

Is routine screening for *Candida auris* necessary in ICU?

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ABSTRACT

Background and Objectives: The capability to cause invasive infection, multi-drug resistance, and health care-associated outbreaks of *Candida auris* have made it a pathogen of great concern. Estimating how many patients in our intensive care unit had *C. auris* colonization and what characteristics put patients at risk for having *Candida* spp. colonization were the primary goals of the study.

Materials and Methods: Swabs from axilla and groin were collected from 229 patients getting admitted to the ICU. Samples were inoculated into CHROMagar™ *Candida* Plus medium. Colonies presumptively identified as *C. auris* by the presence of light blue with blue halo and were confirmed by VITEK-2.

Results: Our study showed that only one patient was colonized with *C. auris*. A total of 47 (20.5%) patients were colonized with *Candida* spp., of which *Candida parapsilosis* was the predominant organism. History of antibiotic use and cerebrovascular accident were independent risk factors in *Candida* colonization.

Conclusion: Active screening for *Candida auris* in all patients is not required in our hospital as the prevalence was very low and not cost-effective. Therefore we plan to modify our screening strategy and use risk factors based surveillance strategy as it may serve as an ideal strategy.

Keywords: Screening; *Candida*; Colonization; Infection; Resistant

INTRODUCTION

A multidrug-resistant fungal pathogen, *Candida auris* is a worldwide hazard due to its potential to induce nosocomial epidemics and invasive infections (1-3). *C. auris* is the first fungal pathogen to be designated as an urgent public health danger by the Centers for Disease Control and Prevention (CDC) (4). In 2009, *C. auris* was reported for the first time from the ear canal of a Japanese patient. In 2011, it was revealed that the fungus had caused blood stream infection in

South Korea (5, 6). *C. auris* has the ability to develop resistance to fluconazole and other antifungal medications (7). Extensive infection control efforts have not been able to control the outbreaks caused by this fungus (8).

Within one month of the CDC releasing a clinical notice about *C. auris* in June 2016, the first cases in the United States were reported (9, 10). Given its ability to colonize patients' skin and other body places for extended periods, as well as its ability to contaminate and remain in healthcare environments, *C. auris* can

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spread easily in these settings (11-13). Approximately 5% to 10% of those who have been identified as colonized may get invasive infection (14). To make matters worse, colonization makes it possible for the organism to be shed into the environment and transmitted to other places (15). The fact that the commonly employed disinfectant quaternary ammonium compounds does not achieve the desired log decrease in *C. auris* for successful disinfection further adds to the difficulty in controlling this yeast (16).

There has been a talk of individuals admitted to the intensive care unit (ICU) with asymptomatic colonization as a potential cause of *C. auris* outbreaks. The risk of invasive illnesses is higher in intensive care units, and there is evidence that they are very contagious and persistent (8). As part of their rigorous infection control efforts, hospitals can reduce the spread of infectious diseases by screening patients upon admission. To further enhance infection control programs, screening aids identification of risk factors linked to *C. auris* colonization. Among the most common hospital-acquired infections, Methicillin-resistant *Staphylococcus aureus* (MRSA) and Carbapenemase-producing Enterobacteriaceae (CPE) are often tested (17, 18). All hospitals should implement a *C. auris* screening program following a local risk assessment to identify patients at high risk of colonization, according to Public Health England (19). It is not recommended that patients need to be tested for *C. auris* upon admission in India according to any national guidelines.

Recognizing *C. auris* is the first step in controlling it. Even with modern biochemical tools, *C. auris* can be misinterpreted (20). When alternative methods of *Candida* identification (VITEK-2, API-20C, BD-Phoenix, Microscan) are unsuccessful and when isolates are interpreted as *Rhodotorula glutinis*, *C. haemulonii*, *C. famata*, *C. sake*, *C. catenulata*, then *C. auris* should be considered (20). *C. auris* detection is now possible thanks to a database update for VITEK-2 (21). Unfortunately, DNA sequencing and Matrix-Assisted Laser Desorption Ionization-Time of Flight Mass spectrometry (MALDI-TOF MS) assays are not readily available in most clinical microbiology laboratories, making it impossible to properly identify *C. auris* (22, 23). In order to properly diagnose *C. auris*, healthcare personnel should be familiar with the diagnostic processes used by their clinical microbiology laboratories (24). The ability to generate a color that is distinctive to a *Candida* species makes

chromogenic agar useful for species identification (25-27). It is not possible to detect *C. auris* using most chromogenic mediums. The time and money will be saved by using chromogenic isolation medium instead of further confirmatory tests, which makes it very popular (28). It is crucial to identify infected and colonized patients as soon as possible in order to implement infection control measures that can limit the spread of *C. auris*, a multidrug-resistant pathogen that poses a global threat. This will help reduce the incidence of nosocomial infections as well as the spread of this fungus.

The primary goal of this research was to find out how well the new chromogenic medium CHROMagar™ *Candida* Plus worked to

1. Determine the proportion of patients admitted to our ICU who are colonized with *C. auris*.
2. Enumerate risk factors associated with colonization.
3. Presumptively identify other *Candida* species.

MATERIALS AND METHODS

This cross-sectional study was done in the ICU of a tertiary care hospital between November 2021 through August 2022 after getting clearance from Ethical Committee.

Inclusion criteria- Swabs collected from all patients more than 18 yrs of age getting admitted to the ICU.

Exclusion criteria- Patients who were not willing to engage in the research or who were 18 years old or younger were excluded.

Prior to admission to the intensive care unit, swabs were taken from the axilla and groin of each patient. Among other things, participants were asked to fill out a detailed questionnaire about their medical history, including if they had recently undergone surgery, the insertion of any devices, and whether they had taken any high-end antimicrobials (such as azoles, amphotericin, echinocandins, carbapenem, and colistin). The CHROMagar™ *Candida* Plus medium, manufactured in Paris, France, was used in the study. Two swabs were taken from each patient's axilla and groin and used for culture. The plates were subsequently incubated at 37°C for one to two days. Species of *Candida* can produce a wide range of colors in this medium, as shown in Figs. 1 and 2. The colonies were initially thought to be *C. auris* because of their light

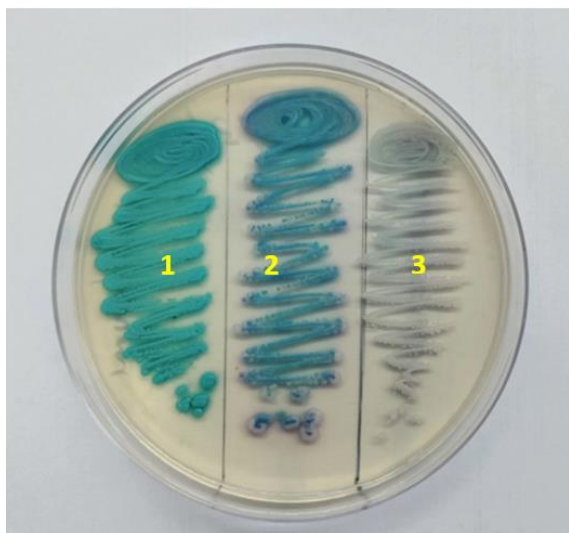


Fig. 1. Colours Produced by Different *Candida* on CHROMagar™ *Candida* Plus

1. Green colored colonies of *C. albicans*
2. Metallic blue-colored colonies of *C. tropicalis*
3. White colored red colonies of *C. parapsilosis*



Fig. 2. *Candida auris* on CHROMagar™ *Candida* Plus

blue coloration and blue halo. The VITEK-2 assay, developed by bioMérieux in France's Marcy l'Etoile, confirmed the identification. Details from medical records were checked for those patients whose swabs grew *Candida*.

Candida colonization. Single Site Colonization- Colonization at one site (axilla or groin) with single or multiple *Candida* species.

Multiple Site Colonization- Colonization at two sites (axilla and groin) with single or multiple *Candida* species.

Statistical analysis. With the exception of age, which is represented by mean and standard deviation, descriptive statistics comprised proportions for

all other variables. The association was tested using a chi-square test. Potential risk factors of *Candida* colonization and the likelihood of infection caused by colonization were estimated using an Odds Ratio with a 95% Confidence Interval. The independent determinants of *Candida* colonization were identified using Logistic Regression.

RESULTS

Axilla and groin swabs (458) were collected from 229 patients among whom 102 patients were transferred from other health care facilities (HCF) and 127 patients were directly admitted from the community. The mean age of the study patients was 64.0 ± 17.3 years with 164 (71.6%) males and 65 (28.4%) females. *C. auris* colonization was found in only one (0.4%) patient in a groin swab and the identification was confirmed by VITEK-2. The same patient was also colonized with *C. parapsilosis* in the axilla. Of the 102 patients from other HCFs, only one (0.4%) patient had colonization with *C. auris*. Of the 127 patients from community, none had *C. auris* colonization. The one patient who was colonized with *C. auris* developed a blood stream infection with *Candida* which was later identified to be *C. famata*. Among patients not colonized with *C. auris*, only one developed a blood stream infection with *Candida* which was later identified to be *C. parapsilosis*. This patient was admitted from the community and had no history of admission in other hospitals in last 3 months.

Colonization with *Candida* at single site (axilla or groin) and multiple sites (axilla and groin) was seen in 25 (10.9%) and 22 (9.6%) patients respectively. Distribution of *Candida* species in these patients is shown in Table 1. In this study 182 (79.5%) patients were not colonized with *Candida*. No change in antifungal usage was done based on the *Candida* colonization status. The one patient who was found to have *C. auris* colonization expired. Among the risk factors, patients admitted from other health care facilities, any history in the last 90 days of hospital admission, the use of central line, foleys catheter, antibiotic use, any history of dementia, cerebrovascular accident were significantly associated with *Candida* colonization ($p < 0.05$) (Table 2). Among the risk factors, history of antibiotic use and history of cerebrovascular accident were independent predictors of *Candida* colonization (Table 3).

DISCUSSION

In this study a total of 229 patients were screened at admission for the presence of *C. auris*. Only one

Table 1. Single and multiple site colonization of *Candida* spp.

<i>Candida</i> species	Axilla + groin	Axilla	Groin
	N,%	N,%	N,%
<i>C. parapsilosis</i>	7 (31.8)	5 (20)	8 (32)
<i>C. albicans</i>	7 (31.8)	3 (12)	4 (16)
<i>C. parapsilosis</i> + <i>C. tropicalis</i>	3 (13.6)	Nil	Nil
<i>C. albicans</i> + <i>C. parapsilosis</i>	2 (9.1)	Nil	1 (4)
<i>C. tropicalis</i>	1 (4.5)	1 (4)	1 (4)
<i>C. albicans</i> + <i>C. tropicalis</i>	1 (4.5)	Nil	Nil
<i>C. parapsilosis</i> + <i>C. auris</i>	1 (4.5)	Nil	Nil
<i>C. tropicalis</i> + <i>C. krusei</i>	Nil	1 (4)	Nil
<i>C. krusei</i>	Nil	Nil	1 (4)
Total	22	10	15

patient was found to be colonized with *C. auris*. The low prevalence of *C. auris* on screening is concordant with the findings of research conducted by Sharp et al who found no evidence of *C. auris* prevalence in 921 patients tested across eight ICUs (29). The Indian subcontinent is the most common site of *C. auris* colonization and infection. Since *C. auris* was found in most intensive care units (19 out of 27) in India, accounting for 5.2% of all *Candida* spp. isolates, hospitalized patients in India are regrettably at a very high risk of colonization or infection (30, 31). Although our finding was surprising, given the high risk in India, a more accurate prevalence estimate might be obtained by a nationally representative survey, like the one that was carried out in 2016 in acute care hospitals in Europe (32). *C. auris* colonization was detected in 6.9% admissions in New York, according to another study that ran from 2017 to 2019. The rates were greater in nursing homes compared to hospitals (33). Our results were at odds with this rather high colonization rate of 6.9%.

Table 2. Risk Factors for Acquiring *Candida* Colonization

Potential Risk Factors	Total (n=229)	<i>Candida</i> Colonization		p Value
		Yes (n=47)	No (n=182)	
Male	164 (%)	32 (68.1%)	132 (72.5%)	0.5
*Patients Received from other HCF	102 (44.5%)	27 (57.4%)	75 (41.2%)	0.046
History in the Last 90 Days				
*Hospital Admission	82 (35.8%)	23 (48.9%)	59 (32.4%)	0.04
Surgery	18 (7.9%)	6 (12.8%)	12 (6.6%)	0.2
Intubation	24 (10.5%)	7 (14.9%)	17 (9.3%)	0.3
*Central Line	8 (3.5%)	4 (8.5%)	4 (2.2%)	0.04
*Foley Catheter	78 (34.1%)	22 (46.8%)	56 (30.8%)	0.04
Tracheostomy	7 (3.1%)	2 (4.3%)	5 (2.7%)	0.6
Microorganism	5 (2.2%)	2 (4.3%)	3 (1.6%)	0.3
*Antibiotic Use	45 (19.7%)	18 (38.3%)	27 (14.8%)	0.0003
Antifungal Use	1 (0.4%)	1 (2.1%)	0 (0.0%)	0.2
Comorbid Conditions				
Diabetes Mellitus	118 (51.5%)	24 (51.1%)	104 (57.1%)	0.9
Neurological Disease	71 (31.0%)	12 (25.5%)	59 (32.4%)	0.4
*Dementia	14 (6.1%)	6 (12.8%)	8 (4.4%)	0.03
Myocardial Infarction	22 (9.6%)	5 (10.6%)	17 (9.3%)	0.8
Congestive Heart Failure	20 (8.7%)	3 (6.4%)	17 (9.3%)	0.5
Peripheral Vascular Disease	12 (5.2%)	2 (4.3%)	10 (5.5%)	0.7
*Cerebrovascular Accident	57 (24.9%)	6 (12.8%)	51 (28.0%)	0.03
Chronic Kidney Disease	29 (12.7%)	3 (6.4%)	26 (14.3%)	0.1
Chronic Liver Disease	35 (15.3%)	7 (14.9%)	28 (15.4%)	0.9

* Significant at $p < 0.05$, HCF- Health care facility

Table 3. Independent Predictors of *Candida* Colonization

Independent Risk Factors	Total (n=229)	Risk of <i>Candida</i> Colonization		
		OR (95% CI)	Adjusted OR (95% CI)	p Value
Male	164 (71.6%)	0.8 (0.4-1.6)	.	
Hospital Acquired	102 (44.5%)	1.9 (1.01-3.7)	ns	
History of the Last 90 Days				
Hospital Admission	82 (35.8%)	2.0 (1.04-3.8)	ns	
Surgery	18 (7.9%)	2.1 (0.7-5.9)	.	
Intubation	24 (10.5%)	1.7 (0.7-4.4)	.	
Central Line	8 (3.5%)	4.1 (1.0-17.2)	ns	
Foley Catheter	78 (34.1%)	2.0 (1.03-3.8)	ns	
Tracheostomy	7 (3.1%)	1.6 (0.3-8.4)	.	
Microorganism	5 (2.2%)	2.7 (0.4-16.3)	.	
Antibiotic Use	45 (19.7%)	3.6 (1.7-7.3)*	3.5 (1.7-7.2)	0.0007
Antifungal Use	1 (0.4%)	n/a		
Comorbid Conditions				
Diabetes Mellitus	118 (51.5%)	0.98 (0.6-1.6)	.	
Neurological Disease	71 (31.0%)	0.7 (0.3-1.5)	.	
Dementia	14 (6.1%)	3.2 (1.05-9.7)	.	
Myocardial Infarction	22 (9.6%)	1.2 (0.4-3.3)	.	
Congestive Heart Failure	20 (8.7%)	0.7 (0.2-2.4)	.	
Peripheral Vascular Disease	12 (5.2%)	0.8 (0.2-3.6)	.	
Cerebrovascular Accident	57 (24.9%)	0.4 (0.2-0.9) *	0.4 (0.2-0.99)	0.047
Chronic Kidney Disease	29 (12.7%)	0.4 (0.1-1.4)	.	
Chronic Liver Disease	35 (15.3%)	1.0 (0.4-2.4)	.	

* Significant at $p < 0.05$, ns: not significant, n/a- not applicable

There were 47 patients who were colonized with *Candida* upon admission to the hospital in this study. *C. parapsilosis* was found in 27 out of the individuals who had colonization, with some having more than one site (Tables 1). All other *Candida* species were either *C. albicans*, *C. tropicalis*, *C. krusei*, or *C. auris*. Our results are at odds with those of a study by Zarei et al. which found that *C. albicans* was the most common colonizer among intensive care unit (ICU) patients (34). Yang et al. found that *C. albicans* was the most common colonizer, with *C. parapsilosis* coming in second (35). The most common kind of *Candida* among Indian ICU patients, according to research by Chakrabarti et al., was *C. tropicalis* (31). In our study there were several risk factors such as history of last 90 days of hospital admission, central line, Foleys catheter, antibiotic use which were significantly associated with *Candida* colonization. However, antibiotic use and cerebrovascular accident were the independent predictors of *Candida* colonization. History of antibiotic use as a predictor of

Candida colonization was also described by Schulte et al. (36).

This study made use of chromogenic medium because it provides a preliminary identification of the yeast type, which is necessary for administering the correct antifungal medication. Despite mixed cultures, the innovative *Candida* Plus medium (CHROMagar™) has demonstrated great sensitivity and specificity for the most frequently isolated *Candida* species. The capacity to accurately detect *C. auris* is the primary benefit of this medium. This medium was found to be completely sensitive and specific for the identification of *C. auris* in samples taken during surveillance, according to the research conducted by Bayona et al. Our study's major organism, *C. parapsilosis*, was also identified using it, and it was reported to be both sensitive and specific (37). One research that found CHROMagar™ *Candida* Plus to be significantly better at recognizing *C. auris* than Hi-Crome *C. auris* MDR selective agar (HiMedia) was the one by De jong et al. (38). To distinguish *C. auris*

from isolates classified as *C. haemulonii* by VITEK, one might utilize CHROMagar *Candida* medium supplemented with Pal's agar, as described by Kumar et al. (39). An article published not long ago by Gaitan et al. demonstrated that chromogenic media supplemented with fluconazole can be helpful for the probable diagnosis of *C. auris* (40).

The patient who was colonized with *C. auris* had a blood stream infection with *C. famata*. However, since *C. auris* can be misidentified as *C. famata* by VITEK-2, identification of this isolate should have been confirmed by MALDI-TOF. This was a major limitation in this study.

CONCLUSION

As far as we are aware, this is the first study to report on *C. auris* screening upon admission from the southern state of Kerala. Our research revealed that a single patient had *C. auris* colonization and a subsequent *C. famata* infection in their bloodstream. A total of 47 (20.5%) patients were colonized with *Candida* on admission, of which *C. parapsilosis* was the predominant organism. Other than the patient who was colonized with *C. auris*, none of the colonized patients developed an invasive infection with *Candida*. History of antibiotic use and cerberovascular accident were found to be independent risk factors of *Candida* colonization. Based on the findings in the study, active screening for *C. auris* in all patients is not required in our hospital as it will not be cost-effective. We plan to modify our screening strategy and a risk factor based surveillance strategy is ideal.

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