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THE INCREASING PACE OF *CANDIDA AURIS* IN BLOODSTREAM INFECTIONS – AN OBSERVATIONAL STUDY

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ABSTRACT The unique attributes of Candida auris, high rates of multidrug resistance, ability to grow in conditions with high salinity and high temperatures, causes a wide spectrum of infections, especially bloodstream infection. Candidemia by C. auris carries a mortality rate of up to 60%, even with correct antifungal treatment. Furthermore, C. auris accounts for most Candida bloodstream isolates, around 20% to 38% of patients. The present study was taken up to know the prevalence of Candida auris in bloodstream infections. **Methods:** A total of 1571 blood samples received in BHI Broth were processed as per standard laboratory protocols after obtaining IEC approval. For all the identified bacterial pathogens antibiotic sensitivity testing was done by Kirby Bauer disk diffusion method, and for fungal yeast pathogens identification was done in Vitek 2 compact. **Results:** Out of 1571 blood culture samples processed, 278(17.6%) were culture positive. Of these positives 213 (76.6%) isolates were bacterial pathogens, 65(23.3%) isolates were Candida spp. Of these Candida isolates majority were Candida tropicalis(36.9 %) followed by Candida auris (20%). **Conclusions:** Most of the microbiology laboratories don't have access to MALDI-TOF MS or Vitek2 system, an especially glaring deficiency for detection of C. auris. It is essential to strengthen all clinical microbiology laboratories to be capable of rapidly and accurately detecting C. auris in clinical samples. A robust response that involves the laboratory, clinicians, and public health agencies is needed to identify and treat Candida auris infections and prevent transmission.

KEYWORDS :

INTRODUCTION:

Candida auris was first isolated in Japan in 2009 from the external auditory canal of the patient[1]. *Candida auris* is an emerging pathogen that results in nosocomial infections and is considered a serious global health problem[12]. *Candida auris* accounts for most candida bloodstream isolates in several areas, varying from around 20% to up to 38% of patients[3]. Candidemia by *Candida auris* carries a staggering mortality rate of up to 60% even with correct antifungal treatment [3]. Candida spp. account for 70 to 80% of invasive bloodstream fungal infections, particularly in ICU patients, and they represent the fourth most common nosocomial bloodstream infection[11]. Bloodstream fungal infections are a significant cause of mortality in immunocompromised patients, including AIDS, organ transplant recipients, haematology and oncology patients and patients requiring invasive therapies[11].

Major risk factors for invasive *Candida* infections include multiple comorbidities, such as extremes of age, being hospitalized in ICU, total parenteral nutrition, diabetes mellitus, neutropenia, pneumonia or chronic pulmonary diseases, cardiovascular diseases, sepsis, the presence of central venous catheters, urinary tract infection, urinary catheters or acute renal failure, malignancy, prior or concomitant bacterial infection, the use of broad-spectrum antibiotics and antifungal agents, and immunosuppressive therapy[9]. Especially ICU patients with medical devices such as central venous catheters (CVC) or urinary catheters, major surgery and immunosuppressive therapy are affected.

The unique attributes of *Candida auris*, high rates of multidrug resistance, ability to grow in conditions with high salinity and high temperatures, causes a wide spectrum of infections, especially bloodstream infection[2]. Because of higher drug-resistance rate, *C.auris* more difficult to treat, requires longer hospitalization periods, and results in higher morbidity and mortality than other Candida species[11]. *Candida auris* can be transmitted between patients in healthcare settings and cause a wide spectrum of infections, ranging from deep-seated to bloodstream infections due to candidemia [2]. In addition, *C. auris* can spread to internal organs through systemic bloodstream infection known as candidemia and is associated with 30 – 70% crude mortality rate. The pathogenicity of *Candida* species is due to virulence factors, which include but not limited to secreted proteases and lipases, mannosyl transferases, oligopeptide, siderophore-based iron transporters, and biofilm formation. The participation of these factors is observed in aspects of pathogen invasion, colonization, and acquisition of nutrition [10].

Candida auris is commonly misidentified by conventional methods in clinical laboratories**.** Due to this misidentification, infection prevention may be delayed resulting in increased transmission.*C. auris* has the attribute to transform into a persistent yeast capable of surviving under harsh physical and chemical conditions [10]. Although most fungi do not survive at normal physiological temperatures (36.5 C to 37.5C) or during conditions of pyrexia and are thus unable to colonize humans and cause infections, *C auris* is capable of growing at higher temperatures (>40 C). *C auris* is also able to tolerate high salt concentrations (>10% Nacl).

C. auris has several unique characteristics, which include its ability to persist, despite the use of common disinfectants, and remain viable for several months, likely due to biofilm formation on plastic surfaces, the hospital environment, and medical devices. Furthermore, very high rates of resistance to fluconazole and variable susceptibility to other azoles, amphotericin B, and echinocandins make the management of *C. auris* infections extremely difficult.[5]

Aims And Objectives:

To evaluate the various Candida spp. isolated in bloodstream infections

To study the prevalence of *Candida auris* in bloodstream infections.

MATERIALS AND METHODS:

A Prospective observational study was conducted in Dept. of Microbiology, Siddhartha Medical College, Vijayawada for a period of two years from Jan 2020 to Feb 2022. Ethics committee approval was obtained for the study. All the blood culture samples received in BHI broth for culture & sensitivity with complete patient information were included in the study. Blood culture samples with incomplete TRF, and leaked samples were excluded from the study. All the blood samples in BHI broths (Himedia) were processed conventionally as per standard laboratory protocol by subculturing onto Blood agar, and MacConkey agar for three consecutive days and incubation at 37^{0}C. On examination of culture plates, if any growth observed smears made and Gram stain performed. For bacterial isolates identification was done by conventional methods & antibiotic sensitivity testing was done by Kirby Bauer disk diffusion method. For yeast isolates, identification was done in Vitek2 compact (Biomerieux) using YST card (Lot 2432117503).

RESULTS & DISCUSSION:

Table 1: Analysis Of Total Blood Cultures Processed

Total no. samples	Males	Females	< 10yrs	11-20 yrs	21-40 yrs	41-60 yrs	>60 yrs
1571	643	928	296	389	432	256	198
	40.9%	59%	18.8%	24.7%	27.4%	16.2%	12.6%

Out of 1571 blood culture samples processed 928 were from female (59%) patients and 643 were from males (40.9%). Among the age groups 27.4%(432) were between 21-40 years, 24.7% (389) were between 11-20 years, 18.8% (296) were in < 10 years age, and 16.2% (256) & 12.6%(198) in age groups of 41-60 years and >60 years respectively (Table-1). Among the total blood cultures processed 278 samples were culture positive. On identification by conventional methods 213(76.6%) were bacterial isolates and 65 were yeast isolates showing 23.4% of candidemia among BSI (Table-2). All the yeast isolates were further tested to identify up to species in automated Vitek 2 compact system. Among the culture positive bacteremia was seen in 29.6% between the age group of 41-60 yrs followed by 23% in 21-40 yrs age group, whereas Candidemia was seen in 40% of cases with less than 10 yrs age(Table 2). Bloodstream infections by *Candida* species is a major cause of morbidity and mortality in hospitalized pediatric and adult patients. The incidence and prevalence of candidemia are on a rise in many countries. Various authors stated that total parenteral nutrition was the foremost risk factor; previous surgery, sepsis, previous exposure to antifungal agents, arterial and central venous catheters, presence of advanced chronic kidney disease and multifocal colonization were proven to be independent predictors of Candidaemia [3].

Table 2: Distribution Of Blood Culture Positives (n=278)

	< 10yrs	11-20 yrs	21-40 yrs	41-60 yrs	>60 yrs	Total
Bacteria	34 (5.9%)	33 (15.5%)	49 (23%)	63 (29.6%)	34 (15.9%)	213 (76.6%)
Candida	26 (40%)	08 (12.3%)	14 (21.5%)	05 (7.7%)	12 (18.5%)	65 (23.4%)
TOTAL	60 (21.6%)	41 (14.7%)	63 (22.7%)	68 (24.5%)	46 (16.5%)	278

Out of 65 Candidemia cases 36.9% (24) were caused by *Candida tropicalis*, 20% (13)were by *Candida auris,* 9.2% by *Candida guillermondii and Candida albicans*(Table-3). A study conducted by Ekadashi Rajni et al;[13] New Delhi India reported that, among 33 candidemia, *Candida auris* was the predominant species (42%) followed by *Candida tropicalis*. While the most common presentation of *Candida auris* infection occurs as bloodstream infection(fungemia), it may spread hematogenously to seed different organs and cause multiorgan dysfunction. Conversely, a localized infection may eventually become an overwhelming bloodstream infection and have further complications such as sepsis, multiorgan system failure involving the kidney, heart, lungs, eyes, brain, liver spleen and ultimately death[12].

Table 3: Distribution Of Candida Spp Isolated From Blood Cultures

NAME	NUMBER	PERCENTAGE (%)
Candida tropicalis	24	36.9
Candida auris	13	20
Candida guillermondii	06	9.2
Candida albicans	06	9.2
Candida parapsilosis	05	7.6
Candida glabrata	05	7.6
Candida kefyr	02	3.0
Candida krusei	02	3.0
Candida ceferrii	01	1.5
Candida rugosa	01	1.5

C.auris has been observed as an important nosocomial pathogen causing bloodstream infections, as most of the patients yielding *C. auris* were in intensive care units. Several studies are showing increasing pace of *C.auris* in bloodstream infections over years. In a meta-analysis conducted by Kaitlin Forsberg et al;[2] (2019)in India, 5.7% of candidemia with *Candida auris* was found in 27 intensive care units across the country, whereas 38% of candidemia by *C. auris* found from Kenya in 3 years. Previous studies have shown that colonization can occur in a new patient with a minimum contact time of just 48 hrs and invasive infections have been acquired by susceptible patients within 48hrs of admission to intensive care settings[9].

Candida auris is increasingly reported as a cause of fungemia and invasive candidiasis worldwide. *C. auris* infection was associated mainly with longer ICU stay, excessive antifungal exposure and respiratory infection [11]. Siva Prakash M et al[6] studied 1400 patients diagnosed with ICU-acquired candidemia, of which 5.3% (74 patients) were due to *C. auris*. Ziauddin Khan et al; 2018[4] reported 9.5% *Candida auris* among Candidemia. Previous antifungal therapy may be risk factor for *C auris.* Candidemia usually occurs after an event, such as placement of new lines or tube, which provides the opportunity to introduce the organism from skin into bloodstream.V. Grace-Bustos et al;[3] in their study mentioned that, 37 of the 206 patients developed candidemia due to *C. auris*, with the frequency of bloodstream infection 17.96%.

Federica Briano et al;[14] Italy in their study reported that, 157 patients admitted to the ICU of our hospital became colonized with *C. auris*, Overall, 27/157 (17%) patients developed at least one episode of *C. auris* candidemia.

Candida auris is a persistent colonizer and difficult to eradicate from the hospital environment. Its ability to form biofilms on a variety of surfaces and lack of activity of some antifungal agents such as fluconazole may have contributed to its persistence and nosocomial transmission[4]. The most compelling explanation by David et al[15] for the sustained *C. auris* transmission that we observed was the persistence of the organism on reusable equipment — in particular, on skin-surface axillary temperature probes[15]. According to certain studies the primary factor contributing to its high mortality rate is its ability to develop resistance to multiple antifungal agents. Biofilm formation allows for drug sequestration within the extracellular matrix, confers antifungal resistance observed in many candida species. Another study found that *candida auris* isolates with biofilm did not show susceptibility to any antifungal agents, including fluconazole, echinocandins and polyenes[12]. On analysing the agewise distribution of *Candida auris*, in the present study 76% of *candida auris* were in children < 10 years age (Table 4). Sivaprakash M et al[6]; 2017 reported in his study that 22 children were infected with *candida auris* in them 6 were neonates and 6 infants. Ziauddin khan et al[4]; kuwait 2018 reported that age prevalence of *candida auris* from bloodstream infections were 13 to 89 years. V. Grace-Bustos et al[3]; 2020 reported that the median age of prevalence of *candida auris* from bloodstream infections were 57.97 years. Available data suggest that the vast majority of infections affect adult critically ill patients in intensive care unit settings, pediatric patients have mostly been reported in Asia and South America [16]. Patients undergoing invasive procedures or the placement of invasive devices are at greater risk of acquiring *Candida auris* bloodstream infections with catheters providing easy access for the fungus to enter the bloodstream [9]. Thermotolerance and osmotolerance are two important characteristics that may help in the persistence and survival of *C auris* on biotic and abiotic surfaces for a long period of time in hospital environment[9,12].

Table 4: Age Wise Distribution Of *Candida Auris* Isolates (n=13)

< 10yrs	11-20 yrs	21-40 yrs	41-60 yrs	>60 yrs
10 (76.9%)	01 (7.6%)	02 (15.3%)	-	-

Patients who have undergone recent surgery, with chronic disease, and/or with recent use of a broad-spectrum antibiotic or antifungal are at a heightened risk of mortality. Specifically, patients who recently had an organ transplant, on immunosuppressant medication, have diabetes, have a history of receiving antibiotics, had indwelling devices such as catheters, and prolonged hospital or nursing home stays have the highest risk for acquiring *C. auris* infection due to its ability to enter the bloodstream and cause invasive infection[8].

CONCLUSION:

Most of the microbiology laboratories don't have access to the MALDI-TOF MS or Vitek2 system, an especially glaring deficiency for the detection of *C. auris*. It is essential to strengthen all clinical microbiology laboratories to be capable of rapidly and accurately detecting C. auris in clinical samples. A robust response that involves the laboratory, clinicians, and public health agencies is needed to identify and treat Candida auris infections and prevent transmission. Without efficient detection, the true prevalence of this menace will never be known, effective management of potential cases will be elusive and mortalities will continually rise.[5]

REFERENCES:

1. Keighley C, Garnham K, Harch SAJ, Robertson M, Chaw K, Teng JC, Chen SC. *Candida auris:* Diagnostic Challenges and Emerging Opportunities for the Clinical Microbiology Laboratory. Curr Fungal Infect Rep. 2021;15(3):116-126. doi: 10.1007/s12281-021-00420-y. Epub 2021 Jun 23. PMID: 34178208; PMCID: PMC8220427.
2. Kaitlin Forsberg, Kate Woodworth, Maroya Walters, Elizabeth L Berkow, Brendan Jackson, Tom Chiller, Snigdha Vallabhaneni, *Candida auris*: The recent emergence of a multidrug-resistant fungal pathogen, *Medical Mycology*, Volume 57, Issue 1, January 2019, Pages 1–12, https://doi.org/10.1093/mmy/myy054
3. V.Gracia-bustos,M.Selavert,A.C.Ruiz-Gaitan et al; A Clinical predictive model of candidemia by Candida auris in previously colonized critically ill patients. Clinical microbiology and Infection; 2020; 26;1507-1513.
4. Ziauddin Khan, Suhail Ahmad, Noura Al-Sweih et al. Increasing prevalence, molecular characterization and antifungal drug susceptibility of serial Candida auris isolates in Kuwait.2018;PLoS ONE 13(4):e0195743.
5. John Osei Sekyere; Candida auris: A systematic review and meta-analysis of current updates on an emerging multidrug-resistant pathogen.2017; Wiley Kumasi, Ghana.
6. Shivaprakash M. Rudramurthy1, Arunaloke Chakrabarti1*, Raees A. Paul et al; Candida auris candidaemia in Indian ICUs: analysis of risk factors; J Antimicrob Chemother 2017; 72: 1794–1801
7. Anuradha Chowdhary, Bansidhar Tarai, Ashutosh Singh, Amit Sharma. Emerging Infectious Diseases; Multidrug-Resistant Candida auris Infections in Critically Ill Coronavirus Disease Patients,India, April–July2020. 2020;26,11.
8. Arunaloke Chakrabarti 1, Prashant Sood, Shivaprakash M Rudramurthy et al; Incidence, characteristics and outcome of ICU-acquired candidemia in India. Intensive care Med; 2015;41,2;285-95
9. Ahmad, S.; Alfouzan, W. Candida auris: Epidemiology, Diagnosis, Pathogenesis, Antifungal Susceptibility, and Infection Control Measures to Combat the Spread of Infections in Healthcare Facilities. Microorganisms 2021, 9, 807. https://doi.org/10.3390/microorganisms 9040807.
10. Adekunle Sanyaolu , Chuku Okorie , Aleksandra Marinkovic , Abu Fahad Abbasi , Stephanie Prakash , Jasmine Mangat , Zaheeda Hosein , Nafees Haider , and Jennifer Chan ; Candida auris: An Overview of the Emerging Drug-Resistant Fungal Infection; 2022 Jun;54(2):236-246.
11. Mohsin J, Weerakoon S, Ahmed S, Puts Y, Al Balushi Z, Meis JF, Al-Hatmi AMS. A Cluster of *Candida auris* Blood Stream Infections in a Tertiary Care Hospital in Oman from 2016 to 2019. Antibiotics (Basel). 2020 Sep 24;9(10):638. doi: 10.3390/antibiotics9100638. PMID: 32987692; PMCID: PMC7598619.
12. Sikora A, Hashmi MF, Zahra F. Candida Auris. 2022 Nov 28. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan–. PMID: 33085444.
13. Rajni E, Singh A, Tarai B, Jain K, Shankar R, Pawar K, Mamoria V, Chowdhary A. A High Frequency of *Candida auris* Blood Stream Infections in Coronavirus Disease 2019 Patients Admitted to Intensive Care Units, Northwestern India: A Case Control Study. Open Forum Infect Dis. 2021 Sep 7;8(12):ofab452. doi: 10.1093/ofid/ofab452. PMID: 34904116; PMCID: PMC8522362.
14. Briano F, Magnasco L, Sepulcri C, Dettori S, Dentone C, Mikulska M, Ball L, Vena A, Robba C, Patroniti N, Brunetti I, Gratarola A, D'Angelo R, Di Pilato V, Coppo E, Marchese A, Pelosi P, Giacobbe DR, Bassetti M. Candida auris Candidemia in Critically Ill, Colonized Patients: Cumulative Incidence and Risk Factors. Infect Dis Ther. 2022 Jun;11(3):1149-1160. doi: 10.1007/s40121-022-00625-9. Epub 2022 Apr 11. PMID: 35404010; PMCID: PMC8995918.
15. Eyre DW, Sheppard AE, Madder H, Moir I, Moroney R, Quan TP, Griffiths D, George S, Butcher L, Morgan M, Newnham R, Sunderland M, Clarke T, Foster D, Hoffman P, Borman AM, Johnson EM, Moore G, Brown CS, Walker AS, Peto TEA, Crook DW, Jeffery KJM. A Candida auris Outbreak and Its Control in an Intensive Care Setting. N Engl J Med. 2018 Oct 4;379(14):1322-1331. doi: 10.1056/NEJMoa1714373. PMID: 30281988.
16. Cortegiani, A., Misseri, G., Fasciana, T. *et al.* Epidemiology, clinical characteristics, resistance, and treatment of infections by *Candida auris*. *j intensive care* **6**, 69 (2018). https://doi.org/10.1186/s40560-018-0342-4).