Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3825-3829 | ISSN:2251-6727

Echinocandin Sensitivity Pattern of Candida krusei Candidemia in NICU at a Tertiary Care Center

Dr. Deepa Hanamaraddi[1*], Dr. Pavithra Jain[2], Dr. Amit Joshi[3], Dr. R D Kulkarni[4]

[1]Professor and Head, Department of Microbiology, KLE Jagadguru Gangadhar Mahaswamigalu Moorusavirmath Medical College and Hospital, Hubli, KLE Academy of Higher Education and Research, Deemed to be University, Belagavi, Karnataka, India: 580028.

[2]Assistant Professor, Department of Microbiology, SDM College of Medical Sciences and Hospital, SDM University, Sattur, Dharwad-580009, India.

[3]Additional Associate Professor, Department of Microbiology, SDM College of Medical Sciences and Hospital, SDM University, Sattur, Dharwad-580009, Karnataka, India.

[4]Professor, Department of Microbiology, SDM College of Medical Sciences and Hospital, SDM University, Sattur, Dharwad-580009, India.

Corresponding Author: Dr. Deepa Hanamaraddi, Professor and Head, Department of Microbiology, KLE Jagadguru Gangadhar Mahaswamigalu Moorusavirmath Medical College and Hospital, Hubli, KLE Academy of Higher Education and Research, Deemed to be University, Belagavi, Karnataka, India: 580028.

Received Date: 11/09/2025 ***Revised Date: 06/10/2025*** ***Accepted Date: 10/11/2025***

KEYWORDS

Candida krusei, Candidemia, Echinocandins, NICU

ABSTRACT:

Background: Over the last two decades, Candida blood stream infections (BSI) have been increasingly reported from various parts of the world. Recent studies on invasive candidiasis (IC) have documented the emergence of Non Albicans Candida (NAC) species as major pathogens. Emergence of Candida krusei as important cause of candidemia is increasingly reported worldwide. This study is done to know the prevalence of Candida krusei candidemia in NICU. The antifungal susceptibility pattern was also analyzed, as Candida krusei is known to be inherently resistant to one of the commonly used antifungal drugs, Fluconazole.

Materials and methods: The study was conducted in a tertiary care center. All suspected BSI were included in this study, a total of 1,838 blood samples were received from NICU for blood culture. Blood culture was performed using automated BACTEC 2D system. Candida from positive blood culture was identified by doing Gram's staining, speciation was done by germ tube test, morphology on corn meal agar (CMA) and sugar assimilation test (Modified Wickerman Burton method). All identified Candida krusei were subjected for antifungal testing using Vitek 2 system.

Results: Out of 1,838 blood culture samples received from NICU, 77 positive samples belonged to Candida species (4.2%) and the predominant species was Candida krusei (n=56, 72.7%). Echinocandins demonstrated very good antifungal activity against Candida krusei.

Discussion: Candida krusei (56/77) was the predominant species isolated from NICU. The other species were Candida albicans, Candida tropicalis and Candida guilliermondi. The Candida krusei demonstrated 85% resistance to Fluconazole, and all were sensitive to Voriconazole and Echinocandins.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3825-3829 | ISSN:2251-6727

INTRODUCTION

Over the past 20 years, there has been a rise in reports of Candida blood stream infections (BSI) worldwide.[1]

Candidemia continues to be the most prevalent invasive nosocomial fungal infection worldwide. Its incidence ranges from 0.33 to 6.51 episodes per 1000 admissions worldwide, and because of its high fatality rates and rising prevalence, it poses a significant public health burden.[2]

Non Albicans Candida (NAC) species have emerged as important pathogens in invasive candidiasis (IC), according to recent investigations. Globally, there are more and more reports of *Candida krusei* emerging as a significant cause of candidemia.[3]

Although *Candida albicans* continues to be the most common species, accounting for over 50% of cases in some series, it has been reported that the incidence of candidemia caused by *Candida krusei*, *Candida tropicalis, Candida glabrata,* and *Candida parapsilosis* is on the rise globally .Three Candida species are commensal organisms that are found in small amounts in the skin and gut of 50–70% of healthy people because of competition within the microbiome.[4]

Numerous host characteristics and the virulence of the infecting species allow Candida to evolve from a commensal organism to a powerful pathogen.[5]

It is harmful due to its ability to attach itself to host tissues and medical equipment and to produce pseudo hyphae. [6]

Total Parenteral Nutrition (TPN), major surgeries, the use of several broad-spectrum antibiotics, a urinary catheter, the insertion of a central venous catheter, mechanical ventilation, persistent neutropenia, renal failure, the use of glucocorticosteroid treatment, burns, and hemodialysis are the factors that are frequently linked to this condition. Breakthrough infections with resistant Candida species have been linked to preexposure to antifungals, especially azoles, mostly as prophylactics, and to a lesser degree with echinocandins. Even though *C. glabrata* and *C. krusei* have been the most common isolates in these environments, and more and more resistant non-albicans Candida species are being noticed.[7]

This is a very unsettling trend that may be related to the growing usage of azoles as a preventative measure, particularly in intensive care and surgical units.[8]

Thus, ongoing surveillance is required to track patterns in the incidence, species distribution, and antifungal medication susceptibility profiles of Candida BSI.[9]

Neonatal *Candida krusei* candidemia is an uncommon but dangerous illness that is especially worrisome because of its inherent fluconazole resistance and possible multidrug resistance.[10]

The broad-spectrum action of echinocandins against the majority of Candida species and their good safety profile make them the recommended first-line treatment for invasive candidiasis. According to clinical research, echinocandins are superior to fluconazole in treating patients with chronic candidemia in terms of mycological eradication. For example, research that compared echinocandins to fluconazole discovered that echinocandin treatment resulted in higher rates of mycological eradication.[11]

The study was done to know the prevalence of *Candida krusei* candidemia in NICU in our hospital and to determine the antifungal susceptibility pattern of *Candida krusei* to Echinocandins as it is known to be inherently resistant to one of the commonly used antifungal drugs, Fluconazole.

MATERIALS AND METHODS

The study was conducted in a tertiary care center. A total of 1,838 blood samples were received from NICU for blood culture. All the blood samples were subjected to an automated blood culture system, BACT/Alert 3D. Candida from a positive blood culture was identified by doing Gram's staining. The Candida was isolated by subculturing the blood in the blood agar and Sabouraud's dextrose (SDA) agar slants and incubating aerobically at 37°d for 24-48 hours. The colonies were then subjected to the germ tube test, morphology on cornmeal agar (CMA), and sugar assimilation test (Modified Wickerham Burton method). [12] Total of 41 identified *Candida krusei* out of 56 were subjected for antifungal testing using Vitek 2 automated system. The antifungals tested in this study were Fluconazole, Voriconazole, Flucytosine, Amphotericin B, Caspofungin and Micafungin.[13,14]

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3825-3829 | ISSN:2251-6727

RESULTS

A total of 11,630 blood samples were received during the study period for blood culture and 1,838 blood samples were from NICU. Out of 1,838 blood culture samples received from NICU, 77 positive samples were positive for Candida species (4.18%) (Table No 1).

All the isolated Candida species were subjected for the speciation and the predominant species was *Candida krusei* (n=56, 72 %), followed by *Candida tropicalis*(n=10, 12.9%), Candida albicans (n=8, 10%), *Candida kefyr* (n=1, 1.2*%), Candida lusitaniae* (n=1, 1.2%) and *Candida guilliermondii* (n=1, 1.2%).

The *Candida krusei* is known to be intrinsically resistant to fluconazole, hence all the *Candida krusei* species were subjected for anti-fungal testing using Vitek 2 automated system. The Echinocandins demonstrated very good antifungal activity against *Candida krusei* with hundred percent sensitivity action. (Table no 3)

Table No 1: Total number of blood sample from NICU

Number of Blood samples received from NICU	1,838
Number of sample positive for Candida species	77

Table No 2: Candida species isolated from NICU

Candida species	**Number (n=77)**
Candida krusei	56
Candida tropicalis	10
Candida albicans	8
Candida kefyr	1
Candida lusitaniae	1
Candida guilliermondii	1

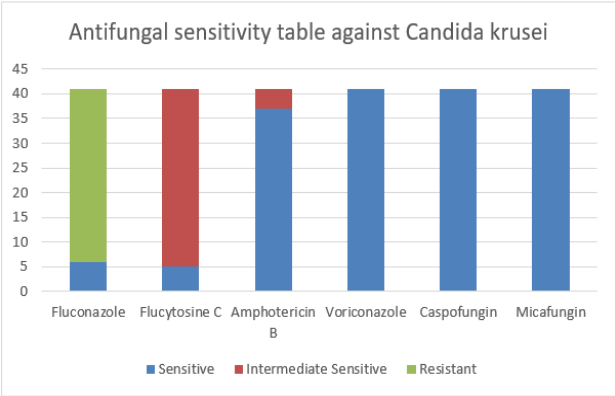

Table No 3: Antifungal activity of *Candida krusei*

DISCUSSION

Among the non-Candida albicans, *Candida krusei* was the most common species isolated in this investigation (56/77; 72.7%). Other species identified included *Candida tropicalis* (10g7; 12_9%), *Candida albicans* (8/77; 10.3%), and one isolate each of *Candida guilliermandii, Candida kefyr, and Candida lusitaniae* (1177; 1.2%). NAC species predominance in neonates has been reported by Pfaller *et al.* (2007) 15 and Chakrabarti *et al.* (2008).[16]

All of the newborns had received injections, according to their clinical histories. As soon as the blood was taken for culture, fluconazole was given. The recommended medication for the empirical therapy of fungaemia is fluconazole. [17]

Babies spent an average of 15.3 days in the NICU before their blood culture revealed the presence of *Candida krusei*, suggesting that the candidemia may be nosocomial in origin. 10 to 15% of nosocomial bloodstream infections are nosocomial candidemia.[18] A variety of host conditions and virulence factors can cause Candida species to transit from commensal to pathogen. [19] Prematurity, extreme low birth weight, the use of central venous catheters, the administration of broad-spectrum antibiotics, TPN, prolonged hospitalization, and prior exposure to antifungals are some of the variables that put newborns, particularly those in NICUs, at increased risk for *Candida krusei* candidemia. [20]

Although the majority of the infants had *Candida krusei* candidemia, which is considered to be inherently resistant to fluconazole, it is noteworthy that 76% of them recovered following empirical fluconazole

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3825-3829 | ISSN:2251-6727

treatment. A second blood culture, a few days later, would be useful in determining the isolate's pathogenicity. It will help in knowing the pathogenicity of *Candida Krusei* candidemia and also to know whether it is temporary/transient in nature. *Candida krusei* was the only isolate that exhibited fluconazole and voriconazole resistance, with 85% of the isolates exhibiting fluconazole resistance. According to Pfaller *et al.* (2008), 80% of *Candida krusei* exhibit fluconazole resistance. Nonetheless, every *C. krusei* isolate exhibited a fair pattern of sensitivity to Amphotericin B, Caspofungin, Micafungin, Flucytosine, and Voriconazole.

For every isolate of *Candida krusei* that was intrinsically resistant, echinocandins displayed a 100% sensitivity pattern. The rarity of acquired echinocandin resistance highlights how well echinocandins work to treat invasive candidiasis. Optimizing treatment methods against invasive candidiasis requires ongoing monitoring of echinocandin resistance patterns. [21]
In preterm and critically ill babies, especially in neonatal intensive care units (NICUs), neonatal candidemia is a major cause of morbidity and mortality. Because of its inherent resistance to fluconazole and capacity to acquire resistance to other antifungals, *Candida krusei* is a less prevalent but clinically significant species of Candida.

Accurate and timely identification of Candida species is essential for successful therapy, and species identification in non-Candida albicans aids in this process. The best antifungal treatment is chosen based on susceptibility testing, particularly when newborn candidemia is resistant. Outbreaks can be avoided in NICUs by strictly adhering to hygiene guidelines. Early detection and intervention can be facilitated by routinely monitoring at-risk infants and conducting surveillance cultures.

CONCLUSION

Echinocandins play a critical role in the management of neonatal candidemia due to *Candida krusei*, especially when fluconazole resistance is present. Their use should be guided by species identification, antifungal susceptibility testing, and careful assessment of infection site. They provide a useful therapeutic option, but in order to maximize their use in this susceptible population, more study and monitoring are required.

REFERENCES

1. Deorukhkar SC. Saioi S. Echinocandin susceptibility profile of fluconazole resistant Candida species isolated from blood stream infections. infect 2015 Dec 9.
2. Agnelli C, Guimaraes T, Sukiennik T, *et al.* Prognostic Trends and Current Challenges in Candidemia: A Comparative Analysis of Two Multicenter Cohorts within the Past Decade. J Fungi. 2023;9(4):468. doi: 10.3390/jof9040468.
3. Bac ND, Anh LT, Quang LB, *et al.* Prevalence of Candida bloodstream isolates from patients in two hospitals in Vietnam. Iran J Microbiol. 2019;11(2):108-113.
4. Soriano A, Honore PM, Puerta-Alcalde P, *et al.* Invasive candidiasis: current clinical challenges and unmet needs in adult populations. J Antimicrob Chemother. 2023;78(7):1569-1585. doi: 10.1093/jac/dkad139.
5. Deorukhkar SC, Roushani S. Virulence Traits Contributing to of Candida Species. J Microbiol Exp. 5(1):00140. doi: 10.15406/jmen.2017.05.00140)
6. Siddiqui R, Mendiratta DK, Siddiqui AF, Rukadikar A. A study of the association between virulence factors and antifungal susceptibility profile of Candida species recovered from cases of vulvovaginal candidiasis. J Family Med Prim Care. 2023;12(1):152-159. doi: 10.4103/jfmpc.jfmpc_1479_22
7. Gupta P, Prateek S, Chatterjee B, Kotwal A, Singh AK, Mittal G. Prevalence of Candidemia in ICU in a Tertiary Care Hospital in North India. Int J Curr Microbiol App Sci. 2015;4(6):566-575)
8. Kothari A, Sagar V. Epidemiology of candida bloodstream infections in a tertiary care institute in India. Indian J Med Microbiol. 2009;27(2):171-172. doi: 10.4103/0255-0857.49440)

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 3825-3829 | ISSN:2251-6727

9. Behera SR, Panda RK, Khatua S, Majhi S, Swain M. Prevalence And Antifungal Susceptibility Profile of Candida Species Isolated from Blood Stream Infections in Neonates in a Tertiary Care Hospital. Int J Acad Med Pharm. 2023;5(6);237-242 doi: 10.47009/jamp.2023.5.6.48.

10. Amaral-Lopes S, Moura A. Neonatal fungal sepsis by *Candida krusei*: A report of three cases and a literature review. Med Mycol Case Rep. 2012 Apr 16;1(1):24-6. doi: 10.1016/j.mmcr.2012.04.002. PMID: 24371729; PMCID: PMC3854703.

11. Kuan-Yin Lin, Pao-Yu Chen, Yu-Chung Chuang, Jann-Tay Wang, Hsin-Yun Sun, Wang-Huei Sheng, Yee-Chun Chen, Shan-Chwen Chang. Effectiveness of echinocandins versus fluconazole for treatment of persistent candidemia: A time-dependent analysis, Journal of Infection.2018: 77(3): 242-248. ISSN 0163-4453, https://doi.org/10.1016/j.jinf.2018.05.011

12. Lemons D. Medically important fungi. Washingtort,D.C.:ASM Press; 2002; 88-180.

13. CLSI. Performance standards for antifungal susceptibility testing of yeasts. CLSI supplement M60. https://clsi.org/media/1895/m60ed1_sample.pdf Wayne, PA: Clinical and Laboratory Standards Institute. 2020

14. VITEK® 2 AST cards. Cards for antimicrobial susceptibility testing. VITEK® 2 AST Cards. https://www.biomerieux-diagnostics.com/vitekr-2-ast-cards-0 2021.

15. Pfaller MA, Diekema DJ. Epidemiology of invasive candidiasis: a persistent public health problem. Clin Microbiol Rev. 2007;20:133–63.

16. Chakrabarti A, Chatterjee SS, Shivaprakash MR. Overview of opportunistic fungal infections in India. Nihon Ishinkin Gakkai Zasshi. 2008;49(3):165-72. doi: 10.3314/jjmm.49.165. PMID: 18689964.

17. Hay RJ, Merz W. Eurnyoelomas, Tooley& Wilson's Microbiology and Microbial Infections, 2010 Mar 15;5:1658-90

18. GiriS, KindoAJ, A review of Candida species causing blood stream infections, Indian Journal of Medical Microbiology 2012130(3): 270-278.

19. Mohanraj H, Vinodhini VM, Vajravelu LK. Evaluation of Epidemiological Pattern of Candida Species Associated with Candidemia from A Tertiary Care Facility in South India. J Pure Appl Microbiol. 2024;18(3):1949-1958. doi: 10.22207/JPAM.18.3.45

20. van Schalkwyk E, Iyaloo S, Naicker SD, Maphanga TG, Mpembe RS, Zulu TG, Mhlanga M, Mahlangu S, Maloba MB, Ntlemo G, Sanyane K, Mawela D, Govender NP. Large Outbreaks of Fungal and Bacterial Bloodstream Infections in a Neonatal Unit, South Africa, 2012-2016. Emerg Infect Dis. 2018 Jul;24(7):1204-1212. doi: 10.3201/eid2407.171087. PMID: 29912684; PMCID: PMC6038734.

21. Axner-Elings M, Botero-Kleiven S, Jensen RH, Arendrup MC. Echinocandin susceptibility testing of Candida isolates collected during a 1-year period in Sweden. J Clin Microbiol. 2011 Jul;49(7):2516-21. doi: 10.1128/JCM.00201-11. Epub 2011 May 4. PMID: 21543574; PMCID: PMC3147820.