# Molecular characterization, Antifungal susceptibility to fluconazole and Analysis of risk factors in patients with *Candida auris* blood stream infection from Tertiary Care Hospital in North India

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**Abstract**

**Aim and objectives:** To analyse the risk factors, molecular characterization and detection of drug resistance to fluconazole in *Candida auris* candidemia.

**Material and methods:** BACTEC blood culture positive for candida on Gram stain from January 2017-December 2020 were inoculated on SDA plate and incubated for at 37ºC for the isolation of yeast colonies. The isolates were subjected to phenotypic identification, PCR and MALDI-TOF MS and antifungal susceptibility testing to fluconazole by Etest method. Demographic details of the patients were recorded and significant associated risk factors were analysed.

**Results:** A total of 59689 blood cultures were received during the study period from admitted patients. There was 623 episodes of candidemia during the study and 111 episodes was due to *C. auris*. Incidence of candidemia due to *C. auris* was 17%. The associated risk factors were diabetes mellitus ($p < 0.024$), underlying respiratory illness ($p < 0.013$), mechanical ventilation ($p < 0.009$), dialysis ($p < 0.034$), prolonged ICU stay ($p < 0.009$), hypertension ($p < 0.035$) and others included use of broad-spectrum antibiotics (94.5%) and steroids (23.4%). Only 9% (n=10) isolates were sensitive to fluconazole; 85.6% (n=95) were resistant and 5.4% (n=6) were sensitive dose-dependent. Study showed mortality in 36%.

**Conclusions:** Emergence of *Candida auris* infection has caused a significant threat in patients admitted to the ICUs and is known to cause outbreaks in healthcare facilities. Strict precautions like barrier nursing, hand hygiene and proper infection control practices must be followed as well as use of appropriate antifungal therapy to prevent and control the spread of *C. auris.*

Keywords: Fungemia, Etest, drug resistance, PCR

## Introduction

Candidemia is the most frequent infection among invasive fungal infections. The prevalence of candidaemia has risen over time as a result of improvements in medical and surgical procedures, the use of broad-spectrum antibiotics, a growing pool of people who are at the extremes of age and a susceptible population with transplant recipients and haematological malignancies[1-3]. Globally, the epidemiology of invasive Candida infection has changed in the last ten years, with a clear shift in the species that cause candidemia from *Candida albicans* to a predominance of non-albicans Candida (NAC)[4,5]. In industrialised countries, *Candida glabrata, Candida tropicalis,* and *Candida parapsilosis* are prevalent. *Candida tropicalis*, *Candida parapsilosis*, and the recently reported development of *Candida auris* are all considered to be multidrug resistant (MDR) species[6,7]. *Candida auris* is becoming an important cause of nosocomial blood stream infections (BSIs) in Asia, Africa, America and Europe. [7-13]

A multidrug-resistant, healthcare-associated fungal pathogen, *C. auris* was initially discovered in the external ear canal of a person in Japan in 2009 and has since been identified from every continent except Antarctica[14-17]. *C. auris* has been linked to outbreaks in a variety of hospital settings[18,19] and has been identified as the pathogen responsible for several invasive fungal infections, including bloodstream infections[20-22]. Intensive care unit (ICU) admission, use of central venous and urinary catheters, immunocompromising diseases, chronic renal disease, and exposure to broad-spectrum antifungal and antibiotic drugs are risk factors for *C. auris* infection that are comparable to other Candida infections[23-25]. Fluconazole resistance is common in *C. auris* isolates, while the susceptibility to other antifungal medications varies[24,26].

In this study, the aim was to successfully identify all the isolates by phenotypic method later confirmed by MALDI-TOF MS and colony PCR. Herein, we analyse the risk factors and the

outcome associated with *Candida auris* candidaemia and the antifungal susceptibility testing was performed by concentration gradient strip method (E-test).

## Material and Methods

The study analyzed 623 yeast isolates from cases of fungemia cultured during the period of 04 years from 2017 and 2020. Out of 623 isolates, 111 cases were of *Candida auris* candidemia. All samples were seeded on Sabouraud dextrose agar. The plates were incubated at 37°C for 24 to 48 hrs and the conventional phenotypic identification was done.

## Identification of yeast

Yeast isolated from blood was first initially identified by phenotypic method then confirmed by MALDI TOF MS and molecular method i.e., PCR. On phenotypic method, the isolates were mainly Gram-positive budding yeasts without pseudohyphae and on Germ tube test isolates were only budding yeasts and no pseudohyphae. The isolates were subcultured on Chromogenic agar in which white coloured colonies were observed on Hi-Chrome agar and mauve coloured colonies were on Tetrazolium Reduction medium (TRM). Chlamydospore production test and carbohydrate assimilation test was also performed [27].

## MALDI-TOF MS and Colony PCR:

All preserved *Candida auris* isolates were subcultured Sabouraud's Dextrose Agar (SDA) and checked for purity. These isolates were subjected to MALDI-TOF MS and colony PCR for confirmation of the candida species.

**Matrix Assisted Laser Desorption Ionization Time of Flight Mass Spectrometry (MALDI-TOF MS) Sample preparation:**

**Identification of *Candida* species by MALDI-TOF MS:** The pure subcultured Candida blood isolates were uniformly spotted on the MALDI target plate, after drying 1.0 ul of formic acid was added and on complete drying 1ul of CHCA matrix solution (α-cyno-4 hydroxy cinnamic acid) was added to the spot on the MALDI plate. *Escherichia coli* (ATCC 8937) was spotted as a positive control and processed by MALDI TOF MS. The data was collected and interpreted and the Candida isolates were identified after matching with the reference profiles in the MALDI data base.

**Protocol for identification of *Candida auris* by colony Polymerase Chain Reaction (PCR) Assay:**

The PCR was performed after extraction of the DNA using manual phenol-chloroform isoamyl alcohol method and amplification was carried out using primers ITS 1 (5'- TCC-GTA GGT GAA CCT GCG G -3') and ITS 4 (5'- TCC TCC GCT TAT TGA TAT GC -3')[28]. The electrophoresis of the PCR result was done in 1.5% agarose gel in Tris-Acetate-EDTA (TAE) buffer at 50 volts for 45 minutes. Ethidium bromide (0.1 ul/ml) was used to stain the gel, which was visualized under an ultraviolet light. The size of PCR products was immediately assessed by directly comparison with 100 bp molecular size marker (Invitrogen).

**Antifungal susceptibility testing for azoles (fluconazole) by Concentration Gradient Strip Method (E-test) on RPMI 1640 medium**

The minimal inhibitory concentration (MIC) of fluconazole was performed by concentration gradient strip method (E-test, bioMerieux) on RPMI 1640 medium. On Sabouraud agar, each isolate was cultured for 24 hours at 37°C. Using an inoculation culture and a cell suspension calibrated to a 0.5 McFarland standard, the E-test strip was placed on the inoculated plates and incubated for 24 hours at 37°C. The drug concentration at which the inhibition ellipse intercepted the scale on the antifungal strip read after 24 hours was the MIC of that particular antifungal agent. The CLSI recommended quality control stains *Candida parapsilosis* (ATCC 22019) and *Candida krusei* (ATCC 6258) were also put up along with the blood isolates. The isolates are categorized as susceptible (S), susceptible-dose dependent (SDD) or resistant (R).

## Results

**Fungal isolates and identification**

A total of 59689 blood cultures were received during the study period from 2017 to 2020. There were 623 episodes of candidemia during the study period; of which111 episodes of candidemia was due to *C. auris.* Yeasts other than *Candida auris* like *Candida albicans, Candida glabrata, Candida parapsilosis, Candida tropicalis* etc, *Cryptococcus* spp., Trichosporon spp., etc was excluded from the study.

**Case patient description**

An overall higher prevalence was observed in male patients (59.45%; n= 66) than in females (40.55%; 45). Mostly the patients were residents from urban population (96.3%; n=107) and few were from rural areas (3.7%; n=4). Higher prevalence of *C auris* candidemia was seen in patients between the age group of 61-70 years (23.4%; n=26) followed by the age group of 51-60 years (18%; n=20), 41-50 years (12.6%; n=14), 21-30 years (10.8%; n=12) and 15.3% of the patients were from the paediatric age group (9%; < 10 yrs.; n=10) and 6. 3% in the age group of 11-20 yrs. (n=7).

We studied the cases of *C. auris* candidemia from different departments and found that majority of the cases were admitted to Emergency Department (33.3 %; n=37), followed by Critical Care Medicine (CCM) (19.81%; n=22), Nephrology (9.0%; n=10), Gastroenterology (7.2%; n=8). 5.4% (n=6) was seen in Pulmonary Medicine and Neonatology. Fewer cases (n=3; n=2, n=1) was seen from other departments also

**Table 1. Distribution of *Candida auris* in various departments**

| Sl. No. | Department | Patients (n=111) |
|---|---|---|
| 1. | Emergency Department | 37 |
| 2. | Critical Care Medicine (CCM) | 22 |
| 3. | Nephrology | 10 |
| 4. | Gastroenterology | 8 |
| 5. | Pulmonary Medicine | 6 |
| 6. | Neonatology | 6 |
| 7. | Neurosurgery | 5 |
| 8. | Hematology | 3 |
| 9. | Cardiology | 3 |
| 10. | Endocrinology | 2 |
| 11. | Apex Trauma Center | 2 |
| 12. | Anaesthesia | 1 |

| | | |
|---|---|---|
| 13. | Endocrine Surgery | 1 |
| 14. | Neurology | 1 |
| 15. | Paediatric Gastroenterology | 1 |
| 16. | Surgical Gastroenterology | 1 |
| 17. | Transplant Unit | 1 |
| 18. | Urology | 1 |

## Risk Factors Associated with Candidemia

During the study period, it was observed that the majority of the patients with *C. auris* candidemia had many underlying risk factors use of broad-spectrum antibiotics, mechanical ventilation, respiratory illness, diabetes mellitus, patient on dialysis, etc. Majority group of patients had received broad-spectrum antibiotics (94.5%; 105) before the onset of candidemia, some patients had respiratory illness (75.6%; 84), patients were on mechanical ventilation (73%; 81), some had comorbidities like diabetes mellitus (32.4%; 36), some suffered from chronic kidney disease (34.3%; 38)

**Table 2. Associated Risk factors in patients with *Candid auris* candidemia**

| Sr. no. | Associated Risk factors | Patients (n=111) |
|---|---|---|
| 1. | Use of broad-spectrum antibiotics | 105 (94.5%) |
| 2. | Respiratory illness | 84 (75.60 |
| 3. | Mechanical ventilation | 81 (73%) |
| 4. | Hypertension | 50 (45.1%) |
| 5. | Chronic kidney disease | 38 (34.3%) |
| 6. | Diabetes mellitus | 36 (32.4%) |
| 7. | Dialysis | 30 (27%) |
| 8. | Use of steroids | 26 (23.4%) |

| | | |
|---|---|---|
| 9. | Neurological disorder | 20 (18%) |
| 10. | Pancreatitis | 14 (12.6) |
| 11. | Malignancy (Solid organ/Hematology) | 13 (11.7%) |
| 12. | Chronic liver disease | 11 (9.9%) |
| 13. | Renal Transplant recipients | 3 (2.8%) |

A univariate analysis of risk factors using Logistic regression showed that diabetes mellitus ($p < 0.024$), respiratory illness ($p < 0.013$), ICU stay ($p < 0.009$), mechanical ventilation ($p < 0.009$), dialysis ($p < 0.034$) and hypertension ($p < 0.035$) had significant correlation in those with mortality.

Out of the 111 patients with *Candida auris* candidemia; 81.9% (n=91) were admitted in the ICU and 18.1% (n= 20) were admitted to different wards of the hospital.

## Acquisition of Candidemia

During the study, it was observed that the acquisition of candidemia (*C. auris*) occurred early after admission; as early as 3rd day. It was seen that infection occurred as early as 1st and 2nd week in 28 cases; however maximum cases (44.7%) were blood culture positive by the 3rd week and 4th week. Blood culture positivity with *C. auris* was seen in 15.3% (n=17) prior to 48 hrs. of admission indicating that these were non-HAI and these patients may have acquired the infection from other healthcare facilities. However, 84% (n=94) of the patients acquired the infection after 48 hrs of admission to the hospital and out of this 44.7% (n=42) acquired the infection on the 3rd and 4th week of admission suggesting poor infection control practices.

## Molecular identification of clinical isolates of Candida spp. by PCR

Universal primers IT S1 (5'- TCC-GTA GGT GAA CCT GCG G -3') and ITS4 (5'- TCC TCC GCT TAT TGA TAT GC -3') were able to successfully amplify the ITS1-5.8S rRNA region of *C. auris.* All 111 *Candida auris* isolates were successfully amplified by the standardized PCR

protocol and the PCR products were of approximately 400 bp; which was seen as a clear band parallel to the DNA ladder of the desired size.

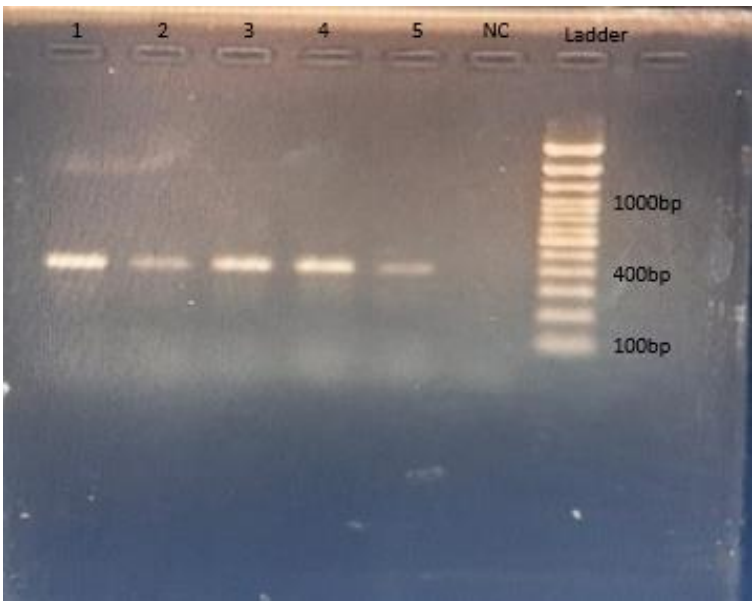


**Fig. 1:** PCR products from blood isolates of *Candida* species on agarose gel electrophoresis. Lanes 1, 2, 3,4 and 5 are the PCR products of *C. auris*. Lane 6 Negative control. Lanes 7: 100 bp DNA ladder.

## Antifungal susceptibility testing

Antifungal drug susceptibility testing was carried out on all 111 isolates by the concentration gradient strip method (E-test) on RPMI 1640 medium. Out of 111 isolates tested, 9.0% (n=10) were sensitive to fluconazole with MIC range from 0.25 to 3 µg/ml, 5.4% (n=6) of the isolates were sensitive dose -dependent (SDD) with MIC range from 16 to 32 µg/ml and 85.6 % (n=95) isolates were resistant to fluconazole with MIC of > 64-256 µg/ml. Most of isolates of *Candida auris* were found to be resistant to fluconazole during the study period.

## Patient Outcome

We studied the outcome of the patients and found that out of 111 patients with candidemia; 63.9 % (n=71) were resolved and were discharged and attended OPD for follow up. Mortality was

seen in 36% (n=40) of the patients; maximum mortality was seen in the 61-70 yrs. age group (30% (n=7) followed by 81-90 yrs. age group (17.5% (n-7); 15% (n=6) in 41-50 yrs. and 12.5% was in seen 31-40 yrs. No mortality was seen below 10 years of age.

## Discussions:

The study highlights the identification and differentiating *C. auris* from other candida species through conventional phenotypic methods as well as their rapid identification by MALDI-TOF MS and colony PCR from archived isolates. A total of 111 *C. auris* isolates were correctly identified by MALDI-TOF MS with an accuracy of 100%.

The demographic profile of patients showed higher prevalence of candidemia among males (59.45%; n= 66) than in females (40.55%; n=45). In a study previously conducted in Oman by Mohsin *et al* [(29)] from 2016-2019 also showed a male (60%) preponderance. In Hu *et al* [(30)] in 2021 showed that out of 827 patients studied, 508 (61.4%) were male and 319 (38.6%) were female. These studies showed similar results as our study.

During the study, the age group ranged from 3 months to 83 years of age. The highest prevalence (23.4%) was seen in the age ranging from 61- 70 years irrespective of gender. The median age in the present study was 52 years (IQR 30-65.5 year). A study by Shastri *et al* [(31)], showed the median age of the patients with *C. auris* candidemia was 56.5 year (IQR 43.3-70.5 year).

Majority of the cases with *C auris* candidemia was seen in patients admitted to Emergency Department (33.3 %; n=37), followed by Critical Care Medicine (CCM) (19.81%; n=22), Nephrology (9.0%; n=10), Gastroenterology (7.2%; n=8). 5.4% (n=6) was seen in Pulmonary Medicine and Neonatology. Fewer cases (n=3; n=2, n=1) was seen from other departments also. In another study done by Rudramurthy SM *et al* [(32)] in 2017, he studied candidemia (n=1400) in 27 ICU setting and showed that 5.3% *C auris* candidemia was seen in 19/27 ICUs and there was also male predominance (62.2%).

Major associated risk factors seen in our patients was the use of broad-spectrum antibiotics (94.5%), ICU stay (81.9%), respiratory illness (75.6%), patients on mechanical ventilation (73%), chronic kidney disease (34.3), Diabetes mellitus (32.4%), patient on dialysis (27%), steroid use (23.4%) and neurological disorder (18%). 12.6 % patients were suffering from pancreatitis, 11.7%

patients were of malignancy and eleven percent (11%) of our patient was having chronic liver disease. Al-Rashdi *et al* [33] studied 108 patients, he also found similar associated risk factors i. e., the use of broad-spectrum antibiotics (84.25%), mechanical ventilation (78.70%) and ICU stay (78.7%). Rudramurthy SM *et al* [32] conducted a subgroup analysis and comparison of the clinical manifestations of *C. auris* and non-auris cases in 27 Indian ICUs where he found that the major risk factor was pulmonary illness (40.5%) followed by renal disease (21.6%) and liver disease (6.8%). A study by Hu *et al* [30] in 2021 showed that use of broad-spectrum antibiotics was seen in 55.9% followed by patients on mechanical ventilation in 26.4%, Diabetes mellitus (19.9%), renal disease in 18.4% and use of steroid in 10.5%. The variation of these associated risk factors between studies depends on the patient profile and nature of treatment practise and therapeutic interventions observed in that institutions. Knowledge of these risk factors is helpful in adopting centre specific strategies for selective administration of antifungal drugs.

It was observed that the acquisition of *C. auris* candidemia occurred early after admission; as early as 3rd day. Maximum (44.7%) blood culture positivity was seen by the 3rd week and 4th week followed by 29.78% in the 1st and 2nd week. Blood culture positivity with *C. auris* was seen in 15.3% (n=17) prior to 48 hrs. of admission indicating that these were non-HAI and these patients may have acquired the infection from other healthcare facilities. 84% of the patients acquired the infection after 48 hrs of admission and 44.7% acquired by the 3rd and 4th week. Most of the cases were from Emergency department followed by Critical Care Medicine. Therefore, hand hygiene as well as infection control practices should be strictly implemented and reinforced in these departments to prevent the acquisition of healthcare associated infections.

The antifungal susceptibility testing was performed in all 111 *Candida auris* isolates and found that only 9% were sensitive to fluconazole (MIC range 0.25 to 3 μg/ml). This suggests that antifungal susceptibility must be performed in all suspected *C. auris* blood stream isolates and fluconazole should not be used as empirical drug of choice for the treatment of invasive *C auris* infection. As evidenced in certain reports *C. auris,* is usually resistant to fluconazole and Shastri *et al* [31] found 97% of his *C. auris* isolates were resistant and, in our study, too we also found that 86.6% of our *C. auris* isolates were resistant to fluconazole. A multicentric study is done by Chakrabarti A *et al* [6] in ICU setting in which they found 58.1% resistant to fluconazole in their isolates. A study conducted by Lockhart *et al* [34] in 3 continents found 93% of their isolates were fluconazole resistant. These studies were in concordance with our study.

In this study the overall mortality rate for *C. auris* candidemia was 36% (n=40). Maximum mortality was seen in the 61-70 yrs. age group (30% (n=7) followed by 81-90 yrs. age group (17.5% (n-7); 15% (n=6) in 41-50 yrs. and 12.5% mortality was in seen 31-40 yrs. No mortality was seen below the age10 years. The mortality in males (55%; n=22) was slightly higher than females (45%; n=18)). The 30-day crude mortality was 60%. In a multicentric study, done by Chakrabarti *et al* [6] in ICU setting, the crude mortality was 44.7%.

The result of the current study indicates that patient with *C. auris* candidemia had a greater chance for mortality if the patient suffered from diabetes mellitus (**OR=2.6, p=0.024**), had respiratory illness (**OR=3.8, p= 0.013**), undergoing dialysis (**OR=2.99, p< 0.034**), on mechanical ventilation (**OR= 4.0, p< 0.009**) and if patients were admitted in the ICU (**OR=15.3, p< 0.009**).

## Conclusion

Due to the widespread use of antifungals in contemporary medicine, resistant to fungal infections brought on by Candida species, have been on the rise. *Candida auris* candidemia continues to be a threat in hospitalized patients. The incidence of candidemia due to *Candida auris* was 17.8% during our study. All the isolates were identified accurately by MALDI-TOF MS and all isolates were successfully amplified by using conventional colony PCR protocol. *C. auris* is continuously reported from different departments in our institute especially from emergency, critical care medicine and intensive care units. Underlying risk factors seen in *C. auris* candidemia were mainly the use of broad-spectrum antibiotics, mechanical ventilation, respiratory illness, diabetes mellitus, and patient on dialysis. The comorbidities found in the patients were diabetes mellitus, chronic kidney disease, pancreatitis, chronic liver disease, malignancy either solid organ or hematological.

In our study, only few isolates were sensitive to fluconazole; most of the isolates (85.6 %; n=95) showed resistance to fluconazole with MIC of ≥ 64. 36% mortality was seen during the study. The rapid candida species identification, antifungal susceptibility testing along with the medical staff's attentiveness, awareness and infection control procedures will aid in an early diagnosis, appropriate antifungal therapy and control of the spread of *Candida auris*. Empirical therapy must be avoided much as possible in order to reduce the selection of resistant candida strains.

**References**


1. McCarty TP, Pappas PG. Invasive Candidiasis. Infect Dis Clin North Am. 2016 Mar;30(1):103-24.
2. Pappas PG. Invasive candidiasis. Infect Dis Clin North Am. 2006 Sep;20(3):485-506
3. Barchiesi F, Orsetti E, Gesuita R, Skrami E, Manso E; Candidemia Study Group. Epidemiology, clinical characteristics, and outcome of candidemia in a tertiary referral center in Italy from 2010 to 2014. Infection. 2016 Apr; 44 (2): 205-13
4. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. Clin Microbiol Rev. 2007 Jan;20 (1):133-63.
5. Kullberg BJ, Arendrup MC. Invasive Candidiasis. N Engl J Med. 2015 Oct 8;373 (15):1445-56
6. Chakrabarti A et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. Intensive Care Med 2015; 41:285-95.
7. Chowdhary A, Sharma C, Meis JF. Candida auris: A rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. PLoS Pathog 2017;13: e1006290
8. Khan Z, Ahmad S, Al-Sweih N, Joseph L, Alfouzan W, Asadzadeh M. Increasing prevalence, molecular characterization and antifungal drug susceptibility of serial Candida auris isolates in Kuwait. PLoS One. 2018 Apr 9;13(4): e0195743
9. Girard V, Mailler S, Chetry M, Vidal C, Durand G, van Belkum A, Colombo AL, Hagen F, Meis JF, Chowdhary A. Identification and typing of the emerging pathogen Candida auris by matrix-assisted laser desorption ionisation time of flight mass spectrometry. Mycoses. 2016 Aug;59 (8): 535-538
10. Walia K, Chowdhary A, Ohri VC, Chakrabarti A. Multidrug-resistant *Candida auris*: Need for alert among microbiologists. Indian J Med Microbiol. 2017 Jul-Sep; 35 (3):436.
11. Mohsin J *et al.* The first cases of Candida auris candidaemia in Oman. Mycoses. 2017 Sep;60 (9):569-575.

12. Schelenz S *et al.* First hospital outbreak of the globally emerging *Candida auris* in a European hospital. Antimicrob Resist Infect Control. 2016 Oct 19;5: 35.

13. Ruiz-Gaitan A, Moret AM, Tasias-Pitarch M, et al. An outbreak due to Candida auris with prolonged colonization and candidemia in a tertiary care European hospital. Mycoses. 2018. Jul; 61(7): 498-505.

14. Chakrabarti A. Fungal Infections in Asia: Eastern Frontier of Mycology. India: 1st Edtn, Elsevier; 2013.

15. Chakrabarti A, Mohan B, Shrivastava SK, Marak RS, Ghosh A, Ray P. Change in distribution & antifungal susceptibility of Candida species isolated from candidaemia cases in a tertiary care centre during 1996-2000. Indian J Med Res. 2002 Jul; 116:5-12.

16. Johanna Rhodes, Matthew C Fisher. Global epidemiology of emerging Candida auris. Cur Opinion Microbiol 2019; 52:84-89.

17. Satoh K *et al*. 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.

18. Lee WG *et al*. First three reported cases of nosocomial fungemia caused by Candida auris. J Clin Microbiol 2011;49 (9):3139-42.

19. Magobo RE, Corcoran C, Seetharam S, Govender NP. Candida auris–associated candidemia, South Africa. Emerg Infect Dis 2014; 20:1250-1.

20. Schelenz S, *et al*. First hospital outbreak of the globally emerging Candida auris in a European hospital. Antimicrob Resist Infect Control 2016; 5:35.

21. Adams E et al.; Candida auris Investigation Workgroup. Candida auris in healthcare facilities, New York, USA, 2013–2017. Emerg Infect Dis 2018; 24:1816-24.

22. Sarma S, Upadhyay S. Current perspective on emergence, diagnosis and drug resistance in Candida auris. Infect Drug Resist 2017; 10:155-65.

23. Lone SA, Ahmad A. Candida auris-the growing menace to global health. Mycoses 2019; 62:620-37.

24. Osei Sekyere J. Candida auris: A systematic review and meta-analysis of current updates on an emerging multidrug-resistant pathogen. Microbiology open. 2018 Aug;7(4): e00578.

25. Kerins JL *et al*. Rapid Emergence of *Candida auris* in the Chicago Region. Open Forum Infect Dis. 2018 Nov 26;5(Suppl 1): S28.

26. 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; 64:134-40.

27. Marinho SA, Teixeira AB, Santos OS, Cazanova RF, Ferreira CA, Cherubini K, de Oliveira SD. Identification of Candida spp. by phenotypic tests and PCR. Braz J Microbiol. 2010 Apr;41(2):286-94.

28. Vijayakumar R, Giri S, Kindo AJ. Molecular species identification of Candida from blood samples of intensive care unit patients by polymerase chain reaction - restricted fragment length polymorphism. J Lab Physicians. 2012 Jan;4(1):1-4

29. Mohsin J, Hagen F, Al-Balushi ZAM, de Hoog GS, Chowdhary A, Meis JF, Al-Hatmi AMS. The first cases of Candida auris candidaemia in Oman. Mycoses 2017; 60:569-575.

30. Hu S, Zhu F, Jiang W, Wang Y, Quan Y, Zhang G, Gu F and Yang Y (2021) Retrospective Analysis of the Clinical Characteristics of Candida auris Infection Worldwide From 2009 to 2020. Front. Microbiol. 12:658329

31. Shastri P. S., Shankarnarayan, S. A., Oberoi, J., Rudramurthy, S. M., Wattal, C., & Chakrabarti, A. (2020). Candida auris candidaemia in an intensive care unit – Prospective observational study to evaluate epidemiology, risk factors, and outcome. J Crit Care. 2020 Jun;57: 42-48

32. Rudramurthy SM *et al*. Candida auris candidaemia in Indian ICUs: analysis of risk factors. J Antimicrob Chemother 2017; 72:1794-801.

33. Al-Rashdi, A.; Al-Maani, A.; Al-Wahaibi, A.; Alqayoudhi, A.; Al-Jardani, A.; Al-Abri, S. Characteristics, Risk Factors, and Survival Analysis of Candida auris Cases: Results of One-Year National Surveillance Data from Oman. J. Fungi 2021, 7, 31.

34. 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; 64:134-40.