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Original Research Article

Emergence of Non-Albicans Candida Species in Neonatal Candidemia

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Abstract:

Aim: Therefore, following study was conducted to know the occurrence of candidemia in our region, among suspected septicemic patients.

Materials and Methods: This prospective study was conducted between December and April 2017 in the Departments of Microbiology and Paediatrics of tertiary care hospital in central, India. From a total 110 neonates admitted to NICU with clinical suspicion of septicaemia. Blood samples were collected in blood culture bottle and incubated at 37C .then subculture done on blood agar and Mc conkey agar and Sabouraud's dextrose agar with chloramphenicol (0.05%) and incubated at 37C. Only those which yielded pure growth of candida spp. were included in the study. Preliminary identification was done by colony morphology on SDA, chromogenic medium, growth at 45C, germ tube test, chlamydospore formation and was confirmed by carbohydrate fermentation test. Candidemia was defiend as the presence of at least one positive blood culture containing pure growthof candida spp. With supportive clinical feature.

Results: Total 110 neonates included in the study, 65(59%) were females and 45(41%) were males. Candida albicans responsible for 67% cases while NAC species responsible for 33% cases with12% cases by C. tropicalis, 10% cases by C.parapsillosis, 5% by C. gullermondii, 4% by C. krusei, 2% by C.kefyr. Among the risk factors observed for candedimia prematurity and LBW, indwelling catheters are commonest followed by broad spectrum antibiotic use, TPN prolonged hyperalimentation. Various clinical presentations also seen in candidemia.

Conclusion: Candidemia in neonates is an ominous prognostic sign and is an important entity in our hospital. Preventive measures such as use of filters for parenteral nutrition, prophylactic antifungal use, and a restrictive policy of antibiotic use to decrease Candida colonization/ infection rates should be implemented to reduce the morbidity and mortality associated with these infections.

Introduction

Significance of candida spp. in neonatal intensive care units (NICU) is increasingly being recognized. It is third most common cause of late onset sepsis in NICU patients and accounts for 9- 13% of blood stream infections (BSI) in neonates [1]. Although Candida albicans has historically been the most frequently isolated species, recently non-albicans Candida (NAC) have emerged as important opportunistic pathogen, notably Candida tropicalis, C. parapsilosis, C. krusei, and C. glabrata. Number of factors including the use of indwelling devices, broad spectrum antibiotics, low birth weight (LBW), prematurity, total parenteral nutrition (TPN), gastrointestinal surgery, artificial ventilation, and/or history of fungal colonization contribute to the risk.[5] Preterm, very low birth weight (VLBW): ≤1,500 g; extremely low birth weight (ELBW): ≤1,000 g; and critically ill infants are at highest risk of invasive Candida infections[6] Candida spp. can also spread through vertical transmission from maternal flora or via horizontal transmission from hands of healthcare workers (HCW).[7,8] Clinical presentation of candidemia resembles sepsis syndrome and to establish a clinical diagnosis is difficult. The incidence of candidemia can be influenced by several factors including the population at risk, healthcare facility standards, Candida spp. involved, and antifungal resistance.[2] We were noticing an increase in the isolation rate of NAC species over last few months from cases of neonatal septicemia, which prompted us to undertake the present study, to examine the prevalence and epidemiology of neonatal candidemia at our hospital Candida species are the 4th leading cause of nosocomial blood stream infection in the united states and ranks 7th in Europe. although more than 17 different species of candida have been reported to be etiologic agents of invasive

candidiasis in humans, only 5 species (candida albicans, candida glabrata, candida tropicalis, candida parapsillosis, and candida Krusei) accounted for 92% of cases of candidemia. An increase in the isolation of non-albicans Candida (NAC) species can be seen worldwide; however, C. albicans still remains the most common cause of candidemia.[1]

The USA and northern Europe have reported a high number of cases by C. glabrata whereas in Brazil and Spain C. parapsilosis is the predominant species isolated from candidemia patients among the NAC species. Furthermore, globally, it is seen that the frequency of C. albicans is decreasing, while that of C. glabrata and C. krusei is stable, and C. parapsilosis and C. tropicalis are increasing.[7] Nationwide data are lacking from India, but from individual studies, 6%–8% of candidemia rates have been reported with increasing isolation of NAC species [8-10] Polyenes, allylamines, azoles, and echinocandins are the antifungal drugs available for the treatment of systemic and invasive candidiasis.

Epidemiological shift from C. albicans to NAC may be attributed to the increasing use of azoles giving rise to increased isolation of resistant species from candidemia patients such as C. glabrata and C. krusei (intrinsically resistant to fluconazole). They may also show cross-resistance to newer triazoles.[13] The isolation of antifungal resistant Candida is on a rise from such group of patients. As morbidity and mortality are very high in such patients, selection of an effective empirical therapy for invasive candidiasis requires a critical knowledge of local epidemiology and regional variability of the concerned area. Therefore, following study was conducted to know the occurrence of candidemia in our region, among suspected septicemic patients.

Materials and Methods

This prospective study was conducted between December and april 2017 in the Departments of Microbiology and Pediatrics of tertiary care hospital in central, India. Average referrals from outside sources are approximately 200-250/year. Premature infants comprise 15-20% of total number of deliveries in the hospital. From a total 110 neonates admitted to NICU with clinical suspicion of septicaemia. Blood samples were collected in blood culture bottle and incubated at 37C .then subculture done on blood agar and Mc conkey agar and Sabouraud's dextrose agar with chloramphenicol (0.05%) and incubated at 37C. Only those which yielded pure growth of candida spp. were included in the study. Preliminary identification was done by colony morphology on SDA, chromogenic medium, growth at 45C, germ tube test, chlamydospore formation and was confirmed by carbohydrate fermentation test. Candidemia was defined as the presence of at least one positive blood culture containing pure growth of candida spp with supportive clinical feature.

Result and Discussion

Total 110 neonates included in the study, 65(59%) were females and 45(41%) were males. candida albicans responsible for 67% cases while NAC species responsible for 33% cases.

Table 1: Percent of CA and NAC species

Organism	Total no.	Percent
Candida albicans	74	67%
Non albicans	26	33%

Potential risk factors for candidemia among neonates n=110. Among the risk factors observed for candidemia prematurity and LBW, indwelling catheters arecommonest followed by broad spectrum antibiotic use, TPN prolonged hyperalimentation.

Table 2:

Factors	Number of cases	percentage
prematurity	30	27%
Low birth weight	20	18%
Risk Indwelling catheters	20	18%
Broad spectrum antibiotic use	15	13.6%
Total parentral nutrition	15	13.6%
Ventilator support	5	4.5%
Prolonged hyperalimentation	5	4.5%

Various clinical presentations observed in cases of neonatal candidemia n==110. Such as failure tobthrive in 50% case, feed intolrence in 27% cases, respiratory distress etc.

Table 3:

Sign/symptom	Number of cases	percentage
Failure to thrive	55	50%
Feed intolerance	30	27%
Respiratory distress	7	6.3%

Abdominal distention	5	4.5%
lethargy	5	4.5%
Poor perfusion	5	4.5%
convulsions	3	2.7%

Characterization of various Candida species isolated from blood- 12% cases by C. tropicalis, 10% cases by C. parapsillosis, 5% by C. gullermondii, 4% by C. krusei, 2% by C. kefyr.

Table 4:

Organism	
Candida albicans	74(67%)
Candida tropicalis	(12%)4
Candida parapsillosis	(10%)3
Candida krusei	(5%)1
Candida gullerimondii	(4%)1
Cadida kefyr	(2%)1

Table 5: CA and NAC in SNCU and PICU patients

	Candida Albicans	**Non Albicans Candida**	
SNCU	44(60%)	29(40%)	73
PICU	33(89%)	4(11%)	37

Discussion

In the present study NAC species accounted for33 % of the cases of neonatal candidemia, whereas C. albicans was responsible for 67% of cases. This corroborates well with the results of other authors.[15-18] Striking feature of the present study was isolation of C. tropicalis (12 %) 4cases as the most common NAC species and C. parapsilosis (10 %) 3cases as the most second common NAC species similar to the study of Ankhi Dutta et al [27)], , C. Krusei (5%) 1cases and C. gullermondii(4%)1 case C. kefyr (2%) 1case. Although C. parapsilosis is less virulent, but under certain conditions (IV catheters, high IV glucose concentrations) virulence may increase many folds and it is relatively difficult to eradicate this organism. [19]

This subsequently has pharmacotherapeutic and pharmacoeconomic implication as to treat such infections is quite difficult. C. parapsilosis is an emerging fungal pathogen and the major threat for neonates in NICU as it frequently colonizes the hands of HCW, has high affinity for intravascular devices, and parenteral nutrition. [20,21] In the present study, 18 and 13.6% of patients were on indwelling catheters and TPN respectively, Higher affinity of C. parapsilosis to adhere on foreign material and ability to form biofilms are important factors for the development of fungemia. [22] C. Tropicalis causes infections with high mortality in adults and children with hematological malignancies or in immunocompromised individuals.[25] Ability of this organism to produce clusters is one of its major virulence factors. Once introduced into the immunocompromised host, C. tropicalis may be more virulent than C. albicans and can rapidly progress from colonization to invasion. In the present study, C. tropicalis and C. parapsillosis have emerged as predominant species accounting for 22% of Combinations of various risk factors are known to be strongly associated with development of candidemia, and our results also suggest the similarity to the study of Deepak Juyal, munish sharma et al study [28]. The major risk factors identified in our study were prematurity, LBW, indwelling catheters, and broad-spectrum antibiotic therapy. 27% of our cases were premature and 18% LBW, highlighting the significant burden of this disease among such infants. Use of multiple invasive devices (catheters, endotracheal tubes) or surgery causes break in the skin/mucosal integrity, which predisposes these sites for colonization/infection by Candida spp. and leading to 18% of total candidemia. Broad spectrum antibiotics ranging two to four in number were being administered to most of the neonates in the present study leading 13.6% cases. Antibiotics promote fungal overgrowth at the a translocation of yeast across the intact mucosa. The risk of candidemia is known to increase exponentially with each class of antimicrobial used. Ventilator support associated candidemia seen in 4.5% of cases. Prolonged hyperalimentation associated candedimia also seen in 4.5% cases. TPN induces gut mucosal atrophy and has immunosuppressive effects which again predisposes individual for infection. Moreover, certain Candida spp. like C. parapsilosis has higher affinity towards parenteral nutrition, and can be responsible for outbreaks in NICUs.13.6% cases of TPN have candidemia. The hands of HCW and environmental surfaces are newly appreciated potential reservoirs for nosocomial strains of Candida spp. Neonatal candidemia are generally associated with high mortality.

Conclusion

Candidemia in neonates is an ominous prognostic sign and is an important entity in our hospital. Preventive measures such as use of filters for parenteral nutrition, prophylactic antifungal use, and a restrictive policy of antibiotic use to decrease Candida colonization/ infection rates should be implemented to reduce the morbidity and mortality associated with these infections. Reporting of fungal BSI and the spectrum of species involved are essential measures in any ICU in order to implement appropriate preventive and therapeutic strategies. Though powered to detect significant risk factors for fungal sepsis, this is a single center study and our findings may not be generalizable to other institutions. Additional studies are necessary to validate our findings and define more accurately the reservoirs, mode of transmission, emergence of new species, and their sensitivity patterns. Epidemiological data of our study can serve as a template for the development of local guidelines for prevention and appropriate treatment of neonatal candidemia. Based on high perinatal risk factors for early onset sepsis, the current hospital antibiotic policy recommends empiric use of ampicillin-

Gentamicin for neonates born within the facility and cefotaxime - amikacin for neonate's referred from elsewhere. Long-term use of these broad spectrum antibiotics must have created a negative pressure and favorable environment for Candida spp. to flourish. This substantiates the need of prophylactic antifungals to be used in a set up where continuous upsurge in the incidence of candidemia is seen. Colonization/ infection rates should be implemented to reduce the morbidity and mortality associated with these infections. Prior knowledge of species distribution in clinical isolates and drug sensitivity pattern among species help the clinician to choose early empirical therapy. Delay in the initiation of antifungal drug may contribute to elevated mortality rate, in spite of low antifungal resistance.

There should be strengthening of antifungal stewardship policies to minimize acquisition of acquired resistance. However, a nationwide study is the need of the hour to formulate policies and strategies for risk identification and management (i.e., prophylaxis, preemptive therapy, or empirical therapy) for invasive candidiasis.

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