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Original Research Article

Candidemia in neonatal intensive care unit: a cause of concern

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ABSTRACT

Background: Candidemia in neonates is a serious and common cause of late onset sepsis. Candida species are the third most frequent organism isolated in late onset sepsis in very low birth weight (VLBW) infants (i.e., <1,500 g).
Methods: This study was performed to evaluate epidemiology, species distribution, antifungal susceptibility and outcome of candida blood stream infections at a tertiary care centre.
Results: About 1-2 ml of blood was collected aseptically in suspected cases of septicaemia and inoculated in 20 ml of Brain Heart Infusion(BHI) broth. Candida species isolates were confirmed by germ tube production, chlamydospore formation on corn meal agar(HiMedia), pigmentation on Hichrome Candida differential agar (Himedia), and carbohydrate assimilation tests. Non-albicans candida spp. are of special concern, due to their high virulence and low azole susceptibility characteristics, augmenting the high mortality rates.
Conclusions: The emergence on non-albicans Candida merits attention as they display higher degree of resistance to azoles and are associated with higher mortality rates. Additional studies are required to define more accurately the prevalence and sensitivity pattern of Candida spp. which may serve as a template for development of preventive and therapeutic strategies for neonatal candidemia especially at peripheral health centres.

Keywords: Candidemia, Neonates, NICU, Non-albicans candidas

INTRODUCTION

Candidemia in neonates is a serious and common cause of late onset sepsis. *Candida* species are the third most frequent organism isolated in late onset sepsis in very low birth weight (VLBW) infants (i.e., <1,500 g). The incidence of such fungal infections has increased many fold over the past two decades.[1,2] Recently, an increase in incidence has been related to the complex medical and surgical procedures undertaken to improve the survival of critically ill neonates.

Candidemia remains associated with high crude and attributable mortality rates along with increased cost of care and duration of hospitalization. The increase of the attributable mortality of candidemia has driven research into the role of early diagnosis and prompt treatment initiation in order to improve outcomes.[3,4] Furthermore, intrinsic and emerging resistance to azoles represents a major challenge for empirical therapeutic and prophylactic strategies. This study was performed to evaluate epidemiology, species distribution, antifungal susceptibility and outcome of *candida* blood stream infections at a tertiary care center.

METHODS

This was a prospective study conducted in Microbiology Department at Bhagat Phool Singh Medical College for Women, Khanpur Kalan, Sonepat. About 1-2 ml of blood was collected aseptically in suspected cases of septicemia and inoculated in 20 ml of Brain Heart Infusion(BHI) broth. The blood culture bottles were incubated at 37ºC

and shaken periodically. Subcultures were made on 3rd, 5th and 7th day onto the Sabaraud's Dextrose agar slants.[5]

Candida species isolates were confirmed by germ tube production, chlamydospore formation on corn meal agar(HiMedia), pigmentation on Hichrome Candida differential agar (Himedia), and carbohydrate assimilation tests.[5.] Species were confirmed by HiCandida identification kit (HiMedia). This is a standard colorimetric identification system utilizing twelve conventional biochemical tests. Different species were differentiated on the basis of color change in the media. Antifungal susceptibility test was performed by using E-test strips(HiMedia) for amphotericin B and fluconazole as per CLSI recommendations.[6]

RESULTS

A total of 26 *Candida* isolates were obtained from blood samples from neonates, during a period of one year (January 2016 to December 2016). Non albicans candida accounted for 88.46% of the isolates. *C. tropicalis* (26.92%) was the predominant isolate (Figure 1).

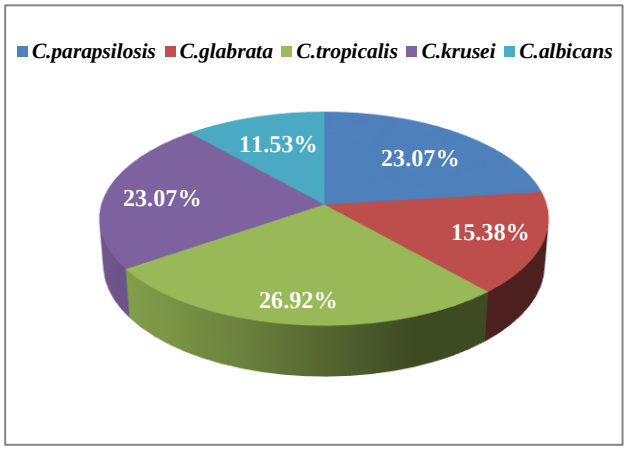

Figure 1: Distribution of candida species in NICU.

Prolonged antibiotic use, preterm and very low birth weight were the most common risk factors associated with candidemia Table 1. However, most of the isolates were sensitive to most of the antifungals Figure 2.

Table 1: Risk factors associated with candidemia in neonates.

Risk Factors	Number (%)
Very low birth weight	12 (46.15)
Thrombocytopenia	12 (46.15)
Preterm	14 (53.84)
Birth asphyxia	4 (15.38)
Ventilator	4 (15.38)
Prolonged antibiotics	24 (92.30)

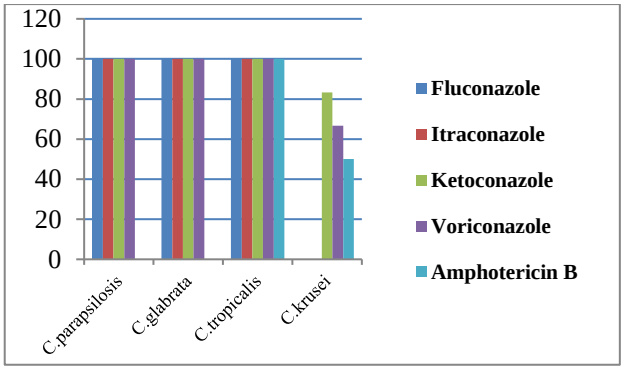

Figure 2: Antifungal susceptibility of candida isolates.

DISCUSSION

Candida species are an increasingly common cause of neonatal sepsis and are responsible for considerable morbidity and mortality.[3,4] Modern day neonatal care has definitely improved the survival rate of neonates but also increased the use of multiple invasive medical equipments, which has further enhanced the acquired sepsis among the newborns. Over the last two decades, non –albicans candida are accounting for a large burden of neonatal septicaemia.[7-9] Agarwal and co-authors reported that 76 out of the 90 isolates were NAC. We also observed 88.46% of the isolates belonged to non albicans group.[10]

C. tropicalis was the most common species isolated in 26.92% cases of candidemia in the present study. Narang and co-workers also found *C. tropicalis* (41.0%) as the major contributor of neonatal candidemia. The predominance of *C. tropicalis* as the main etiological agent has been demonstrated by Bansal and colleagues. [11,12] However, there are several other reports showing frequent isolation of other non albicans species like *C. glabrata*, *C. krusei* etc.[7-9,13] Non-albicans candida spp. are of special concern, due to their high virulence and low azole susceptibility characteristics, augmenting the high mortality rates. This rise is suggested to be a result of fluconazole prophylaxis given as a practice in many tertiary care centers.

Several studies have demonstrated the association of various risk factors with candidemia like low birth weight, preterm delivery, prolonged use of higher antibiotics like third generation cephalosporins and carbapenems, use of intravenous catheters, parenteral nutrition etc.[14,15] These increase the susceptibility to infections because of the immaturity of the immune system and invasive medical equipment needed for improvement of the survival rate of the neonates. VLBW, prematurity and prolonged use of carbapenems were the major risk factors implicated in the present study. Respiratory distress (14/26) and thrombocytopenia (12/26) were consistent clinical findings in our neonatal cases, similar to other studies.[2,4,16]

Bansal and co-workers observed a high degree of antifungal resistance, but on the contrary our study reveals lower rates of resistance to the antifungals tested except *C. krusei*, which is intrinsically resistant to fluconazole. Similar findings have been reported by Gudlaugsson et al.[3,12] The major limitation of our study was lack of colonisation surveillance of the neonates, which serves as a precursor for clinical infection and thus a risk for candidemia.

The emergence on non-albicans *Candida* merits attention as they display higher degree of resistance to azoles and are associated with higher mortality rates. Additional studies are required to define more accurately the prevalence and sensitivity pattern of *Candida* spp. which may serve as a template for development of preventive and therapeutic strategies for neonatal candidemia especially at peripheral health centers.

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