

Non-albicans Candida in Neonatal Septicemia - An emerging clinical entity**Asifa Nazir***

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Abstract

Background:-Over the past two decades the frequency of invasive mycosis in neonates has increased significantly. Candida species account for a significant percentage of all neonatal bloodstream infections and recently non-albicans *Candida* (NAC) have emerged as important opportunistic pathogens, notably *Candida tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. glabrata*.

Aims: This study was undertaken to know the distribution and antifungal susceptibility pattern of *Candida* species in neonatal septicemia cases.

Materials and Methods: In a prospective analysis blood samples from 350 clinically suspected cases of neonatal septicemia were collected aseptically. Only those which yielded pure growth of *Candida* spp. were included in the study. Identification of *Candida* species as well as antifungal sensitivity testing was performed with Vitek2 Compact (Biomérieux France) using vitek 2 cards for identification of yeast and yeast like organisms (ID-YST cards).

Results: Isolation rate of *Candida* from neonatal septicemia cases was 10%. Most common isolate was *C. tropicalis* (57.14%), followed by *C. albicans* (17.1%), *C. krusei* (17.1%), and *C. guilliermondii* (5.7%). Low birth weight and previous antibiotic prophylaxis were the main risk factors found in 100% cases. 62.85% candida isolates were sensitive to fluconazole whereas sensitivity to amphotericin B was 94.28%

Conclusion: Non albicans *Candida* has emerged as an important cause of neonatal septicemia. Therefore speciation & antifungal susceptibility is a must in management of neonatal candidemia cases.

Keywords: Candidemia, *Candida albicans*, non albicans *Candida* (NAC).

1. Introduction

Candida bloodstream infections have become an increasingly important problem in the neonatal intensive care unit (NICU), resulting in significant morbidity and mortality of low-birth-weight infants. *Candida* species are one of the most common causes of invasive fungal infections in the neonatal intensive care unit (NICU) and account for 9-13% of such infections [1]. Also they are the third most common blood culture isolates recovered from cases of late-onset sepsis in the NICU [2-6]. The mortality associated with *C. albicans* is reported to be 44% [7] in very low birth weight (VLBW) infants and 30% to 75% in extremely low birth weight (ELBW) infants [8].

Candidemia has been associated with many risk factors like long-term hospitalization, antibiotic therapy, use of intravascular catheters, and underlying diseases like diabetes and malignancy. [9] Although *Candida albicans* has historically been the most frequently isolated species, recently Non-albicans *Candida* (NAC) have emerged as important opportunistic pathogen, notably *C tropicalis*, *C. parapsilosis*, *C. krusei*, *C. glabrata*. [10,11] This could be because of

selection of lesser susceptible non-albicans species due to frequent use of fluconazole [11-13]. Since there is considerable regional variability, local epidemiological knowledge is critical in the effective management of invasive candidiasis. Also speciation and susceptibility testing of *Candida* sp is still not routinely being done at most of the centres and as such no reliable data are available from India regarding the estimation of antifungal use in hospitals. The present study was conducted to determine the *Candida* species causing candidemia in a neonatal intensive care unit and to find their antifungal susceptibility pattern.

2. Material and methods

The prospective study period was from 1st January 2015 till 30th December 2015 and the study was conducted in the Department of Microbiology of a tertiary care hospital in Kashmir Valley. Candidemia was diagnosed by isolation of *Candida* spp. from at least two blood culture samples or at least one positive blood culture containing pure growth of *Candida* species with supportive clinical features. Prior to the

sample collection, approval from institutional ethical committee and written informed consent from patient's guardian were obtained. A total of 350 peripheral venous blood samples from neonates suspected of septicemia were collected aseptically and inoculated in the BacT/ALERT 3D pediatric culture bottle which was incubated in an automated microbial detection system (bioMerieux) for up to 5 days at 37°C. Any growth indicated was subcultured on sheep blood agar, MacConkey agar plates and Sabouraud dextrose agar slant with antibiotics but without cycloheximide (Hi-Media Pvt Ltd., Mumbai, India). Identification was done by gram staining, colony morphology on SDA and chromogenic media (Hichrome, Himedia Pvt. Ltd.), growth at 45°C, germ tube test and confirmed on VITEK® 2 (Biomérieux) compact systems. Antifungal susceptibility was determined using the Vitek 2 system. The VITEK® 2 (Biomérieux) compact systems is a fully automated growth based technology that performs bacterial / yeast identification by biochemical analysis using colorimetric method. Antifungal sensitivity was performed against Amphotericin B, 5 Flucytosine, Fluconazole, Caspofungin, Voriconazole and Micafungin. Results were interpreted according to CLSI guidelines (2012).

3. Results

A total of 51.42% cases were blood culture positive. Pure growth of *Candida* spp. was isolated from 35 cases. Non *albicans Candida* species were responsible for 82.8% cases

whereas 17.1% of the cases were caused due to *C. albicans*. Among the NAC species, *C. tropicalis* (50%) was the predominant species isolated, followed by *C. krusei* (17.1%) and *C. guilliermondii* (5.7%) [Figure 1].

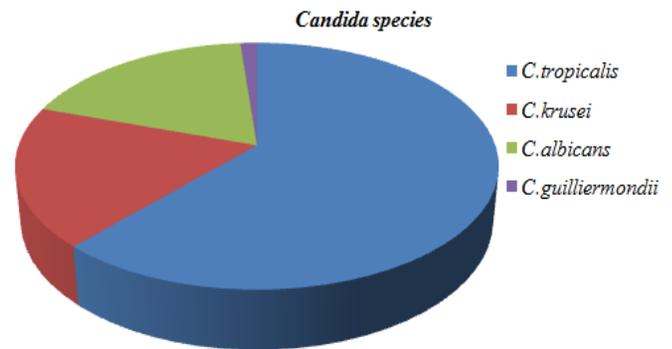


Figure 1: Shows the various *Candida* species isolated from blood (n = 35)

Of the total 35 neonates included in the study 21 (60%) were females and 14 (40%) were males. The average gestational age was 32.2 weeks (30-39 weeks) and average birth weight was 1.2 kg (0.93-2.21 kg).

Antifungal susceptibility testing results showed that 62.85% isolates were sensitive to fluconazole, 68.57% were sensitive to flucytosine and 94.28% were sensitive to amphotericin B, while as all the isolates were sensitive to voriconazole. (Table 1)

Table 1: Antifungal sensitivity pattern of culture positive isolates

<i>Candida</i> Species	Sensitivity (%) to antifungals tested				
	Flucytosine n (%)	Amphotericin B n(%)	Fluconazole n(%)	Voriconazole n(%)	Caspofungin n(%)
<i>C.tropicalis</i>	19(95)	20(100)	17(85)	20(100)	20(100)
<i>C albicans</i>	4(66.6)	5(83.3)	4(66.6)	6(100)	6(100)
<i>C krusei</i>	0(0)	6(100)	0(0)	6(100)	5(83.3)
<i>C guilliermondii</i>	1(50)	2(100)	1(100)	2(100)	2(100)

Among the risk factors observed for candidemia [Table 3] Low birth weight (100%) was the commonest followed by broad spectrum antibiotic use (94.12%), prematurity (80%) prolonged central venous line (48.5%), ventilator support (40%) and corticosteroid therapy (34.3%).

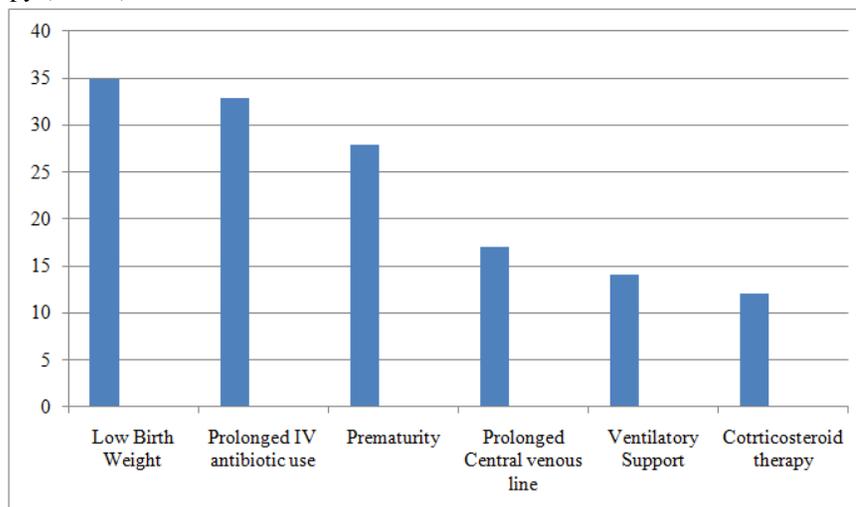


Figure 2: Potential risk factors identified in cases of neonatal candidemia (n=35)

4. Discussion

Candida species have become important nosocomial pathogens over the past two decades. Moreover non-albicans Candida have emerged as important opportunistic pathogen, notably *C. tropicalis*, *C. krusei* and *C. parapsilosis*. [9,14,15] In our study the isolation rate of Candida from neonatal septicemia cases was 10%. This isolation rate is comparable with the findings of other Indian studies conducted by Agarwal et al, and Rani et al who found isolation rates of 14.9% and 11% in their studies.[16,17]. However the prevalence rate was higher than shown in some studies [18].

Studies conducted over past two decades showed that most cases of neonatal candidemia were caused by *Candida albicans*. [19] However, recent studies from different regions of Indian subcontinent have shown emergence of non albicans Candida species as an important cause of neonatal septicemia.[20-22]

In our study, non albicans Candida sp (82.8%) were more commonly isolated than *C. albicans*. These finding are also consistent with other studies where non albicans Candida species predominate in not only India but also in Asia and Europe [23-25].

Emergence of non albicans Candida is probably due to selection of less susceptible species by the pressure of antifungal agent such as fluconazole and due to the greater use of invasive devices, broad-spectrum antibacterial agents, more extensive surgical procedures and use of advance life support on various transplant patients.[26].

In the present study *C. tropicalis* (50%) was the predominant species isolated, followed by *C. albicans* (17.1%), *C. krusei* (17.1%) and *C. guilliermondii* (5.7%). Various other workers have also reported as *C tropicalis* to be the most common isolate.[16,17,20].

Multiple risk factors are associated with neonatal candidiasis including gestational age <32 weeks, central venous catheters, intubation or recent surgery, mechanical ventilation or prolong NICU stay, broad-spectrum antibiotics and colonisation.[27,28]

In the present study prolonged IV antibiotics and low birth weight were the most important predisposing factor associated with candidemia followed by other factors like, prolonged central venous line, prematurity etc. Similar findings have been reported by other authors [16-20].

Antifungal susceptibility in our study revealed that the Candida isolates were 70% sensitive to fluconazole. A significant proportion of *C. tropicalis* isolates (37.25%) in our study were resistant to azoles especially fluconazole. Although resistance to Amphotericin B was quite low (5.8%), but is a matter of concern as emergence of such isolates may pose serious therapeutic challenges and also increases risk of nosocomial infection. Non albicans *Candida* species, especially *C. tropicalis*, *C. krusei*, *C. glabrata* and *C. parapsilosis*, tend to be less-susceptible to azoles, particularly

fluconazole, than *C. albicans*. *C. krusei* is innately resistant to fluconazole.[29-31]

5. Conclusion

The present study emphasizes the clinical importance and mycological shift in neonatal candidemia with predominance of non *albicans Candida* species in a Sub Himalayan Province in Northern India. The changing epidemiology of candidaemia requires close monitoring of the species distribution of Candida isolates by performing antifungal susceptibility tests. Epidemiological data of our study can serve as a template for the development of local guidelines for prevention and appropriate treatment of neonatal candidemia. Additional studies may be necessary to validate our findings and define more accurately the reservoirs, mode of transmission, emergence of new species, and their sensitivity patterns.

Declarations

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Conflict of interest: None

Ethical approval: Was obtained from the institutional Ethical Committee

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