



Research Article

A STUDY OF CANDIDA SPECIES BLOODSTREAM INFECTIONS IN NEONATES IN A TERTIARY CARE HOSPITAL

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Abstract-Background: Fungemia due to *Candida* species is reported commonly and is an increasing problem especially in neonatal intensive care units (NICU). A significant increase in the number of cases of candidemia was observed from November 2015 to January 2016 in NICU of our tertiary care hospital in North Delhi. The species of *Candida* isolated from these cases were diverse and included *C. tropicalis*, *C. krusei* and *C. parapsilosis*. **Methods:** To investigate this increase in the cases of *Non albicans Candida* bloodstream infections, a microbiological study, a case control study and revision of infection control practices was performed. There were total of 8 cases of Candidemia at the time of investigation. The samples for surveillance culture were obtained from various environmental surfaces, from hands of health care workers (HCWs) and from skin and cannulas of the cases. **Results:** Some factors like Preterm deliveries, low birth weight (LBW), parenteral nutrition, presence of central venous catheters and premature rupture of membrane at the time of delivery, were more commonly seen in cases when compared to controls. The surveillance samples on microbiological culture did not yield any *Candida* isolate. Some lapses in infection control practices were observed and with the strict enforcement of infection control measures, the progress of this increase in the number of cases of Candidemia could be halted. **Conclusion:** it was therefore concluded that Candidemia was associated with previously described risk factors and that it is the interplay of host, environment and pathogen which contributed to increase in the number of cases of Candidemia in our hospital.

Keywords- *Candida albicans*, Non-albicans candida, Health Care Workers, Candidemia, Bloodstream Infection

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Introduction

Candida species have emerged as one of the most common cause of nosocomial blood stream infections among neonates in many areas of the world [1,2]. They contribute for 9-13 % of such infections with most surveillance studies reporting a rising trend [3]. Despite the intensive antifungal therapy these infections are responsible for significant morbidity and mortality [4,5]. Although the most common isolated species from such neonatal Candidemia infections is *C. albicans*, however longitudinal studies have shown a shift towards *non-albicans Candida* (NAC) species notably *C. tropicalis*, *C. parapsilosis*, *C. krusei*, and *C. glabrata* [6,7]. The mortality associated with *Candida* species bloodstream infections is consistently high, with estimated figures between 40-50% [1,5,8]. The various risk factors associated with these invasive candida infections include: use of indwelling vascular devices, broad spectrum antibiotics, low birth weight (LBW), prematurity, total Parenteral Nutrition (TPN), gastrointestinal surgery, artificial ventilation and/or history of fungal colonization, cytotoxic chemotherapy and transplantation [6,8,9].

Various earlier studies have associated contaminated milk bottles, parenteral nutrition, glycerine, suppositories, contaminated IV medications, syringes reutilization, HCW hand colonization and contaminated indwelling vascular catheter as the common source of infection responsible for outbreaks of Candidemia in hospitals [1,10-13]. Even in those Candidemia outbreaks where common source of infection could not be found, optimization of infection control practices controlled the outbreaks [11,14].

There was significant increase in the cases of *Candida* bloodstream infection in neonates in NICU from November 2015 to January 2016, in Hindu Rao Hospital, a tertiary care centre at North Delhi, India. All the isolates were recovered in

BactecPeds plus/F culture vials of an automated blood culture system (Bactec 9120, Becton Dickinson, USA). Any growth detected was sub-cultured on 5% sheep blood agar, MacConkey Agar, and Sabourauds Dextrose Agar and incubated at 37°C. The genus level identification was done phenotypically as per the standard mycological techniques [15]. The species level identification of these *Candida* isolates was done by Vitek 2CSystem.

The clustering of *Non albicans Candida* BSI in neonates in NICU of our hospital prompted us to evaluate and to determine the factors contributing to *Candida* spp. BSI so that infection control measures can be optimized to halt this increase in the number of cases of Candidemia.

Materials and Methods

We first performed the preliminary investigation and then a definitive investigation to determine the factors contributing to increase in cases of neonatal Candidemia. The preliminary investigations included establishing a case definition, performing ascertainment, describing clinical characteristics of cases, and review of literature. Cases were defined as the new-borns whom blood culture was positive for *Candida* species and had clinical signs and symptoms of septicaemia, during the course of NICU stay at Hindu Rao Hospital. Case ascertainment was performed by reviewing microbiology laboratory and medical records.

After these preliminary investigations, Definitive investigations were undertaken. These included a case control study, revision of infection control practices in the NICU and a microbiological investigation. Total of 8 cases of neonatal Candidemia were present at the time of investigation. The controls were defined as the new-borns who had clinical signs and symptoms of septicaemia and whom blood culture was positive for organisms other than *Candida* species, during the course

of NICU stay at Hindu Rao Hospital. These controls were randomly selected from inpatients of NICU during the outbreak period. One control patient was included for each case patient. The case and control patients were matched for age, length of hospitalization prior to a positive culture with the case patient.

The demographic and clinical data of cases and controls was taken from medical records using a standardized form. The data collected included age, gender, gestation age at delivery, Birth weight, type of delivery, any significant obstetrical history, date of admission, procedure done, use of CVCs, medications, infusion history, history of mechanical ventilation, history of catheterization, any other nosocomial infection, duration of stay in the hospital, other samples collected and their culture report.

The hospital epidemiology team carried out the revision of behaviour of HCWs and infection control practices through interview of staff of the NICU and observations were made related to common infection control practices.

The microbiological investigations comprised of culture of Health Care workers hands, environmental samples included swabs from Procedure trolley, Gauze piece drums, Chittle forceps, Weighing machine, Bed surfaces, Stethoscope, O₂ Humidifier, SPO₂ probe, Cidex solution, Oxygen hood, Crash cart, Laryngoscope blade, suction jar, syringe pump, hand rub bottle, switch board, Nursing counter, Hand washing soap, Normal saline, lignocaine, Gel 2%, latex gloves. The samples taken from the cases included their iv cannula tips, cannula hub, skin swabs from axilla and iv catheter insertion site. All the samples were collected in Thioglycolate Broth and subcultured after 18 hours on Sheep Blood Agar and Sarbours Dextrose Agar. Further identification of the culture grown was done by standard identification methods [16].

Results

At the time of investigation there were 8 cases of Candidemia. Diverse *Non albicans Candida* species were isolated from the blood cultures of these cases. The isolated species included *C.krusei* (3), *C.tropicalis*(3) and *C. parapsilosis* (2).

The main presenting symptoms of all the cases were respiratory distress associated with diminished spontaneous activity, feeding intolerance and failure to thrive. Disseminated Intravascular Coagulation was seen in 2 out of 8 cases as complication.

All the cases had a history of empiric antibiotic therapy, Central venous catheterization (CVC) and Total Parenteral Nutrition (TPN). Only two babies were on mechanical ventilation. The birth weight of the cases ranged from 820 to 1850 g and the gestational age from 32 to 36 weeks.

The risk factors associated with Candida species BSI in the study included: Preterm deliveries, low birth weight, parenteral nutrition, presence of central venous catheters, and premature rupture of membranes, as these factors were more commonly seen in cases than controls [Table 1]. No associations were observed between Candida species BSI and exposure to a particular Health Care Worker (HCW), IV medications or invasive procedures or mechanical ventilation.

During the inspection of infection control practices by the hospital epidemiology team in NICU, few breaches in the infection control practices were identified: poor hand hygiene practices, no dedicated room for preparation of iv solutions, cleaning of working areas was not properly done, there were only few hand rubs by the sides of beds, suction bottles were filled with turbid solutions and were dirty, general housekeeping was not up to the mark.

Laboratory Studies

We cultured the swab specimen from the hands of all the HCWs. However none of the sample yielded Candida species rather Methicillin Resistant *Staphylococcus aureus*, and *Enterococcus species* were isolated from the hand swabs. None of the environmental samples yielded Candida isolate.

The samples from the skin of the cases also did not yield any Candida species. The peripheral IV catheter tip and hub samples culture from the case patients also did not yield any Candida isolate.

Discussion

This report describes the emergence of *Non albicans Candida* (NAC) species as the cause of Candidemia in NICU of our hospital. Although *C. albicans* is the most

frequently isolated Candida species in several centres, however the role of NAC species is increasing in causing outbreaks. Various previous reports have explained the outbreak caused by NAC species in the NICU settings, mainly caused by *C. parapsilosis* and *C. tropicalis* [11-13].

All the 8 neonatal Cases in our study had Central Venous catheter inserted, were on broad spectrum antibiotics and had received TPN. 6 cases in addition were premature and had LBW. 5 cases had history of mother with leaking per vagina. All these factors have been described as the major risk factors associated with Candidemia. Any break in the integrity of skin/mucosa caused by use of multiple invasive devices such as catheters, endotracheal tubes and surgery predispose these sites for colonization and infection by Candida species. In our study all the cases were on broad spectrum antibiotics. Prolonged use of antibiotics suppresses the normal flora and promotes the fungal growth and encourages the translocation of yeast across the intact mucosa. Also TPN has been known to be a risk factor for Candida spp. infection as it induces gut mucosal atrophy and has immunosuppression effects. Also it is known that LBW and critically ill neonates are at highest risk of invasive Candida infections [3, 8]. Previous studies have reported the risk of systemic fungal infections in premature neonates weighing less than 1000 gm to be as high as 67% with mortality rate around 40% [3,8].

Bloodstream infections associated with Candida species usually originates from the endogenous sources [2,16], however various studies have described the relevance of Candida species also as a nosocomial pathogen [4]. Candida species can be transmitted to patients from hospital environmental sources and from hands of the health care workers. All the risk factors which have been described above, puts the neonates with more frequent contact with healthcare worker, magnifying the impact of lapses in appropriate hand hygiene which can facilitate cross transmission of yeast from transiently colonized HCW hand to patients. Several previous studies have linked the hands of HCW with Candida BSI outbreaks [17- 22].

The cause of the increase in the number of cases of Candidemia is known to be multifactorial, resulting from interplay of host, environment and pathogen as contributors. Various environmental sources may play a vital role in transmission of the infection. In a resource limited settings usually the environmental surfaces are more likely to be problematic. Various earlier studies have shown many environmental factors contributing to Candidemia outbreak [8]. The report of Deepak Juyal [8] implicated the use of handmade alcohol swabs as the cause of Candidemia outbreak in their hospital. Grandoz *et al* [1] have implicated the cause of outbreak in their hospital as the use of non-sterile cotton swabs, plastic transportation bags and plastic IV medication containers, which facilitated the emergence of Candida species as the nosocomial bloodstream pathogen.

Table-1 Clinical and demographic characteristics for cases and controls

Variable	Cases n=8 (%)	Controls n=8 (%)
Low Birth weight	6(75)	2(25)
Preterm	7(87.5)	1(12.5)
CVC in place	8(100)	1(12.5)
TPN	8(100)	1(12.5)
Premature rupture of membrane	6(75)	1(12.5)

The different Candida species can adhere to different environmental surfaces and this property of the yeast plays an important and major also in the pathogenesis of human colonization and invasion as well as in the establishment and perpetuation of infection [23, 24]. Also it is seen that different Candida species can adhere to similar environmental reservoirs and contaminate them thereby causing human infection through similar pathophysiological processes [1]. In our study, we undertook the epidemiological study to trace the source, which could have lead to increase in the number of Candidemia cases; however, no source could be identified. After observation of Infection control policies, Infection control measures were intensified. These included improvement in personnel and visitors hand hygiene, specific and timely antibiotic therapy, antibiotics were given as single dose prescription, correct preparation and use of various solutions, alcoholic solution dispensers were installed in every patient bed side, a dedicated tray was set up for use of daily medical and hygiene instruments (stethoscope, thermometer, gauze, ointments), reprocessing of multi-use semi critical medical

devices was done in correct manner, a clean area was set up and was dedicated to aseptic preparation. The strict enforcement of these infection control measures was able to halt the progress of this increase in the number of Candidemia cases. This signifies that it is the interplay of host, environment and pathogen, which contributed to this increase in the number of cases of Candidemia in our hospital.

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