ORIGINAL ARTICLE

The Dominance of *Candida auris*: A Single-center Experience of 79 Episodes of Candidemia from Western India

Parikshit S Prayag[1], Sampada Patwardhan[2], Shweta Panchakshari[3], Prasad A Rajhans[4], Amrita Prayag[5]

Abstract

Introduction: Invasive candidiasis is a serious infection seen in hospitalized or immunocompromised patients. Mortality rates for candidemia can be as high as 30–60%. *Candida auris* is an emerging species of *Candida* and is increasingly becoming a global public health problem.

Methods: This was a retrospective observational study, in which we analyzed 79 episodes of candidemia. Blood cultures were done using the Bactec™ FX blood culturing instrument (Becton, Dickinson and Company Sparks, Maryland, USA). Species identification was done using VITEK® 2 YST panels (bioMérieux Inc., Durham, North Carolina, USA). Antifungal susceptibility testing was performed using VITEK® 2 AST-YSO8 panels (bioMérieux Inc., Durham, North Carolina, USA).

Results: Among the 79 episodes, the most common species was found to be *C. auris* (43.03% of all the episodes). *Candida tropicalis* was found to be the second most common species in patients admitted to our hospital with candidemia. All the isolates of *C. auris* were resistant to fluconazole, while 32.35 % of the isolates were also resistant to amphotericin B. Crude mortality in patients with *C. auris* candidemia was higher than the crude mortality for the other species.

Conclusion: This is the first study from India where *C. auris* was seen as the most predominant species among patients admitted with candidemia. This is a serious issue given the high rates of fluconazole resistance, mortality, and cost of therapy associated with *C. auris* bloodstream infections. Urgent attention needs to be diverted to infection control practices and antimicrobial stewardship programs.

Keywords: *Candida*, *Candida auris*, Candidemia, Invasive candidiasis.

Indian Journal of Critical Care Medicine (2022): 10.5005/jp-journals-10071-24152

Introduction

Invasive candidiasis is a serious infection seen in hospitalized or immunocompromised patients and can be associated with significant mortality. Mortality rates for candidemia can be as high as 30–60%.[1] The distribution of *Candida* species can vary by geographic locations, and so can the rates of resistance to antifungal drugs. Different species of *Candida* have varying levels of susceptibility and tolerance to different classes of antifungal agents, and hence, correct characterization of species is important for selecting the right antifungal agent for empiric therapy.

In a large multicenter epidemiological study of candidemia in the intensive care unit (ICU) published in 2015, *Candida tropicalis* (*C. tropicalis*) was found to be the most common species.[2] Also in the same study, public-sector hospitals reported a higher presence of *Candida auris* (*C. auris*) than private-sector hospitals (8.2 vs 3.9%).[2] The rate of azole resistance in this study was 11.8%.[2]

In a study of 114 isolates of *Candida* species from a tertiary center in India published in 2018, *C. tropicalis* was the most prevalent species (39.4%), followed by *C. auris* (17.5%), *Candida albicans* (*C. albicans*) (14%), and *Candida parapsilosis* (*C. parapsilosis*) (11.4%).[3] This study demonstrated the rising incidence of *C. auris*, which was the second most common species in this study.

C. auris is an emerging species of *Candida*, which is first isolated from Japan in 2009.[4] It is increasingly becoming a global public health problem. It has been isolated from six continents so far, with five genetic clades described: the South Asia Clade (I), the East Asia Clade (II), the South Africa Clade (III), the South America Clade (IV), and a potential fifth clade recently reported from Iran.[5,6] The South Asian Clade of *C. auris* (prevalent in India) is very often resistant to fluconazole and may be resistant to polyene antifungals, while echinocandin resistance is rare.[7] It presents a considerable diagnostic and therapeutic challenge in India.

In this retrospective observational study, we analyzed 79 episodes of candidemia (in 79 patients) admitted to a tertiary care center in western India, with respect to the relative prevalence of species, antifungal susceptibility rates, risk factors, and the therapy used. We also analyzed the adherence to the practices of line removal, fundoscopy, echocardiography, and repeating the blood

[1]Department of Transplant Infectious Diseases, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

[2]Department of Microbiology, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

[3]Department of Infectious Diseases, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

[4]Department of Critical Care and Emergency Medicine, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

[5]Deenanath Mangeshkar Hospital, Pune, Maharashtra, India

Corresponding Author: Parikshit S Prayag, Department of Transplant Infectious Diseases, Deenanath Mangeshkar Hospital, Pune, Maharashtra, India, Phone: +91 7420079058, e-mail: pprayag100@gmail.com

How to cite this article: Prayag PS, Patwardhan S, Panchakshari S, Rajhans PA, Prayag A. The Dominance of *Candida auris*: A Single-center Experience of 79 Episodes of Candidemia from Western India. Indian J Crit Care Med 2022;26(5):560–563.

Source of support: Nil

Conflict of interest: None

cultures to document clearance, as well as involving an infectious diseases (ID) specialist in the management of these patients.

Materials and Methods

This was a retrospective observational study conducted in a large 900-bed tertiary care multispecialty center in Western India. Ethics committee approval was obtained prior to the study. Due to the retrospective nature of the study, the requirement for obtaining patient consent was waived.

Isolation and Identification of *Candida*

Blood cultures were done using the Bactec™ FX blood culturing instrument (Becton, Dickinson and Company Sparks, Maryland, USA). Ten milliliters of blood was inoculated into BD Bactec™ Aerobic/F or BD Bactec™ Mycosis IC/F blood culture vials, which were loaded into the machine with onboard incubation at 37°C and continuously monitored for growth. *Candida* was identified in bottles flagging positive by Gram stain showing yeast forms, subculture onto blood agar or Sabouraud's dextrose agar to obtain colonies, and germ tube test to differentiate between *albicans* and non-albicans species. Species identification was done using VITEK® 2 YST panels (bioMérieux Inc., Durham, North Carolina, USA). Serial blood cultures were advised to document clearance of candidemia. In patients with central lines *in situ*, paired blood cultures were drawn to determine the differential time to positivity.

Antifungal Susceptibility Testing

This was performed using VITEK® 2 AST-YSO8 panels (bioMérieux Inc., Durham, North Carolina, USA). Drugs tested were fluconazole, voriconazole, amphotericin B, caspofungin, micafungin, and 5-flucytosine. Interpretation of the obtained minimum inhibitory concentrations (MICs) as susceptible, resistant, or susceptible dose-dependent was done with reference to the clinical breakpoints and interpretive categories via the Clinical and Laboratory Standards Institute (CLSI) and EUCAST standards of broth microdilution. Susceptibility interpretation of *C. auris* was done with tentative CDC breakpoints and published tentative ECVS in multicentric Indian studies.[8]

Data regarding the risk factors, treatment, and outcomes were obtained from the hospital's electronic medical records.

Results

A total of 79 episodes of candidemia were studied from December 2019 to July 2021. The most common species was found to be *C. auris*. *C. tropicalis* was found to be the second most common species in our hospital (Fig. 1 and Table 1).

All but one of the patients were on broad-spectrum antibiotics at the time of developing candidemia. Of note, 62.02% of patients were colonized with *Candida* (either in the sputum or in the urine) at the time of developing candidemia (Table 2).

All the isolates of *C. auris* were resistant to fluconazole. Nearly one third of the isolates of *C. auris* were resistant to amphotericin B (Table 3). Crude mortality for *C. auris* was higher than the crude mortality for the other species (Tables 4 and 5).

Discussion

Our study reflects the changing epidemiology of candidemia in India. Unlike previous large studies of *Candida* infections from India, our study showed that *C. auris* was the most common *Candida* species in patients admitted to our center with candidemia. *C. tropicalis*, which has previously been shown to be the most common species in India, was the second most prevalent species in patients admitted with candidemia to our center. To the best of our knowledge, this is the first study in India that shows *C. auris* as the most predominant species. Of note, 19 of 34 patients were referred to our center from outside. The rise of *C. auris* is alarming, and stringent infection control measures need to be implemented across the country. The VITEK 2 automated identification system (bioMérieux) has only recently included *C. auris* in its database (version 8.01). Laboratories across the country use a variety of methods and commercial systems, and it is very likely that *C. auris*

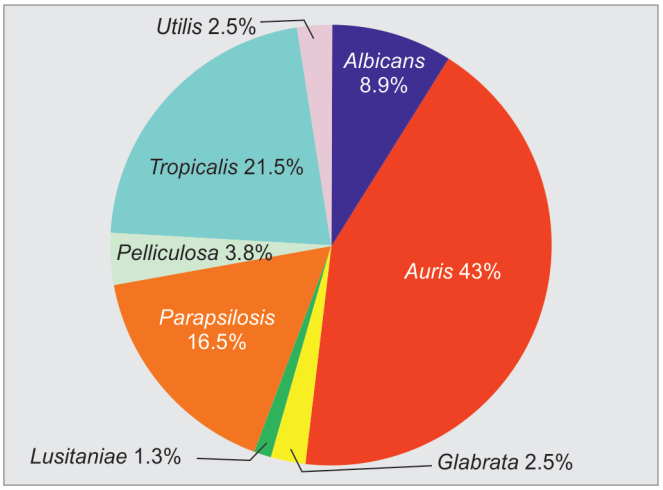

Fig. 1: Species distribution

Table 1: The relative prevalence of the species of *candida*

Species of candida	*Number (%)*
C. auris	34/79 (43.03)
C. tropicalis	17/79 (21.51)
C. parapsilosis	13/79 (16.45)
C. albicans	7/79 (8.86)
C. glabrata	2/79 (2.53)
C. lusitaniae	1/79 (1.26)
C. utilis	2/79 (2.53)
C. pelliculosa	3/79 (3.79)

Table 2: Prevalence of risk factors in patients with candidemia

Risk factor	*Number (%)*
Broad-spectrum antibiotics	78/79 (98.73)
Diabetes mellitus	43/79 (54.43)
Kidney failure on dialysis	20/79 (25.31)
Neutropenia	7/79 (8.86)
Central line	72/79 (91.13)
Steroids	35/79 (44.30)
Immunosuppressive therapy	22/79 (27.84)
Total parenteral nutrition	9/79 (11.39)
Abdominal surgery	22/79 (27.84)
Colonization with candida	49/79 (62.02)

Table 3: Antifungal susceptibility rates for the different species isolated in our center

Species	*Fluconazole resistance (%)*	*Amphotericin resistance (%)*	*Caspofungin resistance (%)*	*Micafungin resistance (%)*	*Voriconazole resistance (%)*	*5-Flucytosine resistance (%)*
C. auris	34/34 (100)	11/34 (32.35)	2/34 (5.88)	1/34 (2.94)	2/34 (5.88)	5/34 (14.70)
C. tropicalis	2/17 (11.76)	2/17 (11.76)	0/17 (0)	0/17 (0)	0/17 (0)	0/17 (0)
C. parapsilosis	7/13 (53.84)	0/13 (0)	0/13 (0)	1/13 (7.69)	0/13 (0)	0/13 (0)
C. albicans	0/7 (0)	0/7 (0)	0/7 (0)	0/7 (0)	0/7 (0)	0/7 (0)
C. glabrata	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	1/2 (50)	1/2 (50)
C. lusitaniae	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)	0/1 (0)
C. utilis	1/2 (50)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)
C. pelliculosa	1/3 (33.33)	0/3 (0)	0/3 (0)	0/3 (0)	0/3 (0)	0/3 (0)
All species	45/79 (56.96)	13/79 (16.45)	2/79 (2.53)	2/79 (2.53)	3/79 (3.79)	6/79 (7.59)

Table 4: Crude mortality for various species associated with candidemia

Species of candida	*Day 28 mortality (%)*
C. auris	11/34 (32.35)
C. tropicalis	5/17 (29.41)
C. parapsilosis	4/ 13 (30.76)
C. albicans	3/17 (17.64)
C. glabrata	1/2 (50)
C. lusitaniae	0/1 (0)
C. utilis	0/2 (0)
C. pelliculosa	0/3 (0)
All species	24/79 (30.38)
Non-*C. auris* species	13/45 (28.88)

Table 5: Adherence to certain practices, such as line removal, performing a fundoscopic eye examination, echocardiography, involving infectious diseases (ID) specialists, and sending repeat blood cultures in patients with candidemia

Action	*Number of patients in which performed (%)*	*Remarks/findings*
Removal of the CVC	65/72 (90.27)	
Fundoscopy	41/79 (51.89)	• 3/41 patients showed evidence of endophthalmitis
Transthoracic echocardiography	65/79 (82.27)	• Two patients showed evidence of candida endocarditis
Repeat blood cultures	Culture repeated once: 65/79 (82.27) Culture repeated twice: 37/79 (46.83)	• 7/65 patients were found to have the first repeat culture positive • 1/37 patient was found to have the second repeat culture positive
Involving an ID specialist in the management	67/79 (84.81)	

is currently being underreported. Adaptation of methods, like VITEK 2 (version 8.01) or identification using matrix-assisted laser desorption/ionization-time of flight (MALDI-TOF) mass spectrometry (MS), is essential to determine the true burden of this problem.

Table 2 shows the risk factors present in patients who developed candidemia in this study. Of note, except one patient, all were on broad-spectrum antibiotics at the time of being found to have candidemia. This calls for meticulous implementation of antimicrobial stewardship programs and reducing the use of unwarranted antibiotic therapy.

The fluconazole resistance rate for *C. auris* in our study was 100%, which is consistent with the rates described previously for the South Asian Clade.[7] The predominance of *C. auris* and the very high rates of fluconazole resistance make fluconazole a poor choice for empiric therapy for candidemia in our center. This impacts antimicrobial stewardship programs adversely. Amphotericin resistance was seen in 32.35% of the isolates of *C. auris* in this study, which is higher than the previously reported rates from India.[7] Resistance was seen only in two isolates for caspofungin and in one isolate for micafungin. This is in congruence with previously published data, which makes echinocandins the preferred therapeutic option for *C. auris*. However, this increases the cost of treating patients with candidemia, as echinocandins are significantly more expensive than fluconazole. Echinocandins have poor penetration into the central nervous system, genitourinary system, as well as the aqueous and vitreous humors, and hence, infections at these sites with *C. auris* are particularly challenging.

The Infectious Diseases Society of America (IDSA) guidelines for the management of candidemia strongly recommend removal of the central venous catheter (CVC).[9] Among patients who had a CVC, the compliance for removal in our center was 90.27%. The IDSA guidelines for candidemia also strongly recommend a dilated retinal examination for all patients with candidemia, preferably performed by an ophthalmologist, within the first week of therapy to establish whether endophthalmitis is present.[9] Among the 79 patients with candidemia in our center, 41 patients underwent an eye examination. Of these, three patients showed evidence of *Candida* endophthalmitis. None of these three patients had candidemia with *C. auris* (one with *C. parapsilosis* and two patients with *C. albicans*). This has clinical significance as the management of endophthalmitis requires using drugs that achieve adequate concentrations at the site of infection and considering intravitreal therapy.

There is evidence to suggest that consultation with an ID expert improves mortality in patients with candidemia.[10] Among patients with candidemia in our center, 84.81% were referred to ID specialists. Involving ID specialists in the management of candidemia should be a part of the protocol. Also 82.87% of patients in this study underwent repeat blood cultures. Clearance of candidemia is important to document since persistent candidemia can be a sign of endocarditis or failure of therapy (which may be related to resistance to antifungal agents or their inability to achieve optimal levels at the site of infection).

Limitations of this study include its retrospective nature and the relatively smaller number of isolates, which makes it difficult to assess the factors affecting mortality. Also, this is a single-center experience, and collaborative studies from multiple centers are needed to confirm whether *C. auris* is now the predominant species in India. Also, the antifungal susceptibility testing was done using VITEK® 2 AST-YSO8 panels (bioMérieux Inc., Durham, North Carolina, USA). This has been reported to be less reliable for detecting resistance to caspofungin.[11]

However, the rise of *C. auris* shown in this study is startling. With the high rates of azole resistance and the predominance of *C. auris*, there is an urgent need to establish robust infection control practices as well as antimicrobial stewardship programs. Further larger studies need to be planned in India to study the rise of *C. auris*, its epidemiology, risk factors, and attributable mortality.

Conclusion

This is the first study from India where *C. auris* was seen as the most predominant species among patients admitted with candidemia. This is a serious issue given the high rates of fluconazole resistance, mortality, and cost of therapy associated with *C. auris* bloodstream infections. Urgent attention needs to be diverted to infection control practices and antimicrobial stewardship programs.

Orcid

Parikshit S Prayag https://orcid.org/0000-0003-2102-7627
Sampada Patwardhan https://orcid.org/0000-0003-0998-5742
Shweta Panchakshari https://orcid.org/0000-0002-5708-3287
Prasad A Rajhans https://orcid.org/0000-0002-0111-6123
Amrita Prayag https://orcid.org/0000-0002-2498-9576

References

1. Flevari A, Theodorakopoulou M, Velegraki A, Armaganidis A, Dimopoulos G. Treatment of invasive candidiasis in the elderly: a review. Clin Interv Aging 2013;8:1199–1208. DOI: 10.2147/CIA.S39120.
2. Chakrabarti A, Sood P, Rudramurthy SM, Chen S, Kaur H, Capoor M, et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. Intensive Care Med 2015;41(2):285–295. DOI: 10.1007/s00134-014-3603-2.
3. Mathur P, Hasan F, Singh PK, Malhotra R, Walia K, Chowdhary A. Five-year profile of candidemia at an Indian trauma centre: High rates of *Candida auris* blood stream infections. Mycoses 2018;61(9):674–680. DOI: 10.1111/myc.12790.
4. Satoh K, Makimura K, Hasumi Y, Nishiyama Y, Uchida K, Yamaguchi H. *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol 2009;53(1):41–44. DOI: 10.1111/j.1348-0421.2008.00083.x.
5. Lockhart SR, Etienne KA, Vallabhaneni S, Farooqi J, Chowdhary A, Govender NP, et al. Simultaneous emergence of multidrug-resistant *Candida auris* on 3 continents confirmed by whole-genome sequencing and epidemiological analyses. Clin Infect Dis 2017;64(2):134–140. PMID: 27988485.
6. Chow NA, de Groot T, Badali H, Abastabar M, Chiller TM, Meis JF. Potential fifth clade of *Candida auris*, Iran, 2018. Emerg Infect Dis 2019;25(9):1780–1781. PMID: 31310230.
7. Chowdhary A, Prakash A, Sharma C, Kordalewska M, Kumar A, Sarma S, et al. A multicentre study of antifungal susceptibility patterns among 350 *Candida auris* isolates (2009–17) in India: role of the ERG11 and FKS1 genes in azole and echinocandin resistance. J Antimicrob Chemother 2018;73(4):891–899. DOI: 10.1093/jac/dkx480.
8. Arendry MC, Prakash A, Meletiadis J, Sharma C, Chowdhary A. Comparison of EUCAST and CLSI reference microdilution MICS of eight antifungal compounds for *C. auris* and associated tentative epidemiological cut off values. Antimicrob Agents Chemother 2017;61:e00485–e00517. DOI: 10.1128/AAC.00485-17.
9. Pappas PG, Kauffman CA, Andes DR, Clancy CJ, Marr KA, Ostrosky-Zeichner L, et al. Clinical practice guideline for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. Clin Infect Dis 2016;62(4):e1–e50. DOI: 10.1093/cid/civ933.
10. Kobayashi T, Marra AR, Schweizer ML, Eyck PT, Wu C, Alzunitan M, et al. Impact of infectious disease consultation in patients with candidemia: a retrospective study. Systematic literature review, and meta-analysis. Open Forum Infect Dis 2020;7(9):ofaa270. DOI: 10.1093/ofid/ofaa270.
11. Astvad KM, Perlin DS, Johansen HK, Jensen RH, Arendrup MC. Evaluation of caspofungin susceptibility testing by the new Vitek 2 AST-YS06 yeast card using a unique collection of FKS wild-type and hot spot mutant isolates, including the five most common candida species. Antimicrob Agents Chemother 2013;57(1):177–182. DOI: 10.1128/AAC.01382-12.