International Journal of Contemporary Pediatrics
Sundaram SC et al. Int J Contemp Pediatr. 2018 Nov;5(6):2199-2202
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20184280

Original Research Article

Profile of fungal blood stream infection (BSI) in neonate at tertiary care hospital in South India

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Received: 17 July 2018
Revised: 06 September 2018
Accepted: 27 September 2018

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ABSTRACT

Background: Advancement in neonatal care has led to remarkable improvement in survival of new-born. Fungal infections in new born are an important health problem associated with substantial morbidity and mortality. The objective of this study was to assess the prevalence and epidemiology of neonatal fungal blood stream infection and to analyze risk factor associated with mortality due to fungal septicemia.
Methods: This is a retrospective study of all neonatal fungal cases admitted from July 2016 to June 2017 to a tertiary care hospital in South India.
Results: Isolation rate of fungal blood stream infection was 3.3%. Risk factors observed for candida blood stream infection were Broad spectrum antibiotic usage >7 days (91.18%) followed by central line >7 days (58.9%) and total parenteral nutrition (50.68%). Poor weight gain (71.23%), respiratory distress (68.4%) are common clinical presentation. Mortality among candida blood stream infection was 29 (39.72%). On step-wise logistic regression analysis, prolonged rupture of membrane and endotracheal tube placement for more than 7 days were significant independent predictors of mortality in neonatal candida blood stream infection.
Conclusions: Candida blood stream infection is significant problem in our unit. It occurs in 3.3 %of neonates admitted in our unit and accounts for 34% of blood culture positive sepsis. Non-albican candidiasis is the predominant agent causing candida blood stream infection. Fungal prophylaxis may be recommended in neonates with risk factors like birth weight less than 1500 gms, those requiring ventilation for more than 7 days, those on total parenteral nutrition for more than 7 days and those on prolonged broad-spectrum antibiotics. It reemphasizes the need for aseptic insertion, maintenance, early identification of catheter related infection and early removal of central line.

Keywords: Fungal blood stream infection, Neonate

INTRODUCTION

Advancement in neonatal care has led to remarkable improvement in survival of new-born. Fungal infections in new born are an important health problem associated with substantial morbidity and mortality.Candida species are the leading cause of invasive fungal infections in neonatal intensive care units.[1] Systemic candidiasis in neonates is increasing in frequency, especially because of increased survival of extremely low birth weight and lower gestational age preterm neonates. Candida blood stream infection are the third most common blood culture isolates in late-onset neonatal sepsis (LOS).[2] Candida albicans has historically been the most frequently isolated species, recently Non-albicans Candida (NAC) have emerged as an important opportunistic pathogen.[3] To evaluate the disease burden and to plan for an early and effective intervention, a thorough knowledge of the local

epidemiology of Candida infection is needed. This study was undertaken to evaluate the prevalence of fungal blood stream infection, common species type, potential risk factors and their association with mortality. Aim and objective of this study were to assess the prevalence and epidemiology of neonatal fungal blood stream infection. Risk factor associated with mortality due to fungal septicaemia.

METHODS

This was a retrospective study conducted at a tertiary care outborn neonatal unit in South India between July 2016 and June 2017. Medical records of all culture proven fungal blood stream infection were reviewed. Candida BSI was defined as at least one pure growth of Candida species in blood culture within 72 hours of inoculation, in presence of clinical features suggestive of sepsis such as respiratory distress/apnea, tachycardia/bradycardia, poor perfusion, feeding intolerance, temperature instability, lethargy, or seizures.[4] In our laboratory blood culture, paired samples were inoculated in sheep brain heart infusion broth in 1:10 dilution and incubated at 37°C for 48 hours. Any growth observed was sub cultured on, Sabouraud's dextrose agar (SDA). Species was identified by colony morphology on SDA, germ tube test, growth at 45°C. Statistical analysis was done using SPSS 20. Risk factors were analysed by univariate and stepwise multivariate logistic regression analysis.

RESULTS

During the analysis period 2172 neonates were admitted to our neonatal unit of which 322 (14.8%) were diagnosed to have clinical sepsis.

Table 1: Percentage of risk factors candida blood stream infection (n = 73).

Risk factors	No of neonates	%
Neonates exposed to PROM	33	45.21
Central line	43	58.9
Broad spectrum antibiotic duration >7 days (n = 66)	62	91.18
Postnatal steroid treatment	18	24.66
Endotracheal tube >7 days	33	45.21
Total parental nutrition >7 days	37	50.68

Table 2: Univariate regression analysis of significant risk factors associated with mortality of candida blood stream infections.

Risk factors	Odds ratio	P value
Birth weight <1500 gms	7.73 (2.08, 28.76)	<0.001
Central line	8.68 (2.57, 29.31)	<0.001
Steroids used	5.36 (1.63,17.63)	0.01
ET used >7 days	28.6 (5.65, 144.64)	<0.001
TPN >7 days	12.57 (3.18, 49.7)	<0.001

Table 3: Baseline characteristics between survivor and non-survivor of Candida blood stream infection excluding AMA.

Variables	Survivors n (%)	Non-survivors n (%)	P value
Birth weight (gms)			
<1500	11 (35.45)	20 (60.52)	<0.001
1500-2500	15 (75)	5 (25)	
>2500	17 (80.95)	4 (19.05)	
Sex			
Male	23 (60.53)	15 (39.47)	0.88
Female	20 (58.82)	14 (41.18)	
PPROM			
Yes	12 (36.36)	21 (63.64)	<0.001
NO	31 (79.49)	8 (20.51)	
CRP			
Positive	21 (46.67)	24 (53.33)	0.005
Negative	22 (81.48)	5 (18.52)	
Central line			
Yes	18 (41.86)	25 (58.14)	<0.001
No	25 (86.21)	4 (13.79)	
Intubation			
NO	26 (92.86)	2 (7.14)	
<7 days	12 (100)	5 (41.67)	0.02
>7 days	10 (31.25)	22 (40.28)	<0.001
Antibiotics			
<7 days	5 (83.33)	1 (16.67)	0.2
>7days	33 (33)	28 (45.9)	
Steroids used			
Yes	5 (29.41)	12 (70.59)	0.01
No	38 (69.09)	17 (30.91)	
TPN			
No	24 (88.89)	3 (11.11)	
< 7days	5 (55.56)	4 (44.44)	0.04
>7 days	14 (38.89)	22 (61.11)	<0.001
Platelet count			
<50000	17 (39.53)	21 (72.41)	0.007
>50000	26 (60.47)	8 (27.59)	
Leucocyte count			
<5000	18 (41.86)	14 (48.28)	0.59
>5000	25 (58.14)	15 (51.72)	
Blood glucose			
<45mg/dl	4 (9.3)	6 (20.69)	0.18
>45mg/dl	39 (90.7)	23 (79.31)	
Duration of hospital stay			
<7 days	3 (6.98)	1 (3.57)	0.55
>7 days	40 (93.02)	27 (96.43)	

Blood stream infection was positive in 66% (212 out of 322) of them with clinical sepsis. Candida species was isolated from 34% (73 out of 212) of neonates with blood stream infection. The incidence of fungal sepsis was 3.3% (73 out of 2171) on the whole.

Among the 73 neonates with candida blood stream infection 39 (53.42%) were male and 34 (46.58%) were female. 52 (71.23%) were born by vaginal delivery and

21 (28.77%) by LSCS. Thirty-three (45.21%) were born through prolonged rupture of membrane.

Non-Albican candida Species constituted 86.3 (63 out of 73) of the candida blood stream infection. Among the risk factors observed for candida blood stream infection (Table 1), broad spectrum antibiotic usage for more than 7 days (91.18%) was commonest followed by presence of central line (58.9%) and total parenteral nutrition for more than 7 days (50.68%). Poor weight gain (71.23%) and respiratory distress (68.4%) were the most common clinical presentation followed by lethargy and poor perfusion (Table 4). Twenty-nine (39.72%) of the 73-neonate died due to candida blood stream infection. One was discharged against medical advice and forty-three (41.09%) survived. Of the 29 deaths due to candida blood stream infection 24 were due to Non-albican candidiasis (OR 0.57 with 95% CI 0.13-2.15)

On univariate regression analysis the risk factors associated with mortality in candida blood stream infection (Table -2) were Birth weight <1500 gms(7.73,95% CI 2.08,28.76), placement of central line (8.68, 95% CI 2.57,29.31) steroid usage during hospital stay(5.36, 95% CI 1.63,17.63), Endotracheal intubation >7 days (28.6, 95% CI5.65, 144.64)and total parenteral nutrition>7 days (12.57 95% CI 3.18,49.7).

Clinical features significantly associated with mortality in candida blood stream infection were poor weight gain (9.72, 95% CI 2.04, 46.2), respiratory distress, lethargy (3.14, 95% CI 1.04, 9.48) and poor perfusion (OR 3.09, 95% CI 1.06,8.97). Platelet count of <50000 cell/cu mm was significantly associated with mortality in candida blood stream infection (OR 4.01, 95% CI1.45,11.11) (Table 3).

DISCUSSION

In the present study isolation of candida BSI among neonates admitted to neonatal unit is 3.3% which is similar to a study publishes by Narang et al.[5] Predominant isolate was Non-albican candida blood stream infection which accounts for 86.3% which is similar to study by Garbino J et al.[6]

Present study shows neonates delivered through vaginal delivery 71.23% and having prolonged rupture of membrane (45.21%) prior to delivery are more likely to get candidemia following colonization as reported by Kari A et al.[7]

Several risk factors have been cited as predisposing to candidemia in neonates including underlying illness, VLBW, prolonged use of antibiotics, invasive interventions, hyperalimentation and TPN, etc.[8]

In the present study use of antibiotics for >7 days was the commonest associated finding present in 91.18%neonates with candida blood stream infection (Table 1). In the present study common clinical features associated with neonatal candidemia are respiratory distress and poor weight gain followed by lethargy and poor perfusion (Table 4).[9]

Table 4: Clinical features of candida infection.

Clinical features	No. of cases (n=73)	%
Respiratory distress	50	68.49
Poor weight gain	52	71.23
lethargy	18	24.66
Poor perfusion	20	27.4

Table 5: Multivariate logistic regression.

Mortality	Odds ratio	95% Conf Interval		P value
PPROM	**Cc**			
Yes	9.31	1.48	58.59	0.017
No	Ref			
Mod				
LSCS	1.93	0.18	21.08	0.591
NVD	Ref			
CRP				
P	2.67	0.49	14.5	0.254
A	Ref			
Birthweight (gms)				
<1500	4.79	0.15	154.67	0.377
1500-2500	2.91	0.2	42.14	0.433
>2500	Ref			
Central line				
Yes	1.83	0.18	18.96	0.614
No	Ref			
Steroid used				
Yes	0.99	0.16	6	0.991
No	Ref			
ET tube				
<7days	19.78	0.78	499.04	0.07
>7days	33.97	1.78	646.45	0.019
No	Ref			
TPN				
<7days	4.23	0.21	84.76	0.346
>7days	5.79	0.57	58.58	0.137
No	Ref			
Poor weight gain				
Yes	5.23	0.38	71.53	0.215
No	Ref			
Respiratory distress				
Yes	0.11	0	3.2	0.197
No	Ref			
Lethargy				
Yes	0.39	0.03	5.22	0.473
No	Ref			
Poor perfusion				
Yes	0.46	0.04	5.1	0.525
No	Ref			

CRP was positive in 63.01%. Severe thrombocytopenia of platelet <50000 cells/cumm was present in 52.78% of neonate with candida blood stream infection. However, when combined both was significantly associated with mortality. High CRP, severe thrombocytopenia and leukopenia were predictor of mortality in candida blood stream infection in a study done by Hung-Wei Chi et al.[10] But in the present study Leukocyte count <5000 was not a significant risk factor with P-value.

Mortality among candida blood stream infection was 29 (39.72%). Mortality was less in non-albican candida compared to *Candida albicans* with (OR .57 95% CI 0.13, 2.51) even though there is a shift in epidemiology of Candida species from albicans to non-albicans as quoted by Asifa et al.[11] On univariate analysis of risk factors significantly associated with mortality in candida blood stream infection (Table 3) were birth weight <1500 gms (OR 7.73, 95% CI, 2.08, 28.76). Presence of central line >7 days (OR 8.68, 95% CI, 2.57, 29.31), presence of endotracheal tube for >7 days (OR 28.6, 95% CI, 5.65, 144.64), steroid used during hospital stay (OR 5.36, 95% CI, 1.63, 17.63) and total parenteral nutrition for >7 days (OR 12.57, 95% CI, 3.18, 49.7).

On step-wise logistic regression analysis, prolonged rupture of membrane and endotracheal tube placement for more than 7 days were independent predictors of motility in neonatal candida blood stream infection (Table 5). Limitation of the present study was that it is a retrospective analysis. The species identification and sensitivity pattern were not analysed.

CONCLUSION

Candida blood stream infection is significant problem in our unit. It occurs in 3.3% of neonates admitted in our unit and accounts for 34% of blood culture positive sepsis. Non-albican candidiasis is the predominant agent causing candida blood stream infection. Fungal prophylaxis may be recommended in neonates with risk factors like birth weight less than 1500gms, those requiring ventilation for more than 7 days, those on total parenteral nutrition for more than 7 days and those on prolonged broad-spectrum antibiotics. It reemphasises the need for aseptic insertion, maintenance, early identification of catheter related infection and early removal of central line.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sundaram SC, Kamalarathnam CN. Profile of fungal blood stream infection (BSI) in neonate at tertiary care hospital in South India. Int J Contemp Pediatr 2018;5:2199-202.