



Candida krusei in neonatal septicemia an emerging entity: A prospective study in tertiary care hospital of Kashmir Valley

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ABSTRACT

Background

Fungal infections are the emerging threat to the neonates in the hospitals taking over to bacteria. Candida infections are major cause of morbidity and mortality in immunocompromised hosts such as neonates. Most neonatal fungal infections are due to Candida species. This study was done with objectives to identify the predominant organisms causing septicemia in neonates and their pattern in Kashmir Valley.

Methods

A prospective study was conducted in the Department of Microbiology GMC Srinagar in Neonates in the age group ranging from one day to four weeks admitted in the associated hospitals of the institution and suspected blood borne infections have been studied in the laboratory and blood culture samples were incubated in BacTAlert 3D (Biomerieux, India®) machine-driven blood culture system *test*

Results

1090 sample were collected from neonates admitted in the NICU. The isolation rate was 868 (79.6%) and among them positive cultures 570 (65.6%) were Candida Krusei. 101 (11.6%) candida albicans, 30 (3.4%) Acinetobacter baumani and other bacterial growth was seen in 167 (19.2%)

Conclusions

There is emerging trend of multi-drug-resistant organisms isolation from septicemic neonates. Nonalbicans Candida particularly Candida krusei has emerged as an important cause of neonatal septicemia. Routine susceptibility testing of Candida isolates by DD method should be confirmed by BMD-MIC method

Keywords: Neonates, Septicemia, Mortality, Candida krusei

INTRODUCTION

The term neonatal sepsis, means a clinical syndrome characterized by the blood stream infection of neonates and inflammatory response by the neonate, it usually presents as septicemia, pneumonia, meningitis, and rarely as arthritis, osteomyelitis, and urinary- tract infection.

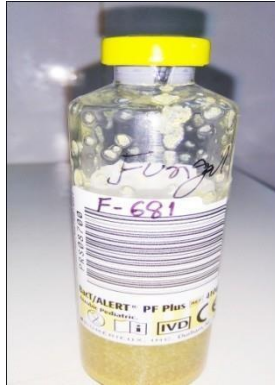
Superficial infections like oral thrush and pustules are generally termed as local infections [1]. Neonatal infections remain a major cause of morbidity and mortality in newborn infants [2]. Septicemia is a systemic illness caused by spread of microbes or their toxins via the blood stream [3]. Importance of Candida species in Neonatal Intensive Care Units (NICUs) is increasingly being

recognized. *Candida* species accounts for 9%–13% of all blood isolates in NICUs [4]. *C. albicans* is the most commonly isolated species and accounts for 50%–70% of cases of invasive candidiasis [5,6]. Neonatal sepsis is a major cause of mortality and neurodevelopmental impairment among neonates. It contributes to nearly 30 % of neonatal deaths in developing countries [7,8]. Inherent factors like immature innate immune system, poorly developed skin barrier, mucosal defense mechanisms and blood brain barrier contribute to the increased susceptibility of the neonates to infection. Although Group B Streptococcus, *E. coli*, and *Listeria monocytogenes* happen to be the most common organism, and in late-onset sepsis is mostly coagulase negative Staphylococci (CONS), *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella* species, and *Pseudomonas aeruginosa* usually acquired in the neonatal intensive care unit (NICU) but over the years the importance of *Candida* species in nursery and intensive care units (ICUs) is increasingly being recognized [9]. *Candida* species account for 9-13% of all blood isolates in neonatal intensive care units (NICUs) [10]. Although *C. albicans* has historically been the most frequently isolated species, infections caused by the non-*albicans* *Candida* have been diagnosed with increasing frequency in recent years. *Candida krusei* has been recognized as a potentially multidrug resistant fungal pathogen due to its intrinsic fluconazole resistance and reports of decreased susceptibility to both flucytosine and amphotericin B [11,12].

Over the last few years it was observed in the microbiology department of Government Medical college, that there has been increased isolation of Yeasts than the Bacteria from the blood samples of NICU. So, we decided to conduct a study with objectives to identify the predominant organisms causing septicemia in neonates and their pattern in Kashmir Valley.

MATERIALS AND METHODS

This prospective study was conducted in the Department of Microbiology GMC Srinagar. Neonates in the age group ranging from one day to four weeks admitted in the associated hospitals of the institution and suspected blood borne infections have been studied in the laboratory over the last 2 year from (March 2017 to Feb 2019). Under all sterile precautions, 1–2 ml of blood was drawn from these newborns. Blood culture samples were incubated in BacTAlert 3D (Biomérieux, India®) machine-driven blood culture system. One milliliter of blood was inoculated into ready to use BacT/ALERT PF and culture bottles (yellow color coded) for pediatric use with all due precautions and shaken well. The culture bottles were loaded into the instrument when scanning the barcode of the bottle and incubated. Positive or negative culture bottles were determined by BacT/ALERT microorganism Detection System. Blood cultures were considered negative solely when seven days of incubation. Positive samples were examined by microscopy of Gram-stained preparations and sub-cultured on agar plate, MacConkey agar plates, and Sabouraud dextrose agar slant with antibiotics however without cycloheximide (Hi-Media Pvt. Ltd., Mumbai India) in aerobic atmosphere. The preliminary identification was done by colony morphology on SDA, chromogenic media (HiChrome, Himedia, Pvt., Ltd.), growth at 45°C, germ tube test, and by carbohydrate fermentation and assimilation tests [13]. Identification of the organism was confirmed with automated Vitek 2 compact sixty system (BioMérieux India®) using Vitek 2 cards. The Vitek ID and AST cards were chosen per the results of the Gram staining and used according to the manufacturer's directions. The Vitek-2 ID and AST cards were logged and loaded into the Vitek-2 Compact system.



Bac T Alert Positive Blood



Positive Conventional Blood Bottle



Candida chrome agar with Candida krusei and other Candida

RESULTS

A sample size was calculated using WHO formula with following parameters, minimum prevalence of Candida isolates as 9%, margin of error 2.5 % at 80% power and 95% confidence interval. The sample size calculated was 504 and after accounting for isolation rate of only 50%, the total sample size was doubled to 1008. Ultimately 1090 sample were collected from neonates admitted in

the NICU. Among them, blood cultures were positive (isolation rate) for 868 (79.6%), 222 (20.4%) samples remained sterile after 7 days of incubation. Among positive cultures 570 (65.6%) were Candida Krusei. 101 (11.6%) candida albicans, 30 (3.4%) Acinetobacter baumani and other bacterial growth was seen in 167 (19.2%) with confidence interval calculated by Wilson's method as shown in Table 1:

Table 1: Distribution of Candida and Bacterial isolates

Isolates (N = 868)	Number (%)	Confidence interval
Candida krusei	570 (65.64%)	62.45%-68.75%
Candida albicans	101 (11.63%)	9.67%-13.94%
Acinetobacter baumani	30 (3.45%)	2.43%-4.89%
Other bacteria	167 (19.23%)	16.76%-22.06%

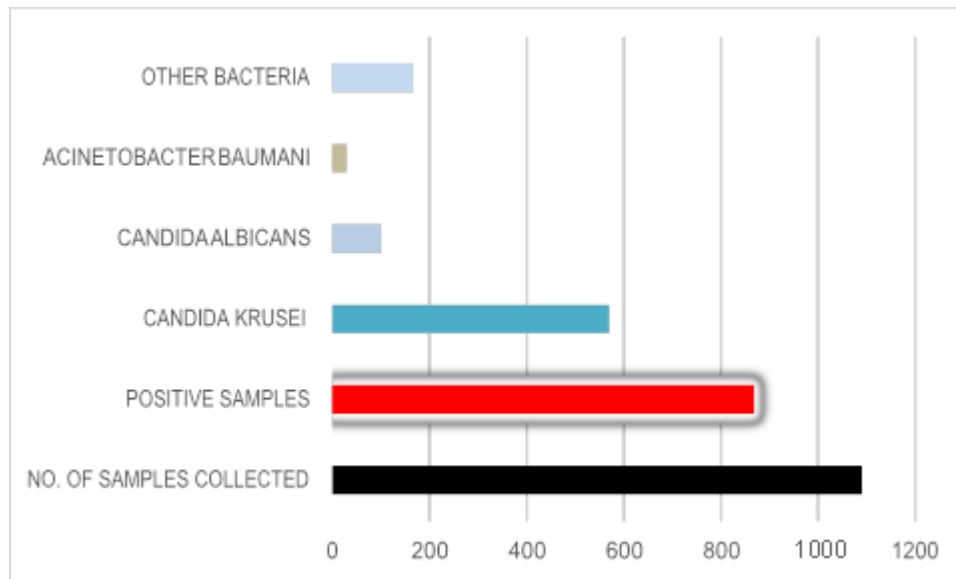


Figure 1: Clustered bar chart comparing values of samples collected and different isolates obtained

DISCUSSION

In this study a high isolation rate of 79.6 % was found which is in concurrence with some of the studies done in India. Nayak *et al* reported blood culture positivity rate in neonatal septicemia in 46.6% cases [14]. Similar results were also revealed by Roy *et al.*, and Kairavi. J. Desai *et al.* [15,16].

Candida krusei was the predominant isolate (65.6%) in current study which is supported by findings by the other researchers in same geographical which also documented predominance of nonalbicans *Candida* although over other *Candida* in neonatal septicaemia [17,18]. Selection of less susceptible species by the pressure of antifungal agent, indiscriminate use of invasive devices, broad-spectrum antibacterial agents and frequent use of advance life support on various patients seem to be the reason for the emergence of resistant Non-albican *Candida* in this cohort of patients [19]. Although many other risk factors are also responsible for emergence of candidemia in neonates including LBW, broad-spectrum antibiotic, hyperalimentation, and total parenteral

nutrition [20]. In current study, use of broad-spectrum antibiotic and low birth weight babies were the most common associated findings present among these neonates.

CONCLUSION

There has been emerging trend of multi-drug-resistant organisms isolation from septicemic neonates. So, great caution is required in irrational use of antibiotic therapy. Also, infection control in NICU, hand washing along with regular surveillance of neonatal sepsis is required to reduce the risk of change in antibiotic susceptibility patterns. Non-albicans *Candida* particularly *Candida krusei* has emerged as an important cause of neonatal septicemia. Routine susceptibility testing of *Candida* isolates by DD method should be confirmed by BMD-MIC method.

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Ethical approval: The study was approved by the ethical committee of Government Medical College Srinagar.

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