



Indian Council of Medical Research *Candida auris* in healthcare settings – India

Date: 16.9.2017

Background: *Candida auris*, a multi-drug resistant yeast, has been reported to cause cutaneous and invasive infections with high mortality. Indian Council of Medical Research (ICMR) is aware of the numerous outbreaks of *C. auris* reported globally and from India. Since 2009, the infection has been reported globally from many countries within a short period of time [1-18]. The whole genome sequence analysis of the isolates collected from different geographical locations showed minimal difference among the isolates suggesting simultaneous emergence of *C. auris* infection at multiple geographical locations, rather than spread from one place to another [14]. The isolation of fungus from patients' environment, hands of healthcare workers, and from skin and mucosa of the hospitalized patients indicate the agent is nosocomially spreading. *C. auris* forms non-dispersible cell aggregates and persists for longer time in environment in addition to its thermotolerant and salt tolerant properties. It has the ability to adhere to polymeric surfaces forming biofilms and resist the activity of antifungal drugs. The yeast is misidentified by common phenotypic automated systems as *C. haemulonii*, *C. famata*, *C. sake*, *Saccharomyces cerevisiae*, *Rhodotorula glutinis*, *C. lusitaniae*, *C. guilliermondii* or *C. parapsilosis*. [18, 19]. Definite confirmation of the species can be done by either MALDI-TOF with upgraded database or DNA sequencing, which are not frequently available in diagnostic laboratories. The high drug resistance and mortality (33-72%) are other challenges associated with *C. auris* candidemia. [11, 18, 19]

Unlike other *Candida* species, the fungus acquires rapid resistance to azoles, polyene and even echinocandin. *C. auris* infection has been reported from many hospitals across this country since 2011 [2, 3, 10]. The conventional phenotypic methods fail to identify the species and require molecular techniques. Globally several warnings and advisories have been provided: Centers for Disease Control and Prevention (CDC), Atlanta; Public Health England (PHE), London; European Centre for Disease Prevention and Control (ECDC), Europe. The present advisory note is for all hospitals of this country

The emergence of *C. auris* in India was noted in sporadic outbreaks and in a multicentre study of candidemia across 27 ICUs in 2011 [2-3, 10-11]. The fungus was the causative agent in 5.3% (74/1400) of these episodes, ranking fifth of the agents causing candidemia [10, 11]. The isolates from India had been found to be clonal and genotypically distinct from Japanese and Korean isolates [2, 3]. The significant risk factors associated with *C. auris* candidemia included admission in over-capacity public sector hospitals, previous antifungal exposure, respiratory illness, vascular surgery and multiple interventions. The multiple medical interventions in ICU patients may account for high rate of the disease even in less morbid patients. Other than blood, the fungus has been isolated from a young girl with vulvovaginitis and a case of fatal pericarditis with end stage liver disease [20, 21]. Healthcare providers need to be vigilant for *C. auris* infections and colonization particularly in those patients who have long ICU stay and are previously exposed to antifungals.

Identification and susceptibility testing Rapid and accurate identification of *C. auris* and adherence to infection control practices, along with ongoing public health surveillance and investigations, are needed to combat the spread of *C. auris* in India. The agent requires specialized method of identification, as commonly used automated phenotypic systems like Vitek 2, API20C-AUX, Auxacolor, Phoenix and Microscan can label *C. auris* as *C. haemulonii*, *C. famata*, *C. sake*, *S. cerevisiae*, *R. glutinis*, *C. lusitaniae*, *C. guilliermondii* or *C. parapsilosis* [18, 19]. Reliable identification is given by either MALDI-TOF with upgraded database or sequencing of internal transcribed spacer and D/D2 regions of ribosomal DNA. However, it has been

observed that *C. auris* grows at 42° C, but fails to grow in presence of 0.01% or 0.1% cycloheximide, and can ferment dextrose, dulcitol, mannitol [22, 23].

There are challenges in antifungal susceptibility testing for *C. auris*. Epidemiological cut off values (ECVs) or clinical breakpoints are still not defined, and variation has been noted by different methods of susceptibility testing [24].

Treatment *Candida auris* is often multidrug resistant and can lead to high mortality (33-72%) in candidemia[11, 18, 19]. At present, overall resistance pattern is seen as: Resistance to fluconazole - >90%, voriconazole ~ 50%, Amphotericin B ->30%, Echinocandins - 7-10% [2-19].

- There is no consensus for optimal treatment due to variation of susceptibility.
- Uniform opinion – fluconazole should be avoided.
- Antifungal susceptibility testing is highly desirable.
- Echinocandins remain the first-line therapy for *C. auris* infection, however, caspofungin shown to be inactive against *C. auris* biofilms.
- Flucytosine (MIC50, 0.125–1 µg/ml) has shown good activity for urinary tract infection, but the drug should not be used alone.
- Posaconazole (range, 0.06–1 µg/ml) shows excellent in vitro activity against *C. auris*, but no data available on use in patients.

Prevention and Infection control [25-27] *Candida auris* has caused outbreaks in many hospitals. Patients can get rapidly colonized by the yeast after admission in healthcare facilities. Colonization occurs most commonly in the axilla, followed by the groin and rectum. Patients with diarrhoea in intensive care unit may be at a higher risk for persistent colonization. Patient care-articles that are shared between patients have a high chance of getting contaminated after use on infected and colonized patients. Temperature probes and ECG and other leads attached to ventilator have been reported in studies to get contaminated and help in spread to non-colonized patients.

Infection Prevention Measures for the infected or colonized patient: Standard as well as contact precautions should be implemented while caring for patients with suspected or confirmed *C. auris* infection

- Wherever feasible, these patients should be kept in isolated rooms or with other patients with the same infection. Patients with diarrhoea may be at a higher risk to transmit the organism to other patients and self-colonization at multiple sites. It may be useful to cohort or semi-cohort these patients away from other patients.
 - Hand-hygiene using WHO recommended all six steps should be followed strictly by all staff and patient attendants before and after contact. Both soap and water and alcohol hand sanitisers with or without chlorhexidine have been found to be equally effective in eradicating hand carriage of *C. auris*. Wearing of gloves should not be used as a substitute for hand hygiene.
 - There should be a dedicated routine equipment for these infectious individuals (ventilators etc.)
 - Catheter care bundles and care of tracheostomy sites.
- If a procedure (e.g. dialysis) has to be performed on an infected or a colonized patient, then he/she should be the last patient of the day, if possible.

Environmental control measures: As *C. auris* is known to persist in environment for long time, it is important to disinfect surfaces around infected and colonized patients. The routinely used disinfectants (hypochlorite, hydrogen peroxide, quaternary ammonium compounds, phenol and alcohols) are effective to remove *C. auris* from environmental surfaces. However, it is important that the manufacturers' recommended concentration and contact time be followed strictly. The two-bowl or three-bowl method should be adopted for the disinfection of surfaces. For terminal cleaning, fogging by hydrogen peroxide vapor has been used to disinfect patient rooms.

All patient care equipment should be cleaned and disinfected daily. Single use devices should be preferred. Autoclaving or ethylene oxide/gas plasma sterilization should be preferred over high-level disinfection of reusable items, especially semi-critical and critical instruments, which come into contact with mucous membranes or sterile tissues. In case of any spill of body fluids such as saliva, there should be prompt removal of the same followed by routine disinfection.

Colonization screening: Colonization occurs most commonly in the axilla, followed by the groin and rectum. Patients with diarrhoea may be at a higher risk for persistent colonization. Suggested screening sites based on the predilection of *Candida* spp. to colonize the skin and mucosal surfaces are:

- axilla
- groin
- oral mucosa
- urine/urethral swab
- perineal or low vaginal swab
- sputum/endotracheal secretions
- drain fluid (abdominal/pelvic/mediastinal)
- cannula entry sites
- wounds

At least the axilla and the groin and the body site from which *C. auris* was previously isolated, should be tested at periodic intervals. A composite swab of the axilla and groin may reduce resources utilized. If a site is positive, there is no need to test for three months [28]. For decolonization of skin, patients should be sponged with 2% chlorhexidine gluconate (Annexure I). Oral decolonization can be done by using 0.2% chlorhexidine mouthwash or 1% chlorhexidine dental gel in patients on ventilator support. Oral nystatin has been used in oropharyngeal colonization. Chlorhexidine-impregnated protective disks for central vascular catheter exit sites may be used to reduce line-associated *C. auris* bloodstream infections.

When you should suspect *C. auris*?

- If the patient is from ICU or high-dependency area
- Transferred from another hospital after a long stay
- Multiple intervention & prior antifungal exposure in any patient
- If one identifies in a commercial system -*Candida haemulonii*, *C. famata*, *C. guilliermondii*, *C. lusitaniae*, *C. parapsilosis*, *Rhodotorulaglutinis*, *Candida sake*, *Saccharomyces cerevisiae*
- If the *Candida* appears to be resistant to fluconazole & high MIC to voriconazole

Notification Whenever there is a suspected or confirmed case of *C. auris* infection or *C. auris* colonization in the hospital, the details should be notified to Prof. Arunaloke Chakrabarti, Professor and Head, Mycology Reference Laboratory, Department of Medical Microbiology, PGIMER, Chandigarh.

The suspected *C. auris* isolates can be sent to labs at PGIMER Chandigarh and/or Vallabhbhai Patel Chest Institute, University of Delhi, Delhi 110 007 for identification and characterisation as per the details given below:

- Prof. Arunaloke Chakrabarti, Professor and Head, Mycology Reference Laboratory, Department of Medical Microbiology, PGIMER, Chandigarh 160012 arunaloke@hotmail.com
- Prof Anuradha Chowdhary, Department of Medical Mycology, ESCMID Collaborative Centre, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi 110007
Email: dranuradha@hotmail.com; chowdhary.anuradha@gmail.com
Phone: 91-11-27667560

Further reading:

1. Satoh K, Makimura K, Hasumi Y, 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;53:41–4.
2. Chowdhary A, Anil Kumar V, Sharma C, et al. Multidrug-resistant endemic clonal strain of *Candida auris* in India. *Eur J Clin Microbiol Infect Dis* 2014;33:919–26.
3. Chowdhary A, Sharma C, Duggal S, et al. New clonal strain of *Candida auris*, Delhi, India. *Emerg Infect Dis* 2013;19:1670–3.
4. Emara M, Ahmad S, Khan Z, et al. *Candida auris* candidemia in Kuwait, 2014. *Emerg Infect Dis* 2015;21:1091–2.
5. Magobo RE, Corcoran C, Seetharam S, et al. *Candida auris*-associated candidemia, South Africa. *Emerg Infect Dis* 2014;20:1250–1.
6. Kim MN, Shin JH, Sung H, et al. *Candida haemulonii* and closely related species at 5 university hospitals in Korea: identification, antifungal susceptibility, and clinical features. *Clin Infect Dis* 2009;48: e57–61.
7. Lee WG, Shin JH, Uh Y, et al. First three reported cases of nosocomial fungemia caused by *Candida auris*. *J Clin Microbiol* 2011;49:3139–42.
8. Sarma S, Kumar N, Sharma S, et al. Candidemia caused by amphotericin B and fluconazole resistant *Candida auris*. *Indian J Med Microbiol* 2013;31:90–1.
9. Schelenz S, Hagen F, Rhodes JL, et al. First hospital outbreak of the globally emerging *Candida auris* in a European hospital. *Antimicrob Resist Infect Control* 2016;5:35.
10. Chakrabarti A, Sood P, Rudramurthy SM, et al. Incidence, characteristics and outcome of ICU-acquired candidemia in India. *Intensive Care Med* 2015;41:285–95.
11. Rudramurthy SM, Chakrabarti A, Paul RA, et al. *Candida auris* candidaemia in Indian ICUs: Analysis of risk factors. *J Antimicrob Chemother*. 2017; 72, 1794–1801.
12. Morales-Lopez SE, Parra-Giraldo CM, Ceballos-Garzon A, et al. Invasive infections with multidrug-resistant yeast *Candida auris*, Colombia. *Emerg Infect Dis* 2017;23:162–4.
13. Vallabhaneni S, Kallen A, Tsay S, et al. Investigation of the first seven reported cases of *Candida auris*, a globally emerging invasive, multidrug-resistant fungus—United States, May 2013—August 2016. *Am J Transplant* 2017;17:296–9.
14. Lockhart SR, Etienne KA, Vallabhaneni S, et al. Simultaneous emergence of multidrug-resistant *Candida auris* on 3 continents confirmed by whole genome sequencing and epidemiological analyses. *Clin Infect Dis* 2017;64:34–40.
15. Ben-Ami R, Berman J, Novikov A, Bash E, et al. Multidrug-Resistant *Candida haemulonii* and *C. auris*, Tel Aviv, Israel. *Emerg Infect Dis*. 2017; 23. doi: 10.3201/eid2302.161486
16. Mohsin J, Hagen F, Al-Balushi ZAM, et al. The first cases of *Candida auris* candidaemia in Oman. *Mycoses*. 2017; Jul 7. doi: 10.1111/myc.12647.
17. Al-Siyabi T, Al-Busaidi I, Balkhair A, et al. First report of *Candida auris* in Oman: Clinical and microbiological description of five candidemia cases. *J Infect*. 2017; Jun 1. pii: S0163-4453(17)30164-0. doi: 10.1016/j.jinf.2017.05.016
18. Chowdhary A, Voss A, Meis JF. Multidrug-resistant *Candida auris*: 'new kid on the block' in hospital-associated infections? *J Hosp Infect*. 2016;94:209–12.
19. Chowdhary A, Sharma C, Meis JF. *Candida auris*: A rapidly emerging cause of hospital-acquired multidrug-resistant fungal infections globally. *PLoS Pathog*. 2017; May 18; 13:e1006290. doi: 10.1371/journal.ppat.1006290
20. Kumar D, Banerjee T, Pratap CB, et al. Itraconazole-resistant *Candida auris* with phospholipase, proteinase and hemolysin activity from a case of vulvovaginitis. *J Infect Dev Ctries*. 2015; 9:435–7.
21. Khillan V, Rathore N, Kathuria S, et al. A rare case of breakthrough fungal pericarditis due to fluconazole resistant *Candida auris* in a patient with chronic liver disease. 2014, *JMM Case Reports* 1: doi: 10.1099/jmmcr.0.T00018
22. Welsh RM, Bentz ML, Shams A, et al. Survival, persistence, and isolation of the emerging multidrug-resistant pathogenic yeast *Candida auris* on a plastic healthcare surface. *J Clin Microbiol*. 2017 Jul 26. pii: JCM.00921-17. doi: 10.1128/JCM.00921-17
23. Kordalewska M, Zhao Y, Lockhart SR, et al. Rapid and accurate molecular identification of the emerging multidrug-resistant pathogen *Candida auris*. *J Clin Microbiol*. 2017;55:2445–52.
24. Kathuria S, Singh PK, Sharma C, et al. Multidrug-resistant *Candida auris* misidentified as *Candida haemulonii*: Characterization by Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry and DNA sequencing and its antifungal susceptibility profile variability by Vitek 2, CLSI Broth microdilution, and Etest method. *J Clin Microbiol* 2015;53:1823–30.
25. Global Emergence of Invasive Infections Caused by the Multidrug-Resistant Yeast *Candida auris*. Clinical Alert to U.S. Healthcare Facilities - June 2016. <https://www.cdc.gov/fungal/diseases/candidiasis/candida-auris-alert.html>.
26. The characteristics, diagnosis and management of *Candida auris* (*C. auris*). Gov. UK (2016). <https://www.gov.uk/government/collections/candida-auris>.
27. CDC (2016). *Candida auris*: Questions and Answers. <https://www.cdc.gov/fungal/diseases/candidiasis/candida-auris-ganda.html>.
28. CDC (2017) Recommendations for Infection Control for *Candida auris*. <https://www.cdc.gov/fungal/diseases/candidiasis/c-auris-infection-control.html>

Annexure I

Protocol for Chlorhexidine (CHG 2%) body wash: ATC ICU

1. Bring the articles to bed side :

Gloves

Gauze pieces 5 each for area abdomen, arms, back, legs and groin

Two towels

Bowl to make CHG solution

Bowl for fresh water

Chlorhexidine 2% [1 (CHG 4%): 1 (RO water)]

Clean gown

2. Maintain privacy
3. Wet the areas with towel
4. Apply CHG 2% with different gauze pieces to respective areas using the following sequence

Area	
I.	Neck to trunk (Front)
II.	Fingers to axilla (both arms)
III.	Toes to thigh
IV.	Neck to trunk (Back)
V.	Buttocks to groin

5. Pay special attention to axilla and groin.
6. Make sure that all areas have minimum contact period of two minutes.
7. Start wiping the area with 2nd wet towel using the same sequence (I to V)
8. Put fresh gown to the patient.
9. Terminate the procedure.