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Original Article

Paediatrics Section

Neonatal Candida Blood Stream Infection in A Tertiary Care Hospital

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ABSTRACT

Introduction: Candidemia or Candida Blood Stream Infection (BSI) is associated with medical advancements. Since the survival of Very Low Birth Weight (VLBW) and Extreme Low Birth Weight (ELBW) babies has improved, there is a surge of Candida BSI.

Aim: The aim of the study is to describe the clinical profile of Candida BSI in neonates including the risk factors, symptoms and signs associated with mortality.

Materials and Methods: This is a retrospective descriptive study conducted in NICU of Government Mohan Kumaramangalam Medical College, Salem. The inclusion criteria were to include all neonates with Candida species in blood culture during the study period. The neonates who left against medical advice were excluded.

Results: The incidence of Candida BSI is 1.43% (n=60). About 86% of the neonates weighed less than 2.5kgs and 84% were preterm. More than half neonates received an Aminoglycoside and about one fourth received third generation Cephalosporins. About 82% stayed in the NICU for more than 10 days. More than half of the neonates had clinical features of lethargy, apnoea, temperature instability, feeding intolerance, shock, thrombocytopenia and hypo/hyperglycemia. About 39% of neonates expired.

Conclusion: Candida BSI is an important morbidity in NICU with a high mortality rates. Every NICU should have a written antifungal policy to prevent the morbidity and mortality associated with Candida BSI.

Keywords: Candidemia, Fungal sepsis, Neonatal Intensive Care Unit, Neonatal Mortality

INTRODUCTION

Candidemia or Candida Blood Stream Infection (BSI) is primarily a condition associated with medical advancements in intensive care arena. Since the survival of Very Low Birth Weight (VLBW) and Extreme Low Birth Weight (ELBW) babies has increased in recent years, there is a surge of candidemia in Neonatal Intensive Care Unit (NICU). It is recognized as a major cause of morbidity and mortality in VLBW babies [1]. It causes a diverse spectrum of clinical condition with increased length of hospital stay and the cost of treatment [2]. Candida BSI is caused because of impaired innate immunity in neonates and because of increased interventions in VLBW [3]. Incidence of Candida BSI in ELBW ranges from 2-20% in various studies [1,3,4]. Candida BSI is associated with 25-40% of mortality and 73% of end organ damage involving brain, heart, kidney and eyes [5]. Birth weight and gestational age are the non-modifiable risk factors that predict mortality in Candida BSI. In Candia BSI, 40% mortality is seen in less than 750 grams birth weight babies and 20% mortality in 1000 to 1500 grams birth weight babies [6]. Mortality is three times higher than the uninfected neonates of similar gestational age and weight [7]. High index of suspicion is essential for diagnosis of Candida BSI and thus treatment [8]. Blood culture is the gold standard for diagnosis of Candida BSI. But the sensitivity to detect candidemia in ELBW is low because of less amount of blood culture volume [9]. Prompt diagnosis and early initiation of antifungal treatment is utmost important for the survival and long term neuro developmental outcome. Empiric antifungal therapy reduces the disseminated infection and reduced mortality [10,11].

The aim of the study is to describe the clinical profile including the risk factors, symptoms and signs associated with mortality in neonates with Candida BSI admitted in NICU of the hospital.

MATERIALS AND METHODS

This is a retrospective descriptive study conducted in NICU of Government Mohan Kumaramangalam Medical College, Salem. The study period was from January 2017 to March 2018. The inclusion criteria were to include all neonates with candida species in blood culture admitted during the study period. Fungal cultures were done in Sabouraud's dextrose agar and candida species were identified by morphology, gram stain and Lactophenol cotton blue mounts. Those neonates who

left against medical advice were excluded as their complete clinical profile could not be obtained. The case records of these neonates were collected and analysed for presence of risk factors for Candida BSI like gender, gestational age, birth weight, Apgar score, duration of hospital stay, use of antibiotics, parenteral hyperalimentation, Ranitidine and steroid usage and indwelling central venous catheters. The clinical features like feeding intolerance, temperature instability, apnoea, hypo/hyperglycemia, ventilator support, thrombocytopenia and final outcome were analysed. Institutional ethical committee approval was obtained. Standard case definitions of National Neonatology Forum were used for all neonatal conditions [12].

STATISTICAL ANALYSIS

Univariate and multiple logistic regression analysis of the parameters were done and Odds ratio for death was obtained.

RESULTS

The results are tabulated in [Table/Fig-1 and 2]. There were 60 neonates with Candida BSI during the study period. During the study period, there were 4185 admissions in the NICU and the incidence of Candida BSI is 1.43% (n=60). Excluding the nine neonates who left against medical advice, 51 neonates were considered for analysis. More than half of the neonates in the study group received an Aminoglycoside and about one fourth of the neonates received third generation Cephalosporins. About 82% of the neonates stayed in the NICU for more than 10 days. About 61% of the neonates survived and were discharged and 39% of neonates expired in the study group.

Parameter	No (%)	Univariate analysis	
		Odds ratio for death (95% CI)	p-value
Sex distribution			
Male	28(54.9)	0.72(0.23-2.23)	0.573
Female	23(45.09)		
Birth weight distribution			
< 1 Kg	3(5.88)	8.25(0.82-82.67)	0.073
1-1.5 Kgs	16(31.37)		
1.5-2.5 Kgs	25(49.01)	2.82(0.29-27.54)	0.372
>2.5 Kgs	7(13.72)		
Gestational age distribution			
<28 wks	7(13.72)	7.5(0.76-74.16)	0.085
29-32 wks	21(41.17)	2.25(0.37-13.87)	0.382
32-36 wks	15(29.41)	1.09(0.15-7.8)	0.931
>37 wks	8(15.68)		
Place of delivery			
Intramural	31(60.78)	0.52(0.16-1.71)	0.282
Extramural	20(39.21)		
Mode of delivery			
Labour natural	24(47.05)		
LSCS	19(37.25)	0.77(0.22-2.75)	0.686
Instrumental	08(15.68)	2.78(0.53-14.5)	0.226
Apgar score			
>7	28(54.90)	1.69(0.54-5.26)	0.363
<7	23(45.09)		

[Table/Fig-1]: Clinical profile of neonates with Candida BSI (n=51)

On univariate and multiple logistic regression analysis of the clinical profile [Table/Fig-1,2], the odds ratio for death in the study group for birth weight less than 2.5 kgs, gestational age less than 36 weeks, instrumental delivery and apgar score less than 7 were significant. The analysis of clinical profile also revealed a significant odds ratio for all the clinical features studied except hypo/hyperglycemia, steroid usage, central venous line usage and concomitant bacterial sepsis. Absence of thrombocytopenia and maternal HIV could not be statistically analysed as their numbers were too small. The multiple logistic regression analysis [Table/Fig-3], established a significant odds ratio for mechanical ventilation, bleeding, feeding intolerance, multi organ dysfunction and blood transfusion.

DISCUSSION

Candida BSI is a very important cause of morbidity and mortality in the premature neonates. The isolation rate of 1.43% in this present study is comparable with many other studies [13,14]. Few other studies showed a higher rate of isolation. Agarwal J et al., demonstrated an isolation rate of 13.6% and Rani R et al., demonstrated an isolation rate of 11% [15,16]. The isolation rates depend on the percentage of preterm babies and the level of care in the NICU.

Low birth weight and prematurity were closely associated with Candida BSI in this study. This is in agreement with many other studies [17,18,19]. In the present study, clinical features like apnoea, feeding intolerance, lethargy shock, thrombocytopenia and temperature instability were commonly observed in more than half of the neonates. A similar finding was observed by James M et al., [20]. Parenteral nutrition and Non Invasive Ventilation were the other significant associated risk factors in this study. It is also in concurrence with other studies [17,18].

Broad spectrum antibiotics were given to all the neonates in the present study. They promote Candida growth at the expense of normal bacterial flora seen in neonates. The risk of Candida BSI increases exponentially with more and more antibiotic usage. In the present study more than half of the neonates received an Aminoglycoside. In many studies the use of third generation Cephalosporin was considered to be an important risk factor [7,11]. But in the present study third generation Cephalosporin was used in only 23.52% of neonates. The usage of third generation Cephalosporins in an NICU varies from time to time

Clinical feature	Present (%)	Absent (%)	Univariate analysis	
			Odds ratio (95% CI)	p-value
Steroid usage	11 (21.56)	40 (78.43)	0.51 (0.12-2.2)	0.365
Parenteral nutrition	44 (86.27)	7 (13.72)	1.73 (0.3-9.92)	0.538
Non invasive ventilation >5days	36 (70.59)	15 (29.41)	2.2 (0.59-8.23)	0.242
Mechanical ventilation >5days	28 (54.91)	23 (45.09)	2.83 (0.86-9.31)	0.086
Nil oral feeds >6 days	32 (62.75)	19 (37.25)	1.69 (0.51-5.56)	0.391
Ranitidine usage	17 (33.33)	34 (66.66)	2.35 (0.71-7.76)	0.16
Central venous line	7 (13.72)	44 (86.27)	0.58 (0.1-3.31)	0.538
Temperature instability	29 (56.9%)	22 (43.1%)	2.49 (0.76-8.16)	0.132
Lethargy	44 (86.3%)	07 (13.7%)	4.56 (0.51-41.13)	0.176
Apnoea	28 (54.9%)	23 (45.1%)	1.98 (0.62-6.31)	0.247
Feeding intolerance	33 (64.7%)	18 (35.3%)	6.04 (1.47-24.89)	0.013
Bleeding	21 (41.2%)	30 (58.8%)	3.67 (1.12-11.98)	0.031
Abdominal distension	18 (35.3%)	33 (64.7%)	2 (0.62-6.47)	0.247
Pneumonia	12 (23.5%)	39 (76.5%)	1.14 (0.31-4.26)	0.842
Intraventricular haemorrhage	09 (17.6%)	42 (82.4%)	1.3 (0.3-5.57)	0.724
Shock	28 (54.9%)	23 (45.1%)	3.2 (0.93-10.98)	0.064
Multi organ dysfunction	09 (17.6%)	42 (82.4%)	7.81 (1.42-42.83)	0.018
Blood transfusion	20 (39.2%)	31 (60.8%)	4.31 (1.29-14.36)	0.017
Platelet transfusion	13 (25.5%)	38 (74.5%)	2.24 (0.62-8.07)	0.216
Bacterial sepsis	09 (17.6%)	42 (82.4%)	0.74 (0.16-3.35)	0.691
Thrombocytopenia	49 (96.1%)	02 (03.9%)	-	-
Absolute neutropenia	12 (23.5%)	39 (76.5%)	2.8 (0.74-10.55)	0.128
CRP positivity	24 (47.1%)	27 (52.9%)	1.98 (0.62-6.31)	0.247
Hypo/ hyperglycemia	24 (47.1%)	27 (52.9%)	0.3 (0.09-0.96)	0.043
Maternal HIV reactivity	01 (02%)	50 (98%)	-	-

[Table/Fig-2]: 2 Clinical features in neonates with Candida BSI (n=51)

Outcome	Odds Ratio	95% Confidence Interval		p-Value
Mechanial Ventilation				
Used	1.46	0.20	10.88	0.71
Not used (Ref)				
Feeding Intolerance				
Present	5.60	0.87	36.07	0.07
Absent (Ref)				
Bleeding				
Present	2.30	0.41	12.98	0.347
Absent (Ref)				
Multi Organ Dysfunction				
Present	14.19	1.20	167.17	0.035
Absent (Ref)				
Blood Transfusion				
Present	6.18	0.63	60.41	0.118
Absent (Ref)				
Hypo/Hyperglycemia				
Present	0.24	0.05	1.32	0.101
Absent (Ref)				

[Table/Fig-3]: 3 Multiple Logistic regression analysis.

depending on the antibiotic policy which again depends on the bacterial pathogens prevalent at that time. During the study period *Klebsiella* was the most prevalent pathogen and it was resistant to Cephalosporins. So the usages of Cephalosporins were limited in the study population.

On multiple logistic regression analysis, Multi organ dysfunction had a significant odds ratio for death. A similar observation was made by Sriparna Basu et al., in 2017 [19].

The mortality rate among the study group is 39.22%. The mortality among the neonates with Candida BSI in a study by Sriparna Basu et al., from Varanasi was 14.9% [19]. Another study from Kerala also reported a mortality rate of 40% [20].

LIMITATION

Limitations of the present study are related to the retrospective nature of the study. Though every effort was taken to collect all the data, we did not have data on specific characteristics of non infected neonates in our NICU. Therefore, it was not possible to risk adjust the rates to compare with other studies. One another limitation was that the Candida sub species were not studied and antifungal sensitivity pattern was not done.

CONCLUSION

Candida BSI is an important condition for neonates in NICU with a high mortality rates. An incidence of 1.43% and a mortality of around 39.22% warrant the need for specific strategies to

prevent it. Further all laboratories should be equipped to identify the Candida species and also perform anti fungal sensitivity tests. Like having an antibiotic policy, every NICU should have a written antifungal policy to prevent the morbidity and mortality associated with Candida BSI.

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