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Original Research Article

Neonatal candidiasis: clinical spectrum and epidemiology in a tertiary care centre

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ABSTRACT

Background: Candidial infections are a serious problem in neonatal intensive care units (NICU) which increases the mortality and morbidity in addition to increasing health care costs. Confirming the diagnosis by laboratory tests is difficult and a high index of suspicion is required. The objective of this study was to identify the clinical spectrum and epidemiology of neonatal candidiasis in a tertiary care NICU.
Methods: The present study was carried out in the NICU of SDM medical college and hospital, Dharwad. All babies who were admitted to NICU and who had positive blood culture for Candida were included in the study. One year Data (1st December 2015 to 31st November 2016) was collected retrospectively from NICU case records. Statistical test used was chi square test.
Results: Total admissions to the NICU during the study period were 2591. Blood cultures were positive in 132 babies. Among these, Candidial sepsis was noted in 39.39% (52) babies. Out of the 52 positive fungal cultures, 15 were Candida albicans, 35 were Candida non albicans and 2 were mixed cultures (Candida albicans and non albicans) showing an increasing incidence of non-albicans Candida infections. Among the non albicans Candida, Candida tropicalis and Candida guilliermondii were the predominant species (11 each) followed by Candida famata (6), Candida krusei (6) and Candida parapsilosis (3). Candidial sepsis was seen to be more common among preterm and low birth weight babies. Usage of antibiotics, Total parenteral nutrition (TPN) and mechanical ventilation were common risk factors noted in our study.
Conclusions: Systemic Candidiasis is a disease of modern neonatal intensive care. It deserves urgent attention for its prevention as well as effective treatment in order to minimize neonatal morbidity and mortality.

Keywords: Candida albicans, Neonatal candidiasis, NICU

INTRODUCTION

Infections are a major cause of mortality and morbidity in newborns.[1] Advances in neonatal management have led to considerable improvement in newborn survival.[2] Incidence of neonatal Candidaemia in Neonatal Intensive Care Units (NICU) has increased over the last two decades. Fungal septicemia is a devastating disease especially in low birth weight and preterm babies. It is associated with prolonged hospital stay and increased health care costs.[3] Candida sepsis has become the third most common cause of late onset sepsis in NICU with the mortality figures varying between 15 to 59%.[4] Candidaemia in hospital NICU has been a recurring health problem.[5] Use of multiple antibiotics, steroids, central catheters, ventilation alter ecology and facilitate colonization of Candida.[6]

Due to absence of specific clinical and laboratory criteria coupled with delay in culturing organisms from body fluids, a high index of suspicion is required for prompt diagnosis and treatment of Candidial sepsis.[7]

Although Candida albicans remains the most common fungal pathogen isolated from blood and body tissues, recent evidence show an increased prevalence of Non albicans Candida species.[3,7,8] As most published data on Candidemia in NICU is from developed countries, this study was undertaken to study the clinical spectrum and epidemiology of Candidial sepsis. The study also aimed to identify maternal and perinatal risk factors for development of Candidial sepsis in our setting.

METHODS

The present study was conducted in NICU of SDM Medical College and Hospital, Dharwad. NICU at SDM medical college is a 50-bedded level 3 care unit with provision of all neonatal and subspecialty care with exception of ECMO and iNO.

A cross sectional study was carried out where in retrospective NICU records from December 2015 to 31st November 31st 2016 were analysed. All babies admitted to NICU and had blood culture positive for Candida during this period were included in the study. Candidaemia was defined as Candida species growth from at least one blood culture sent from peripheral or central venous catheters.

Blood cultures were sent for all babies on the day of admission to NICU and repeated on clinical suspicion of fungal sepsis. Under aseptic precautions, 3 ml of blood drawn from baby is sent to lab in Tripticase soy broth. This bottle is inserted into the Bactialert system. Any organism present in the blood sample will produce Carbon di oxide which is detected in the bactialert system. The positive sample is further subjected to Gram staining. Fungi are identified as gram positive budding yeast like cells, thus differentiated from bacteria. Those samples positive on Bactialert system and turned to be positive on gram staining are inserted into Vitek system for further fungal speciation and antifungal sensitivity.

Data was collected using a proforma which had questions regarding day of life, gestational age, sex, weight, clinical presentation to NICU, risk factors, salient laboratory parameters and Candida speciation in blood cultures.

Descriptive data was expressed as percentage and presented in tables and graphs. Chi Square test was used to find out the association between the type of species and other qualitative variables. Statistical software used was SPSS 18 trial version.

RESULTS

Total number of babies admitted to our NICU during the study period were 2591 of which 73% (1914) were term babies and 27% (677) were preterm babies. Total number of blood cultures positive was 132 out of which 80 were bacterial and 52 had positive fungal cultures. Thirteen cultures were polymicrobial. Incidence of fungal sepsis among NICU admission was 2 %. Among the 52 babies, 75% (39) were born in our hospital and 25% (13) were born outside our hospital setting. Males were 67.30% (35) and females were 32.69% (17).

Table 1: Distribution of risk factors among candidial sepsis babies.

Risk factors	Frequency	Percent
Antibiotics usage	52	100
TPN	44	84.61
UVC	10	19.23
Mechanical ventilation	13	25.0
Urinary catheter	11	21.15
Steroids	8	15.38
H2 blockers usage	11	21.15
Surgical procedures	5	9.61

Table 2. Distribution of Candidial species causing Candidial sepsis.

Candida species	Number	Percent
Albicans	15	28.84
Tropicalis	11	21.15
Parapsilosis	3	5.76
Famata	6	11.53
Krusei	6	11.53
Guilliermondii	11	21.15
Total	**52**	**100**

Candida albicans was the most common offending agent 28.8% (15) followed by Candida tropicalis and Candida guilliermondii 21.15% (11) each.

Table 3: Association between the species (Candida Albicans and non-Albicans) and other variables.

Variables	Chi square	df	P value
Sex	0.004	1	0.950
Gestational age	0.022	2	0.989
Weight	0.889	3	0.828
Duration of stay	2.034	3	0.565
Antibiotics duration	4.242	3	0.236
Outcome	3.911	2	0.141
Thrombocytopenia	5.134	2	0.077

Df - degree of freedom.

Table 3 shows the association between the species and other qualitative variables. Test used is Chi square test and P value of < 0.05 was taken to be significant. None of the variables showed statistically significant values as shown by the p values.

This could however be due to small sample size. Close association was seen between the type of species and thrombocytopenia, but was not statistically significant ($p = 0.077$).

Antibiotic usage was seen among all babies. Total parenteral nutrition was seen in 84.6% followed by mechanical ventilation (25%).

Severe thrombocytopenia i.e. platelet count <50,000 (71.2%) was a consistent lab finding followed by hypoglycemia and hypocalcaemia.

Mean duration of antibiotic usage was 13.9±4 days. Mean duration of hospital stay was 21.7±8 days.

All babies received antifungal treatment and all fungal species were sensitive to Fluconazole and Amphotericin B. Out of the 52 babies, 71.2% (37) improved, 9.6% (5) expired and 10 babies left the hospital with incomplete treatment for various reasons and the clinical outcome of these babies remained unknown.

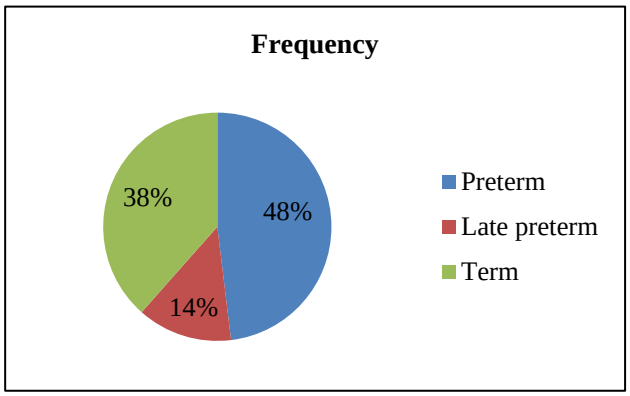

Figure 1: Relationship of gestational age and occurance of candidial sepsis.

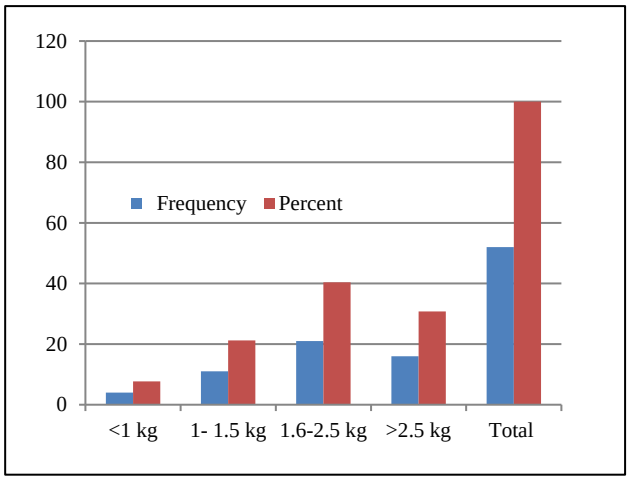

Figure 2: Correlation between birth weight and Candidial sepsis.

DISCUSSION

Documenting fungal blood stream infections with the spectrum of clinical features, species involved are important in NICU in order to adopt appropriate preventive and treatment strategies. In our study, incidence of neonatal candidemia over one year period was approximately 2% which is comparable to incidence reported from developed countries.[9-11] A study done by Ariff et al reported an incidence of 0.93%.[7] However in contrast, Niranjan et al and Benjamin et al reported an higher incidence of upto 7.1% and 9% respectively.[3,12] Our study showed candidial sepsis commonly occurred in preterm and low birth weight babies which is similar to observations made in various studies.[5,8,13] Commonest clinical presentation to NICU was respiratory distress 57.5%. This is comparable with the study done by M.T.Montagna et al documenting respiratory distress in 57.1% and Kapila S et al who documented respiratory distress in 74.55% babies.[4,8]

The major risk factors identified in our study were antibiotic usage (100%), Total Parenteral Nutrition (TPN) 84.6% followed by mechanical ventilation 25%. Similarly, Kumar A et al. in their study showed the risk factors associated to be antibiotics usage 80.46%, TPN 61.25% and intubation in 24.5%.[2] Femitha P et al documented antibiotics usage in 80.6%, H2 blockers usage in 69.4% and mechanical ventilation in 58.3 %.[13] Major laboratory marker for fungal sepsis reported in literature is thrombocytopenia (platelet count<1,50,0000).[7,14] In this study, thrombocytopenia was a consistent finding seen in 100% with severe thrombocytopenia being noted in 71.2%. In a study done by Femitha P et al severe thrombocytopenia was noted in 77.8%.[13] Ariff et al documented thrombocytopenia in 60% babies.[7]

The present study highlights the changing trend of Candidial species in newborn candidaemia that is increasing incidence of non albicans candida 71% compared to Candida albicans 28%. This is similar to study done by Kapila. S et al. who showed non albicans Candida sepsis in 86.4%.[8] A shift towards Non albicans Candida was also noted by Borderon et al, Mendirata et al and Heljic et al.[15-17] Among non albicans Candida, Candida tropicalis and Candida guilliermondii were the predominant species in our study 21% each followed by Candida famata 11.53%, Candida Krusei 11.53% and Candida Parapsilosis 5.76%. Niranjan HS et al demonstrated Candida Krusei to be the predominant non albicans species followed by Candida tropicalis.[3]

All babies received antifungal treatment. It is worth mentioning that in a few babies anti-fungal drugs were initiated on clinical suspicion before the blood cultures yielded positive for fungal growth. 46 babies received Flucanazole and 6 babies received Amphotericin B. 5 babies received initial fluconazole but later were upgraded to Amphotericin B as there was no clinical improvement. Limitation of our study was that the data was collected retrospectively only for a period of one year and hence the number of babies with fungal sepsis were less. The other limitation was that only blood cultures were sent, other body fluids like urine, CSF, peritoneal fluid were not sent for culture. Overall

mortality rate also could not be calculated as some babies left the hospital against medical advice.

CONCLUSION

Systemic Candidiasis is a disease of modern neonatal intensive care. It deserves urgent attention for its prevention as well as effective treatment in order to minimize neonatal morbidity and mortality.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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