

Invasive candidiasis outbreak in a neonatal intensive care unit (NICU), a descriptive study from tertiary care teaching hospital of western part of Maharashtra

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Abstract

Background: Candidemia outbreaks are frequent event take place in NICU accounting about 9-13%. Especially non-albicans *Candida* species emerged as an important cause of various outbreaks in NICU. There are various predisposing factors which may be a culprit for an outbreak. Early on detection and source of infection is helpful in effective management of candidemia outbreak. **Material and methods:** There was remarkable increase in number of candida isolates from blood cultures in Microbiology laboratory. Different laboratory procedures were performed to identify these isolates till species level and also antifungal susceptibility test was done further. Environmental samples were collected from NICU to trace the cause of outbreak. **Results:** Candidemia incidence in current outbreak was 7.71%. The most common species involved was *C.glabrata* in 43(81.13%) followed by *C.tropicalis* 10(18.87%). Among environmental samples these isolates were isolated from in use Total Parenteral Nutrition (TPN) and Dextrose solution used in NICU. **Conclusion:** NICU is always vulnerable unit where standard safety precautions should be at utmost level. Any minor breach in practices can lead to major events. Therefore, if needed surveillance should be done to evaluate source of infection before time and also for effective management of such events.

Key Word: Candidemia, NICU, outbreak

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INTRODUCTION

Blood stream infections (BSIs) are the major problem in Intensive Care Units of the hospital especially Neonatal Intensive Care Unit (NICU). Though bacteria are traditionally the common cause of BSIs, fungal infections are increasing their occurrence in the event. It accounts

for about 9-13% of BSI in neonates. They have been found to be the cause for various outbreaks that occurred in NICU.^{1,2,3,4} Invasive Candidiasis in neonates is a severe and frequent cause of late onset sepsis. Among fungal BSIs *Candida* species, especially non-albicans species is the major cause of infections. Non-albicans *Candida* species emerged as an important cause of Candidiasis includes *C. parapsilosis*, *C. tropicalis*, *C. krusei* and *C. glabrata*. This rise of non-albicans *Candida* species is a concern in the management of Candidiasis event as few species are predominately resistant to anti-fungal drugs such as *C.krusei* being intrinsically resistant to Fluconazole.^{1,3,5,6} In addition, Various predisposing factors are accountable for occurrence of Candidiasis outburst in neonates such as preterm babies or prematurity, low birth weight (LBW), intramedical devices, broad spectrum antibiotics, total parenteral nutrition (TPN), mechanical ventilation, prolonged

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hospitalization, history of surgical procedure and intestinal colonization. It is important to identify risk factors which are likely to influence health outcomes in these patients.^{2,3,5,7,8} Early and prompt diagnosis of such cases can help in effective management of outbreak. Here we report an invasive Candidiasis outbreak in NICU from tertiary care teaching hospital.

MATERIAL AND METHODS

In Microbiology laboratory we observed dramatic increase in isolation of *Candida* strains during Nov-2016 and December-2016, from blood culture of NICU patients compared to the previous laboratory data. Different laboratory procedures were performed (detail procedure given below) to identify the pathogen to the species level and their antifungal susceptibility pattern for epidemiological purpose as well as for effective management. An outbreak was suspected, so we started working on parameters to control the outbreak. We conducted a survey in NICU. Different environmental samples were taken to know the exact source of an outbreak.

Sample collection: Blood cultures were collected from suspected clinical sepsis cases by venipuncture for using all aseptic precautions and transported to laboratory for further processing.

Microbiological processing: Blood cultures were incubated at 37°C in the laboratory. Subcultures were made on 3rd, 5th and 7th day onto the routine media such as Blood agar, MacConkey Agar and Sabaraud's Dextrose agar (SDA) with chloramphenicol and incubated at 37°C. *Candida* isolates were identified by standard methods including colony morphology on SDA, chromogenic media (Hichrome, Himedia Pvt. Ltd.), germ tube formation, chlamyospore formation on corn meal agar (HiMedia).^{9,10,11} Antifungal susceptibility testing was performed for fluconazole (25 mg), itraconazole (ITR, 10 mg), voriconazole (VRC 1 mg), ketoconazole (KTC, 10 mg) and amphotericin B (AMB, 100 units) using standard disc diffusion method on Muller-Hinton agar supplemented with 2% dextrose and methylene blue (5 mg/ml) according to CLSI guidelines and Zone diameters were interpreted as per standard guidelines.¹²

Environmental surveillance: Swabs from potential environmental reservoirs such as nearby surfaces and equipments which included Health Care worker's (HCW's) hands, beds, incubators, ventilators and ventilator tubings, ante-cubital fossa and intravenous medication vials were screened. Simultaneously intravenous fluid administration set and intravenous solutions were collected and processed further. Intravenous solutions collected were Dextrose and Total Parenteral Nutrition (TPN) fluids. In the laboratory,

different environmental samples collected were inoculated on Sheep blood agar and Sabouraud dextrose agar. Further identification and speciation of fungal isolates was done as per standard microbiological techniques. After analysing results outbreak situation was confirmed. Hospital infection control guidelines were provided to the NICU. The concerned staff was trained regarding universal safety precautions to be taken before performing any procedures in babies. At the end of Jan-2017 isolation rate decreased. But again few cases were identified during month of February to June 2017. So again in July-2017 we assessed possible risk factors and tried to re-investigate an outbreak. This time while taking environmental samples we also included inuse total parenteral nutrition (multi-electrolyte fluids) and dextrose solution started to the babies. These samples were included to know the source of colonization as they are extremely good source of nutrients for growth of *Candida*. Data from this investigation were analyzed to formulate outbreak control measures.^{7,8,13,14}

RESULTS

Following earlier cluster of Candidemia cases in NICU, there were constantly new cases found during outbreak. Overall 53 episodes of Candidemia were reported from NICU during November 2016 to July 2017. A total of 687 blood cultures were sent from NICU from clinical septicemia cases during this period, overall incidence of Candidemia found to be 7.71%. (Table 1) The most common species isolated was *C.glabrata* in 43(81.13%) followed by *C.tropicalis* 10(18.87%). We analysed susceptibility testing against antifungals also, results are given as in below Table 3. Environmental samples were collected to find out source of an outbreak. Different samples collected and results has been tabulated in Table 4.

Table 1: overall blood culture results

Blood culture results (n=687)	Isolation rate
Bacterial growth	357(50.94%)
Candida growth	53(7.71%)
No Growth	277(40.32%)

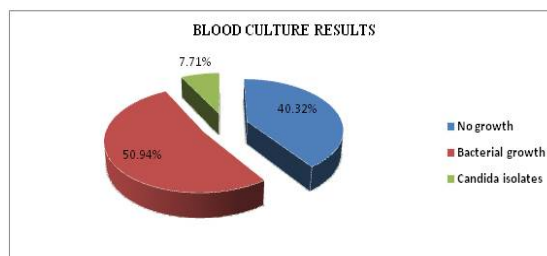


Table 2: Distribution of Various Candida Species

Candida species isolated (n=53)	Total no. of cases
<i>Candida glabrata</i>	43(81.13%)
<i>Candida tropicalis</i>	10(18.87%)

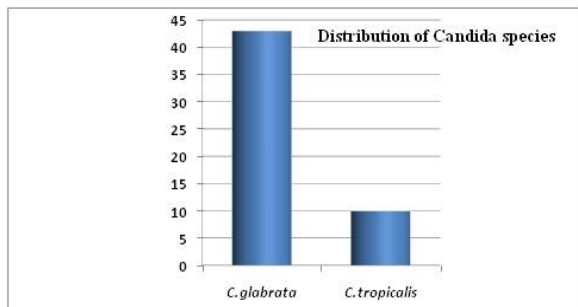


Table 3: Anti-Fungal Susceptibility Pattern Of Isolates

Species	Fluconazole	Amphotericin B	Voriconazole	Itraconazole	Ketoconazole
<i>C. glabrata</i>	30(69.77%)	43(100%)	43(100%)	43(100%)	43(100%)
<i>C. tropicalis</i>	7(70%)	10(100%)	10(100%)	10(100%)	10(100%)

Table 4: Environmental Sampling Results

Samples collected	Growth observed
Bed swabs	No growth
Medication vials	No growth
Endotracheal tube	No growth
Suction catheter	No growth
Antecubital fossa	No growth
Total parenteral nutrition	Candida grown(<i>C. glabrata</i>)
Dextrose solution	Candida grown (<i>C. tropicalis</i>)
Hand prints of Health staff	No growth

DISCUSSION

Outbreaks of invasive candidiasis in hospitalized patients have been reported in various hospitals. Among such outbreaks *Candida* especially non-*albicans* *Candida* species were found to be the culprit. Different possible factors associated with outbreaks were increased use of intramedical devices, colonization of animate and inanimate objects, cross-infection via the hands of health care workers or total parenteral nutrition solutions that may be contaminated during preparation or intravenous administration.⁸ Candidemia event had been very common in NICU due to babies' susceptibility to trivial infections. This may be due to various predisposing factors such as low birth weight, preterm birth, broad spectrum antibiotics, prolonged hospital stay, various intramedical procedures which makes them vulnerable. These various factors prone neonatal babies to septicemia or blood stream infections. Overall prevalence rate of Candidemia in NICU varies from 9- 13%.^{1,2,3,4} In our study, we found prevalence of Candidemia 7.71% which

is correlating with other studies. Few studies have reported greater incidence upto 18% such as by Kothari *et al.*¹⁵ This may be due to non-adherence to aseptic precautions to be followed before various procedures. In reported previous outbreaks, non-*albicans* *Candida* species were commonly isolated as a cause in the event. In our institute, we had also observed non-*albicans* *Candida* species as a common offender. Trend of *Candida* species predominance may vary according to geographical distribution, as in western countries like USA and other countries *C. albicans*, *C. parapsilosis*^{4,5,8,16} were commonly involved while in Asian countries like India change of trend had been observed. In these countries, recently there has been increased predominance of *C. glabrata* and *C. tropicalis* in outbreak in NICU.^{3,5,8} In the present study most common species isolated was *C. glabrata*(81.13%) followed by *C. tropicalis*(18.87%). Our findings are correlating with various studies such as Trick *et al*¹⁷, Kapila *et al*¹⁸ and Sardana *et al*¹⁹. Though few isolated outbreaks had different findings such as Banerji *et al*¹¹, Basu *et al*⁽²⁰⁾ and Narain *et al*²¹ have reported *C. albicans* predominance, while Juyal *et al*³, observed predominance of *C. parapsilosis* in the event. In few studies *C. tropicalis* and other species had been isolated as a causative agent.^{1,22} Due to clustering of cases we did environmental surveillance in NICU to detect the source of event. Various samples were collected as shown in Table 4. We did not find any *Candida* isolation in any samples except multi-electrolyte fluid i.e. total parenteral nutrition which had isolated *C. glabrata* and dextrose solution which grew *C. tropicalis* with similar susceptibility pattern. It was hypothesized that these solutions may have been contaminated during pre-infusion set preparation or dilution.^{8,16} So we advised NICU staff to follow strict aseptic precautions during IV set preparation and strict adherence to hand hygiene practice before and after administration of fluid. At the same time, NICU staff were trained regarding intravenous line care also. After few weeks of following standard safety precautions, we observed significant decrease in incidence of Candidemia cases from NICU and outbreak was curtailed.

CONCLUSION

As neonates are vulnerable to various opportunistic infections including fungal as well as bacterial infections, highest attention must be paid to NICU standard precautions. One should always look for any alarming sign of outbreak and need of necessary surveillance protocol to be followed so as to reduce the event. Breach in safety precautions leads to the spread of infection, so strict adherence to standard work precautions most of the times helps in preventing outbreak in NICU.

Nevertheless, our study emphasizes the importance of passive surveillance by laboratory findings in timely detection of outbreaks.

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