

## Increasing Trend of Non-Albicans Candida Species in Neonatal Septicemia

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### ABSTRACT

**Introduction:** Neonatal septicemia is a life threatening emergency and delays in diagnosis and treatment may have devastating consequences. With the advance in medical and surgical management Candida species has become the most common pathogen involved in neonatal septicemia. Recently Non-Albicans Candida has emerged as important opportunistic pathogens notably *C. tropicalis*, *C. glabrata*, *C. parapsilosis* etc.

**Objective:** This study was undertaken to know the emerging trend of NAC and importance of species identification of candida.

**Materials and Methods:** During the period of December 2015 to December 2016; blood sample from 141 clinically suspected cases of neonatal septicemia were collected aseptically from NICU at RIMS, Ranchi and were processed by automated BD BACTEC FX system. Only those which yielded pure growth of Candida sp. were included in the study. Identification of Candida sp. was done by using germ tube test, growth on corn meal agar, sugar fermentation test and sugar assimilation test.

**Results:** Out of 141 cases 43(30.5%) were found to be positive for candidemia. Out of 43 cases, *Candida albicans* were identified in 9 (20.9%) cases while remaining 34 (79.1%) were identified as NAC species. Among NAC species 26/43(60.5%) were *Candida tropicalis*, 5/43 (11.6%) were *Candida glabrata*, 3/43 (6.9%) were *Candida parapsilosis*. This study indicates *Candida* species as a common cause of

nosocomial bloodstream infection. This may be due to various risk factors like increased low birth weight deliveries (93%), prematurity (81.4%), wide use of broad spectrum antibiotics (67.4%), central venous catheters (51.2%), ventilator support (48.8%).

**Conclusion:** As there is increasing frequency of NAC species, species identification becomes important for early diagnosis and treatment of cases, thus reducing the mortality and morbidity.

**Keywords:** Candidemia, Non-Candida Albicans, *Candida Albicans*, Neonatal Septicemia, Low Birth Weight.

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### INTRODUCTION

Septicemia in neonates refers to generalized bacterial and fungal infection documented by positive blood culture in the first four weeks of life and is one of the leading cause of neonatal mortality and morbidity in India. Neonatal septicemia continues to be a major problem for neonates in neonatal intensive care units around the world. *Candida* sp. has become the fourth most common organism responsible for bloodstream infection in the intensive care unit (ICU).<sup>1</sup>

The advent of candida species as common human pathogens dates to the introduction of modern therapeutic approaches that suppress normal host defence mechanisms. Of these relatively recent advances, the most important is the use of antibacterial agents that alter the normal human microbial flora and allow non-bacterial species to become more prevalent in the commensal flora. The non - albicans candida species now account for

approximately half of all cases of candidemia and hematogenously disseminated candidiasis. Recognition of this change is clinically important, since the various species differ in susceptibility to the newer antifungal agents.<sup>2</sup> As per the initial reports, most cases of neonatal candidemia were caused by *Candida albicans*. However, recent studies from different regions of India have shown changing trends of neonatal candidemia, with emergence of non-albicans *Candida* (NAC) species as an important cause of neonatal septicemia.

Various risk factors for the development of candidemia in neonates include increased low birth weight deliveries, prematurity, use of broad spectrum antibiotics, presence of central venous catheters, ventilator support, etc. Primary site of infection can involve blood stream, meninges or urinary tract, but disease is frequently disseminated to multiple organ system.<sup>3,4</sup>

Clinical presentation of fungaemia resembles sepsis syndrome and to establish a clinical diagnosis is difficult. Respiratory insufficiency, feeding intolerance, abdominal distension, temperature instability, lethargy, and decreased perfusion are the various clinical manifestations associated.<sup>5</sup>

In laboratory findings other than blood culture, these neonates show decrease in leukocytes count, increase in level of ESR and CRP. Presence of band cells in blood in raised number also indicates toward neonatal septicaemia. The majority of preterm infants with fungal sepsis develop thrombocytopenia, but this is a common laboratory finding in patients with sepsis due to other organisms as well.<sup>6</sup>

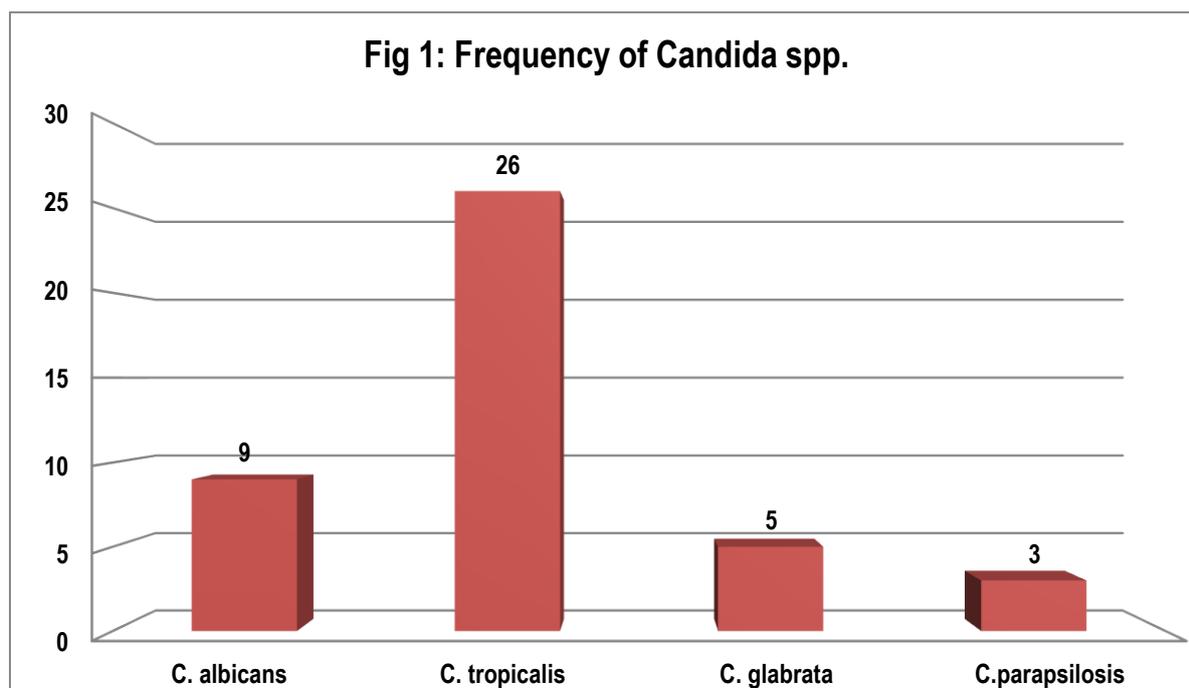
Thus the clinical presentation may be indistinguishable from bacterial septicaemia, thus making it difficult to diagnose, refractory to treatment which may lead to increase in morbidity and mortality. Therefore, the present study was undertaken to assess changing trends of candidemia in NICU and to assess risk factors for candida septicaemia.

**MATERIAL AND METHODS**

The prospective study period was from December 2015 to December 2016 and the study was conducted in the Department of Microbiology, RIMS, Ranchi. 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. Blood sample is taken from peripheral vein under aseptic conditions. The local site is cleansed with 70% alcohol and providine iodine (1%) followed by 70% alcohol again. Approximately, 1-2 ml of venous blood is collected and is inoculated into BD BACTEC pedia plus culture vial and processed by automated BD BACTEC FX system. If bactec shows positive result then subculture was done on sheep blood agar, mac conkey agar and SDA slant. *Candida* species identification was based on cultural characteristics, Gram stain and assessment by Germ tube test. Speciation of all isolates was done by plating on corn meal agar plate. Confirmation was done by sugar assimilation test and sugar fermentation test.

**Table 1: Showing frequency and species identification**

Fungal Isolates	Percentage	Germ Tube Test	Chlamydospore Formation	Carbohydrate Assimilation Test				Carbohydrate Fermentation Test			
				Glu	Suc	Mal	Lac	Glu	Suc	Mal	Lac
<b>C.tropicalis</b>	26 (60.5%)	Negative	Absent	+	+	+	-	AG	AG	AG	-
<b>C. albicans</b>	9 (20.9%)	Positive	Present	+	+	+	+	AG	-	AG	-
<b>C. glabrata</b>	5 (11.6%)	Negative	Absent	+	-	-	-	AG	-	-	-
<b>C. parapsilosis</b>	3 (6.9%)	Negative	Absent	+	+	+	-	AG	-	-	-



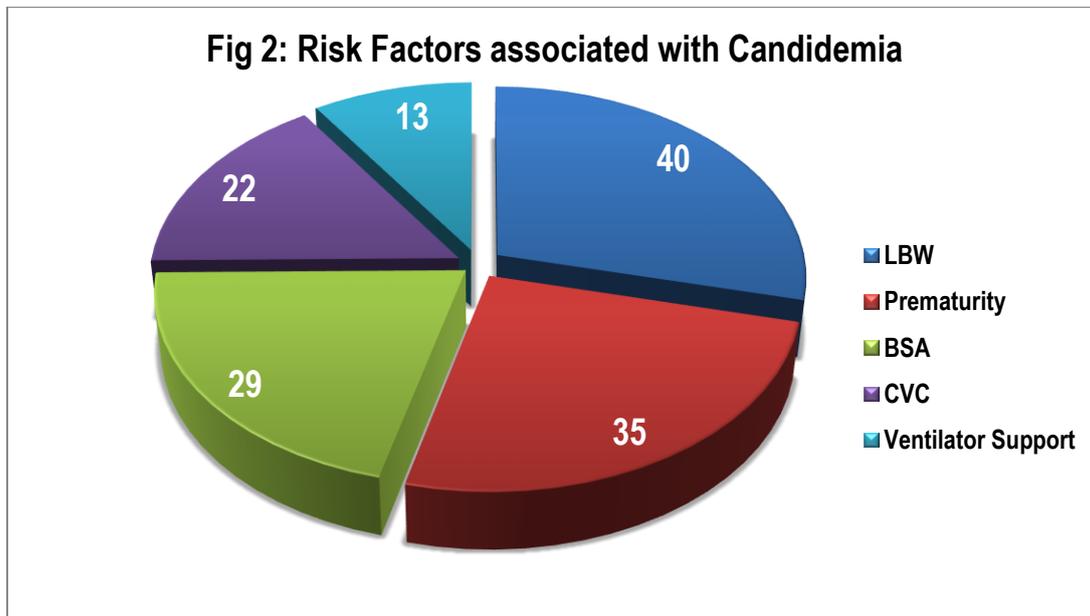
**RESULTS**

During the study period, a total of 141 samples were collected. Out of the 141 samples tested, 43 were found to be positive for candidemia.

Out of the 43, 9 (20.9%) were identified as *Candida albicans* while the remaining 34 (79.1%) were identified as NAC species. Among the NAC species, 26/43 (60.5%) were *Candida tropicalis*, 05/43

(11.6%) were *Candida glabrata* while 03/43 (6.9%) were *Candida parapsilosis*.

Among the various risk factors observed for candidemia increased low birth weight deliveries 40/43 (93%) was the commonest followed by, prematurity 35/43 (81.4%), wide use of broad spectrum antibiotics 29/43 (67.4%), central venous catheters 22/43 (51.2%) , ventilator support 21/43 (48.8%).



## DISCUSSION

In the present study, 43/141 [30.5%] neonates were diagnosed with bloodstream infections due to *Candida* species indicating a common cause of nosocomial bloodstream infection. In V. Sardana et al and R. Rani et al study 30.1% and 34.7% candida spp. were isolated from blood sample which correlates with our study.

In this study, non albicans *Candida* sp (79.1%) were more commonly isolated than *C. albicans*. These finding was also consistent with other studies done by A. Nazir et al (82.8%) and N. Goel et al (80.59%) where non albicans *Candida* species predominate.

In India, *C. tropicalis* is now the most common cause of nosocomial candidemia. Epidemiological studies have implicated *C. tropicalis* in as many as 67-90% of cases of candidemia.<sup>11</sup> The increased use of fluconazole has been determined to be the major cause of predominance of non-albicans *Candida*, especially *C. tropicalis* over *C. albicans*. The emergence of non-albicans species of *Candida*, mainly *C. tropicalis* has been reported from all over the country.<sup>12</sup> In the present study *C. tropicalis* was found to be the most prevalent species of *Candida* isolated from cases of candidemia (60.5%) followed by *C. albicans* (20.9%), *C. glabrata* (11.6%) and *C. parapsilosis* (6.9%). This finding correlates with the study done by N. Goel et al (61.19%) and V. Mishra et al (61.76%).

Though *Candida albicans* was the predominant species causing blood stream infections, during the last few decades, our results are comparable with the present day trends where increasing rates of NAC have been reported by various workers from different regions of India. In general the 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.

Among the various risk factors implicated in the acquisition of candidemia or invasive candidiasis in neonates, the most important factor is low birth weight (LBW) and prematurity. In a study by Lee *et al*, neonates with birth weights less than 1250 g

were found to be at a greater risk of getting candidemia or meningitis caused by *Candida*. Such neonates also had a higher chance of developing complications like intraventricular haemorrhage and greater mortality rate than control neonates.<sup>13</sup> In the present study also low birth weight (93%) and prematurity (81.4%) were the most important predisposing factor associated with candidemia followed by other factors like, wide use of broad spectrum antibiotics (67.4%) prolonged central venous line (51.2%) etc. Similar findings have been reported by other authors also like A. Nazir et al and V. Sardana et al.

## CONCLUSION

This study shows that Non-*Candida albicans* has emerged as an important cause of neonatal septicemia. Candidemia due NAC species has increased morbidity, mortality and complication. As there is increasing frequency of NAC species, species identification becomes important for early treatment and proper selection of appropriate antifungal drugs and to curtail the development of antifungal resistances.

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