A Study of Neonatal Sepsis due to Candida Species

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Abstract

This study was intended to find out the changing trends of fungaemia in cases of neonatal sepsis. Blood culture from 442 neonates admitted in neonatal intensive care unit (NICU) were collected in Brain Heart Infusion Broth (BHIB) and sub cultured on Sabouraud's dextrose agar. Only Candida spp. were encountered. Speciation of Candida was done by Germ tube test, growth on corn meal agar and sugar assimilation tests. Candidaemia was observed in 66 patients (14.9%). Candida albicans was predominant isolate (66.3%), followed by Candida glabrata (19.69%), Candida parapsilosis (10.66%) and Candida tropicalis (6.06%). Important predisposing factors were long term antibiotic therapy, low birth weight, pre-maturity, respiratory distress syndrome and neonates on ventilators. Candida albicans is still the commonest cause of neonatal septicaemia and Candida glabrata is an emerging pathogen. Early diagnosis, treatment and surveillance of hospital infections reduce morbidity and mortality.

Introduction

Fungaemia due to Candida spp is reported commonly and is an increasing problem especially in neonatal intensive care unit (NICU).[1,2] Though Candida albicans is the most common species isolated, there is increase in prevalence of non-albicans Candida septicaemia.[1-3] Multiple risk factors have been identified, e.g. prior antibiotic therapy, presence of central line catheters, endotracheal intubations, pre-maturity, respiratory distress syndrome and prior fungal colonization.[1-4] Isolation rate of Candida spp in NICU varies from 3.2% to 13.6% in Indian studies.[1-5] Primary site of infection can involve blood stream, meninges or urinary tract, but disease is frequently disseminated to multiple organ system.[6] The clinical presentation may be indistinguishable from bacterial septicaemia,[3,4] thus making it difficult to diagnose, refractory to treatment which may lead to increase in morbidity and mortality.[1-6] Therefore, the present study was undertaken to assess changing trends of fungaemia caused by Candida spp in neonatal intensive care unit (NICU) and to assess risk factors for Candida septicaemia.

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Material and Methods

A total of 442 clinically suspected cases of neonatal septicaemia in NICU were studied from March 2005 to February 2007. 1-3 ml of blood was collected from peripheral vein under aseptic precautions and inoculated in blood culture bottles containing 10-20 ml of Brain Heart Infusion Broth (BHIB). The bottles were incubated at 37^0 C and on 3rd, 5th and 7th day subcultures were done on Sabouraud's dextrose agar slants. Speciation of Candida was done by Germ tube test, growth on corn meal agar and sugar assimilation tests. The clinical details of all these patients were taken.

Results

From total number of 442 cases, *Candida spp.* were isolated in 66 cases (14.9%) (Table1).

On further analysis, it was noted that in first year of study i.e. from march 2005 to February 2006, out of 286 cases *Candida spp.* were isolated in 9.1% cases (26/286) while in the second year of study isolation rate was significantly increased to 25% (40/157).

Major outbreak was observed in December 2005, out of 37 suspected cases, 8 were Candida albicans. Another major outbreak was noted in October 2006, out of 15 suspected cases, 10 *Candida species* were isolated, consisting of 3 *Candida albicans*, 4 *Candida glabrata*, 2 *Candida parapsilosis* and 1 *Candida tropicalis*.

Persistent pneumonia (45.45%), failure to thrive (100%), lethargy (100%), tachycardia (100%) were common clinical manifestations. One patient had abdominal distension.

Underlying predisposing factors were antibiotic therapy 100% (66/66), low birth weight 66.66% (44/66), respiratory distress syndrome 45.45% (30/66) and mechanical ventilation 45.45% (30/66).

Discussion

In the present study isolation rate observed was 14.9%. This rate was comparable with Indian study conducted by Agarwal *et al*[1] showing isolation rate of 13.6% and another study conducted by Rani *et al*[3], where isolation rate was 11%. In this study there was significant increase in rate of candidaemia in the second year of study (9.1% to 25%). Similar findings were noted in study by Agarwal *et al*[1] and also Kossoff, Erric H *et al*[8]. Analysis of latter showed that there was >11 fold increase in the rate of candidaemia in 15 years from 1981 to 1995.

Table 1 : Species wise distribution of the isolates (n=66) and percentage

Species	No. of isolates	% of isolates
Candida albicans	42	66.63
Candida glabrata	13	19.69
Candida parapsilosis	7	10.66
Candida tropicalis	4	6.06

In the present study *Candida albicans* was the predominant pathogen (66%) followed by *Candida glabrata* (19.69%), Candida parapsilosis (10.66%) and *Candida tropicalis* (6.06%). The findings of *Candida albicans* as predominant pathogen in neonatal sepsis was noted earlier in the year 2003 from Mumbai[4] in which *Candida albicans* was isolated in 16 out of 30 isolates (53.3%).

However this finding was in contrast to the study conducted by Rani *et al*[3] where *Candida tropicalis* was predominant (92%) isolate followed by *Candida albicans* and *Candida kefyr* (4% each). Agarwal *et al*[1] showed marked increase in non-albicans isolate, showing *Candida parapsilosis* being most prevalent isolate. Kossoff *et al* showed shift from *Candida albicans* to non-albicans i. e. *Candida parapsilosis* over 15 years[8], Narang *et al*[5] showed *Candida tropicalis* commonest isolate followed by *Candida albicans* and *Candida guillermondii*. Another important trend noted in this study was that *Candida glabrata* is emerging as an important pathogen in neonatal sepsis, which is in accordance with the study by Fairchild *et al*.[9]

We tried to explore possible source of infection when there was clustering of cases in a month. In the outbreak of December 2005, *Candida albicans* was isolated from bottles of parenteral fluid given to neonates, which may be the

source of infection. Administration of contaminated intravenous solutions, notably total parenteral nutrition was reported earlier as source of infection.[10]

The sources of candidiasis in NICU are often endogenous, following colonization of babies with fungi. About 10% babies get colonized in first week of life and 64% of babies get colonized by 4 weeks of hospital stay. Gastrointestinal tract is the first organ to get colonized, though multiple sites may be involved.[10] There was evidence showing correlation between fungal colonization and invasive disease in low birth weight babies.[10] Microorganisms including *Candida species* causing pneumonia acquired during labour and delivery may also act as source of candidaemia.[9] Various fungal agents colonize hospitalized infants, healthcare workers and visitors. Pathogenic agents can be transmitted by direct contact or indirectly via contaminated instruments and intravenous fluids.[10] Except parenteral fluid no such source was traced in our outbreaks.

There are multiple factors responsible for emergence of neonatal candidaemia in recent years. These include wide use of broad spectrum antibiotics, loss of mucosal immunity, colonization, low birth weight, prematurity, and respiratory distress syndrome.[1-10] In the present study, all these predisposing factors for septicaemia i. e. antibiotic therapy 100%, low birth weight 66.66%, preterm infants (66.66%), respiratory distress syndrome 45.45% and ventilation 45.45% were observed. Similar predisposing factors are cited in other studies also.[1-10]

In this study only one death due to Candida albicans was reported before administration of Amphotericin B. The low mortality rate in our study is due to use of Fluconazole and Amphotericin B and all preventive measures taken to reduce nosocomial infections by routine surveillance by Hospital Infection Control Committee.

In conclusion *Candida albicans* still remains predominant pathogen causing neonatal candidaemia and *Candida glabrata* is important pathogen. Early diagnosis and treatment is required to reduce mortality and strict vigilance to prevent nosocomial infection by routine surveillance.

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