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# EPIDEMIOLOGY OF NEONATAL CANDIDEMIA: A STUDY FROM EASTERN INDIA

**Microbiology**

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## ABSTRACT

**Introduction:** To assess the epidemiology of neonatal Candida blood stream infection and its significant predisposing factors.
**Methods:** Medical records of neonatal candidemia over 4 years were reviewed. Clinical details and species distribution were noted.
**Results:** Out of 923, 89 neonate developed Candidemia and commonly isolated Candida species were C.parapsilosis, C. albicans and C. tropicalis. Low birth weight was found to be significantly associated with candidemia.
**Conclusions:** Epidemiology of neonatal candidemia is essential for prophylactic initiation of antifungals in risk group and early and appropriate treatment of the patients.

## KEYWORDS

## INTRODUCTION:

There is more than 150 species in genus *Candida*, among them few causes human infection. They are ubiquitously present in nature, distributed worldwide, natural inhabitant in GI tract, skin and genital tract. In developed countries *Candida* species are now among the most common health care-associated pathogens. In United States, Candida spp is the fourth most common pathogen causing blood stream infection in hospitalized patients (1). It is accounted for one of the most common cause of blood stream infections among neonates (9-13%). Although blood stream infection (BSI) due to Candida species (spp.) in neonates is less frequent than that due to bacteria, it has higher morbidity and mortality rates.( 2) The high (25-60%) mortality rate due to candidemia is related to the difficulty to make an early diagnosis (3). Newborns who survive frequently have long-term neurological impairment, including cerebral palsy, blindness, hearing impairment, cognitive deficits, and periventricular leukomalacia ( 4). Although candida albicans remains most common fungal isolates from neonatal candidemia, longitudinal studies have detected shift towards non-albicans candida (NAC) species. After introduction of antifungal drugs, candida infections shifted from C.albicans to Non albican Candida species (NAC).NAC now are the half of all cases of candidemia and hematogenously disseminated candidiasis. (1).There is growing evidence suggesting a role of increasing use of azole agents in this epidemiological shift. Number of factors including use of indwelling device, broad spectrum antibiotics, low birth weight (LBW), prematurity contribute to risk. Preterm, very low birth weight (VLBW), extreme low birth weight (ELBW) are at highest risk for invasive candida infection. Candida spp can also spread through vertical transmission from maternal flora or via horizontal transmission from hands of health care workers. It is generally observed that most infant candidiasis is thought to be endogenously acquired through prior colonization of different parts of the body (5,6,7). C.albicans, C.glabrata, C.parapsilosis, C.tropicalis, C.krusei, these five spp are account for more than 90% of all diagnosed case of candidemia, but the frequency differ according to susceptible host, geographical region, patient age, previous antifungal exposure etc.(8).

## AIMS AND OBJECTIVES:

This study aimed to determine the epidemiology of neonatal Candidemia in a tertiary care hospital during four years of observation and to analyze the trend in species distribution.

## MATERIALS AND METHOD:

Blood samples were collected from every neonate from various ward with signs and symptoms of sepsis during the study period from January 2015 to May 2018 and cultured by conventional blood culture method. Subculture was done on blood and MacConkey agar at regular interval following standard protocol. Pure growths of candida spp obtained on blood agar were included in this study. The isolates were identified as per standard mycological technique (9).

## RESULT:

A total 923 neonates were included in our study from January 2015 to May 2018. Candida species were isolated from 89/923(9.6%) cases. Highest incident of neonatal candidemia seen in NICU (neonatal intensive care unit) ward 53/89(59.5%) but NAC were more prevalent in SNCU (sick neonatal care unit) than MCW (main child ward) and NICU (table1). incidence of candidemia was highest in the year 2013 (table2). The male: female ratio was 1.3:1.The majority of candidemia episodes occurred in Low birth weight (LBW) infants (65.16%). Candidemia was observed to be more in preterm neonates 53(59.55%) and neonates receiving antibiotics 61(68.53%) and who were born by vaginal delivery 55(61.79%).

Out of 89 isolates, 14(15.7%) were C.albicans and NAC spp were responsible for 84% (75) cases. Among NAC spp C.parapsilosis 22.5% (20) was the most predominant, then C.tropicalis 14.6% (13), C.guilliermondii 10.1% (10) and C.glabrata 9%(8) as the other most predominant spp.

With regard to the temporal trend of C. albicans and Candida non-albicans, a variable drift from 20015–2018 was observed, with a considerable percentage increase in non-albicans species in 2018. Predisposing factors associated with C. albicans and non-albicans are listed in Table3. NAC candidemia was associated with late onset sepsis, LBW, prematurity, broad spectrum antibiotics. Association of NAC candidemia with late onset sepsis and LBW were statistically significant.

**Table 1**

| | | | albicans and NAC | | Total |
|---|---|---|---|---|---|
| | | | 1 | 2 | |
| Ward | MCW | Count | 6 | 23 | 29 |
| | | % within Ward | 20.7% | 79.3% | 100.0% |
| | NICU | Count | 8 | 45 | 53 |
| | | % within Ward | 15.1% | 84.9% | 100.0% |
| | PICU | Count | 0 | 1 | 1 |
| | | % within Ward | 0.0% | 100.0% | 100.0% |
| | SNCU | Count | 0 | 6 | 6 |
| | | % within Ward | 0.0% | 100.0% | 100.0% |
| Total | | Count | 14 | 75 | 89 |
| | | % within Ward | 15.7% | 84.3% | 100.0% |

**Table 2**

| | | | Total admission | | | Total |
|---|---|---|---|---|---|---|
| | | | | C.albicans | N\|AC | |
| Year | 15 | Count | 446 | 5 | 34 | 39 |
| | | % within Year | 8.74% | 12.8% | 87.2% | 100.0% |

| | | | | | | |
|---|---|---|---|---|---|---|
| | 16 | Count | 189 | 7 | 12 | 19 |
| | | % within Year | 10.05% | 36.8% | 63.2% | 100.0% |
| | 17 | Count | 129 | 2 | 5 | 7 |
| | | % within Year | 5.42% | 28.6% | 71.4% | 100.0% |
| | 18 | Count | 159 | 0 | 24 | 24 |
| | | % within Year | 15.09% | 0.0% | 100.0% | 100.0% |
| Total | | Count | 923 | 14 | 75 | 89 |
| | | % within Year | 100% | 15.7% | 84.3% | 100.0% |

**Table 3: Clinical characteristics of the patients with candidemia**

| Characteristics | Number | C.albicans | NAC | p-value |
|---|---|---|---|---|
| Late onset sepsis | 53 | 3 | 50 | .0015 |
| Male | 51 | 9 | 42 | .565 |
| LBW | 58 | 5 | 53 | .011 |
| Preterm | 53 | 10 | 43 | .323 |
| Broad spectrum antibiotics received | 61 | 7 | 54 | .103 |
| Vaginal delivery | 55 | 8 | 47 | .696 |

P value significance level at 0.05

**Table 4**

| Species | | Frequency | Percent |
|---|---|---|---|
| | C.albicans | 14 | 15.7 |
| | C.dubliniensis | 1 | 1.1 |
| | C.glabrata | 8 | 9.0 |
| | C.guilliermondii | 9 | 10.1 |
| | C.haemulonii | 5 | 5.6 |
| | C.kefry | 1 | 1.1 |
| | C.krusei | 5 | 5.6 |
| | C.lipolytica | 1 | 1.1 |
| | C.lusitaniae | 5 | 5.6 |
| | C.parapsilosis | 20 | 22.5 |
| | C.rugosa | 3 | 3.4 |
| | C.stelletoidie | 2 | 2.2 |
| | C.tropicalis | 13 | 14.6 |
| | C.zeylanoides | 2 | 2.2 |
| | Total | 89 | 100.0 |

## DISCUSSION

Candida species may produce various infections like mucocutaneous, cutaneous, systemic and allergic disease. Certain patients are at high risk for candidemia like neonates specially low birth weight neonates, critically medical and surgical patients, neutropenic patients, organ transplantation patients with immunosuppressive agents, patients with cytotoxic chemotherapy, parenteral glucocorticoid, indwelling intravenous or urinary catheter, severe burns, HIV-associated low CD4 cell count, antibacterial agents, diabetes etc.(1). Although Candida species exist as commensals on the skin, oropharynx and gastrointestinal tract, invasive candidiasis may occur among preterm neonates due to immaturity of their immune system (10, 11)

Candidemia is a significant cause of mortality and morbidity specifically among the neonates. We aimed to find out the significant predisposing factor(s) of neonatal candidemia and observe the frequency of the candida species causing the same. Susceptibility of the NAC to commonly used antifungals differs, so it is very much essential to find out the common candida species prevalent in that particular hospital before choosing the proper antifungal empirically.

In our study the majority of candidemia episodes occurred in Low birth weight (LBW) infants (65.16%). Low birth weight indicates immune system imaturity and fragile physical barriers and, although neutrophil counts in preterm newborn are similar to those in adults, neutrophil function and mobilisation in preterm newborn are different when facing infections; neutropenia occurs due to small neutrophil bone marrow reserves that are quickly depleted (12). LBW infants are known to be at a high risk of candidemia due to more intensive treatment such as indwelling catheters, mechanical ventilation and longer hospital stay. Candida spp can adhere to foreign substances and forms bioflims and that acts as a reservoir for for systemic infections (2. 4). It is observed that the incidence of candidemia was highest in the year 2016 (table2) and lowest in 2017 with variable drift from 2015 to 2018. The reason behind this drift was not evaluated.

The incidence of late onset sepsis was significantly higher in NAC candidemia in our study. Basu, et al,2017 also have reported NAC candidemia is higher in late onset neonatal sepsis.**(13).**

Shift of the species from C.albicans to non albicans candida (NAC) is now account for approximately half of all cases of candidemia and hematogenously disseminated candidiasis (1). Five candida spp (C.albicans,C.parapsilosis, C.glaabrata, C.tropiclis and C.kruise) are account for most of the cases. The frequency of the various spp depend on geographical region, population involved, previous antifungal used, and patient age (8). Recognition of this change clinically important because many of different species have different antifungal susceptibility pattern specially many of them are intrinsically resistant to many antifungal agents (1).

In the present study the prevalance of Candidemia was 9.6% of total clinically suspected neonatal sepsis cases. Out of 89 isolates, 14(15.7%) were C.albicans and NAC spp were responsible for 84.3%(75) cases .Among NAC spp C.parapsilosis 22.5%(20) was the most predominant. Though C.parapsilosis is a less virulence organism, but its virulence increase in certain circumstances like intravenous catheter, high IV glucose concentrations C.parapsilosis have high affinity to adhere to foreign substances and have ability to produce bioflims and this factors important for development of candidemia (14) have also documented C.parapsilosis as an emerging fungal pathogen and a major threat for future especially among neonates in NICU's and the incidence of C.parapsilosis may continue to rise as it frequently colonises the hands of health care workers and has high affinity for parenteral nutrition Some authors have reported that 96.8% of the isolates causing invasive candidiasis were NAC (15), which is quite higher than our study. Others have reported 50% (16). C. tropicalis, causes infections in adult and children with hematological malignancy or immunocompromised individuals but less frequent in neonates (17). However premature and low birth weight neonates have an immature immune system and that may be the cause behind second most common NAC spp causing candidemia in our study (13) have reported 65% NAC with C. tropicalis, 32 (39%). (18) have reported C. albicans 43.5%, C. tropicalis 21.7%, C. guillermondi 13%, C. parapsilosis 13%, and C. krusei 8.7% as causative agents of invasive candidiasis. C. krusei has more recently emerged as a notable pathogen with clinical manifestations such as fungaemia, endopthalmitis, arthritis and endocarditis which usually occur in compromised patient groups in nosocomial settings (19) and in our study though we found C.krusie is responsible for 5.6% of neonatal candidemia. The high incidence of NAC species causing candidaemia is of concern as many of them are known to be resistant to fluconazole (C.glabrata and C. krusei which are more likely to be drug resistant), and the shift towards NAC is clearly evident.

## CONCLUSIONS:

We found an increasing trend in neonatal candidemia by Non-albicans candida. Recognition of this change is clinically important because many of different species have different antifungal susceptibility pattern specially many of them are intrinsically resistant to many antifungal agents. So where antifungal susceptibility is not readily available, species identification can guide a clinician to choose antifungal agents to start therapy without delay. There is a significant variation in cases of candidemia in different geographic regions, even within the same continent. Therefore, monitoring epidemiological data to facilitate the choice of treatment is important. Also assessing the predisposing factor is important to initiate proper antifungals empirically for the risk group to decrease the mortality and morbidity significantly.

## REFERENCES


1. John E. Edwards, Jr. Candidiasis. 19th edition. United States of America: McGraw-Hill education; 2015
2. D.Testoni,M.Hayashi,M.Cohen-Wolkowiezetal.,"Late-onset bloodstream infections in hospitalized term infants," Pediatric InfectiousDiseaseJournal,vol.33,no.9,pp. 920–923, 2014.
3. Castagnola, E., Buratti, S. 2009. Clinical aspects of invasive candidiasis in paediatric patients. Drugs, 69(Suppl.1): 45-50
4. M.S.Kelly, D.K.Benjamin, and P.B.Smith,"The epidemiology and diagnosis of invasive candidiasis among premature infants," Clinics in perinatology,vol.42, no.1,pp. 17–105, 2015.
5. Asmundsdottir, L.R., Erlendsdottir, H., Haraldsson, G., Guo, H., Xu, J., Gottfredsson, M. 2008. Molecular Epidemiology of Candidemia: evidence of clusters of smoldering nosocomial infections. Clin. Infect. Dis., 47(2): 17-24.
6. Blot, S., Dimopoulos, G., Rello, J., Vogelaers, D. 2008. Is Candida really a threat in the ICU? Curr. Opin. Crit. Care, 14(5): 600-4.
7. Bendel, C.M. 2003. Colonization and epithelial adhesion in the pathogenesis of neonatal candidiasis. Semin Perinatol., 27(5): 357-364.
8. Antinori S et al,candidemia and invasive candidiasis in adult:A narrative review.Eur J internal Med.2016 oct;34:21-28.doi:10.1016.
9. Jagdish Chander. Candidiasis. 3rd edition. India: Mehta publisher; 2013.
10. Kaufman D, Kilpatrick L, Hudson RG, Campbell DE, Kaufman A, Douglas SD, et al. Decreased superoxide production, degranulation, tumor necrosis factor alpha secretion, and CD11b/CD18 receptor expression by adherent monocytes from preterm infants. Clin Diagn Lab Immunol 1999 Jul;6(4):525-529.

11. Marodi, L., and R. B. Johnston, Jr. editor. Fetal and Neonatal Physiology. R.A. Polin, W. W. Fox, and S. H.Abman (ed) ed.: The W.B. Saunders Co., Philadelphia,Pa.; 2004
12. Del Vecchio A, Christensen R. Neonatal neutropenia: what diagnostic evaluation is needed and when is treatment recommended? Early Hum Dev. 2012; 88(Suppl2):S19-24.
13. Basu S, Kumar R, Tilok R and Kumar A. Candida Blood Stream Infection in Neonates: Experience from A Tertiary Care Teaching Hospital of Central India, Indian Pediatrics. 2017March:,vol54:556-59.
14. Trofa, D., Gacser, A., Nosanchuk, J.D. 2008. Candida parapsilosis, an emerging fungal pathogen. Clin. Microbiol. Rev., 21: 606-625
15. Tushar, B.P., Ruchi, N.N., Chandrakant, V.P., Suman Rao, P.N., Kishore, B., Rekha, H.U., Preeti, M. 2007. Fluconazole prophylaxis against fungal colonization and invasive fungal infection in very low birth weight infants. Indian paediatrics, 44: 830 837.
16. Kaufman, D., Boyle, R,. Hazen, K. 2001. Fluconazole prophylaxis against fungal colonization and infection in preterm infants. N Engl. J. Med., 345: 1660–1666.
17. Roilides E1, Farmaki E, Evdoridou J, Francesconi A, Kasai M, Filioti J, Tsivitanidou M, Sofianou D, Kremenopoulos G, Walsh TJ Candida tropicalis in a neonatal intensive care unit: epidemiologic and molecular analysis of an outbreak of infection with an uncommon neonatal pathogen. J Clin Microbiol. 2003 Feb;41(2):735-41.
18. Narang, A., Agarwal, P., Chakrabarti, A., Kumar, P. 1996. Fluconazole in the management of neonatal systemic candidiasis. Indian pediatrics, 33(10): 823 6.
19. Yuthica, H.S., Samaranayake, L.P. 1994. Candida krusei: biology, epidemiology, pathogenecity and clinical manifestations of an emerging pathogen. J. Med.Microbiol., 4: 295 310.