

Trends in Neonatal Septicemia: Emergence of Non-albicans *Candida*

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In a prospective analysis, blood from 660 neonates admitted to Neonatal Intensive Care Unit (NICU) of a teaching hospital with clinical suspicion of septicemia was cultured to look for etiological agents with particular reference to role of *Candida* species. Blood culture specimens from two different sites at same time were obtained to rule out possibility of a *Candida* isolate being a mere contaminant. Due to technical difficulties, this was possible in only 338 neonates (Group I); from remaining 322 neonates only single specimen was available (Group II). *Candida* was isolated from total 90 neonates (isolation rate 13.6%) and it was the single most common isolate. Majority were non-albicans *Candida* (germ tube test negative - 76/90). In group I, *Candida* was isolated from 66 neonates, of these 49 grew *Candida* in both specimens (significant candidemia). 44 records were available for analysis. Low birth weight was found in 73.3%. Crude mortality was 52.6%. A peak in isolation rate of *Candida* was noted (isolation rate 27%, $p < 0.05$) in month of February. In Group I, 49 of the total 66 (74.2%) isolates of *Candida* were significant, suggesting that three in every four *Candida* isolated from blood can be significant. Non-albicans *Candida* are emerging as important pathogens for neonatal septicemia.

Key words: *Candida* species, Candidemia, Neonatal septicemia, Neonatal ICU

Over the last 2 decades, yeasts have become important nosocomial pathogen, *Candida* species being the most frequent isolate. This rise is largely attributed to extensive use of broad-spectrum antibiotics and advances in medical field, which contribute towards the large pool of susceptible population available for these opportunistic pathogens(1,2). Recently, non-albicans *Candida* have emerged as important opportunistic pathogen, notably *C. tropicalis*, *C. glabrata* and *C. parapsilosis*(3). This could be because of selection of lesser susceptible non-albicans species due to frequent use of fluconazole(4). Importance of *Candida* spp in nursery and intensive care setup is increasingly being recognized. *Candida* spp account for 9 to 13% of all blood stream isolates in neonatal intensive care unit

(NICU)(5,6). Common use of broad-spectrum antibiotics, low birth weight (LBW), prematurity and intravenous catheter etc. makes neonates prone to candidemia(2,7-12).

Here we are presenting our findings that were observed while investigating the causes of septicemia in a neonatal ICU.

Subjects and Methods

The study was conducted in Microbiology and Pediatrics department at KGMU, Lucknow, India. This is a tertiary care, 2500 bedded hospital. In a prospective analysis between August 2002 to April 2003; blood from 660 neonates (<28 days) admitted in NICU with clinical suspicion of septicemia was collected for culture. We were noticing an increase in the isolation rate of non-albicans *Candida* over last few months from cases of

neonatal septicemia. Since *Candida* can be part of skin flora of neonates admitted in hospital, its isolation from blood culture may reflect contamination from skin flora. To rule out this, we planned present study with the aim of collecting two blood culture specimens from each neonate enrolled. Due to technical difficulties of collecting blood from a sick neonate; two specimens each were received from only 338 neonates (Group I); 2 mL of venous blood was collected for culture under aseptic conditions simultaneously from two different sites. From remaining 322 neonates, only single specimen of blood was available for culture (Group II).

Blood specimen was inoculated into culture bottle with 20 mL of brain heart infusion broth and subcultures were made on 5% sheep blood agar and Sabouraud's dextrose agar after 24 hours and on 6th day(13). Significant candidemia was defined as growth of *Candida* in both samples from a patient to rule out the possibility of the isolate being a contaminant from skin flora. Germ tube test was put for all *Candida* isolates and they were reported as *C. albicans* or non-albicans *Candida*. Significant *Candida* recovered from fourteen cases of candidemia during the month of February were further identified using sugar fermentation and assimilation tests(14).

Results

Blood cultures from 660 cases with clinical suspicion of septicemia were processed. *Candida* was isolated from a total of 90 neonates (isolation rate 13.6%); Gram negative and Gram positive organisms from 158 and 129 neonates (isolation rate 23.9% and 19.5%) respectively. Infection rate due to *Candida* was calculated to be 77/1000 discharges in NICU.

Of 338 neonates in Group 1, 66 grew

Candida from their blood, 49 of these neonates grew *Candida* in both specimens *i.e.*, significant candidemia (14.5 %). In remaining 17 cases, *Candida* was isolated from only single specimen. From Group II *Candida* was isolated in 24/322 neonates. Majority of the isolates were non-albicans *Candida* (GTT negative, 76/90).

Of 49 neonates who had significant candidemia, records of 44 were available for analysis, one of these neonate had two episodes of candidemia, so a total of 43 cases were further analyzed. Mean age of neonate at the time of investigation was 3.4 days (ranging from just born to 19 days), male is to female ratio was 1:2. Average duration of stay in ICU was 9.6 days. Other associated findings were LBW 73.3% ($P < 0.05$), prematurity 38.6%, perinatal asphyxia 35.7%, respiratory distress 33.3%, jaundice 28.5% and meconium aspiration in 11.9% of neonates.

Crude mortality rate was 52.6% in culture proven significant candidemia group. Details of anti-fungal treatment were not available. On further analysis we noticed a peak in isolation rate of *Candida* in month of February, 14 of the 52 blood specimen received in this month grew *Candida* (isolation rate 27%) and it was found to be significantly higher than in any other month ($P < 0.05$). These 14 *Candida* isolates were further speciated, and 9 were found to be *C. tropicalis*, four *C. glabrata* and one isolate was *C. guilliermondii*.

Discussion

In the present study *Candida* was the commonest isolate from neonates clinically suspected to have septicemia. Majority (76/90) of the isolates were non-albicans *Candida*. Blood stream infection cases due to non-albicans *Candida* have been reported to range from 14-100%(1). In a retrospective analysis

Key Messages

- Non-albicans *Candida* are gaining importance as cause of neonatal septicemia.
- Upto three fourth of *Candida* species isolated from single blood culture specimen from neonates with clinically suspected septicemia, may be significant.

in an NICU, authors found >11 fold increase in rate of candidemia over a fifteen year period (2.5/1000 discharges in 1981 to 28.5/1000 discharges in 1995(15). A shift from *C.albicans* to non-albicans was noted by this group, *C. parapsisosis* being most prevalent isolate in latter years. Similar trend was also observed by an Indian group in their study done over a period of ten years(6). Previous study during year 2001 from our hospital showed candidemia to be present in 6% of neonates with suspected septicemia(17), *Candida* was not further identified. There is marked increase in rate of blood stream infection caused by *Candida*, over last two years at our center.

Various workers have reported *Candida* as cause for neonatal septicemia. Systemic candidiasis in 3.2% of admissions in NICU has been reported by one group(18), in their study mean age at the time of infection was 10.4 days, 95% had LBW and 94% of neonates were preterm. They found *Candida* attributed mortality to be 17%, *C. tropicalis*, *C. albicans* and *C. guilliermondii* were the commonest isolates. Systemic candidiasis was found in 0.57% of neonatal admissions in a prospective multicenter analysis, *C. albicans* being the commonest species and LBW the commonest associated factor(19).

An outbreak of candidemia during month of February (isolation rate 27%) was largely responsible for overall high infection rate due to *Candida* in this study (77/1000 discharges in NICU); apart from that one month the

isolation rate was between 8-16% in accordance with other published reports(5,6,10). High rate of fungemia (22.8%) in neonates has been reported by a group and they also noted that 71.4% of neonates were colonized with yeasts within 24 hours of admission and colonization was more in LBW babies(12).

Candidemia is generally associated with high mortality. In our study crude mortality rate of 52.6% was observed in neonates with significant candidemia. Reported attributable mortality ranges from 6-22%. Mortality rates as high as 60-80% have been reported in candidemia in adult patients(21).

Several risk factors have been cited as predisposing to candidemia in neonates including underlying illness, LBW, broad-spectrum antibiotic, asphyxia neonatorum, invasive interventions, hyperalimentation and TPN, etc. (2,7-12). In our study LBW was the commonest associated finding present in 73.3% neonates with candidemia.

The findings from Group I, in which 49 of the total 66 (74.2%) isolates of *Candida* were significant, suggests that three in every four *Candida* isolated from blood culture is a significant isolate. This is an important finding that emerges from this study, as *Candida* isolated from single blood culture is sometimes ignored as a mere skin contaminant.

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BRIEF REPORTS

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