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Original Research Article

Comparative study of clinic-microbiological profile of fungal and bacterial sepsis in neonates

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ABSTRACT

Background: Neonatal sepsis both bacterial and fungal sepsis is a major cause of neonatal mortality in India. This study is an attempt at determining the spectrum of fungal and bacterial infections in our NICU and ways to differentiate fungal from bacterial sepsis.
Methods: All culture positive cases of bacterial and fungal sepsis from neonates in nursery of JLN hospital Ajmer from November 2016 to November 2017 were included in the study. The bacterial and fungal cases were compared for clinical and laboratory features, complications and outcome. Chi square test was used.
Results: Culture positive sepsis was found in 391 cases out of total 2190 cases (17.8%) out of which 84.9% were bacterial (EONS 30% and LONS 70%) and 15.1% fungal (EONS 33.8% and LONS 66.1%). Fungal sepsis was found more in lower gestational age (55.9% versus 31.3%; p value 0.003) and in lower birth weight babies (76.2% versus 62.9%; p-value 0.004). Mortality rate was higher in fungal group (40% versus 19.5%; p-value: 0.0003). WBC count of <5000, platelet count <1.5 lac, reactive CRP, hyperglycemia, NEC, ventilation was significantly higher in fungal sepsis. While meconium stained liquor, per vaginal exams >3, maternal fever, mode of delivery, hypoglycemia, increased serum creatinine, respiratory distress, deranged CRT, temperature instability, intra cranial haemorrhage and length of hospital stay were found to be insignificant.
Conclusions: In this study fungal sepsis when compared with bacterial sepsis, was found to be associated more with complications and mortality.

Keywords: Bacteria, Fungi, Neonatal sepsis

INTRODUCTION

Neonatal mortality is the major determinant of Infant Mortality Rate in India, of which neonatal sepsis both bacterial and fungal is an important cause.[1] It is estimated that 20% of all neonates develop sepsis and approximately 1% die of sepsis related causes.[2] Sepsis is responsible for about 30-50% of total neonatal deaths in developing countries. According to recent data from National Neonatal Perinatal Database (NNPD) 2000, the incidence of neonatal sepsis has been reported to be 38 per 1000 intramural live births in tertiary care institutions. Sepsis related morbidity can be largely minimized with prevention of sepsis itself and timely recognition, rational antimicrobial therapy and aggressive supportive care. Two forms of clinical presentations of neonatal sepsis have been identified, early onset sepsis (within first 72 hrs of life) and late onset sepsis (after 72 hrs of life).

Blood culture is the gold standard for the diagnosis of septicemia and should be done in all cases of suspected

sepsis prior to starting antibiotics.[3] A positive blood culture and sensitivity of the isolate is the best guide to antimicrobial therapy. Blood culture is time consuming and not available at small centres, so we can use some surrogate markers of infection like sepsis screen. Sepsis screen is positive when 2 or more parameters are positive out of following investigations (WBC count <5000, absolute neutrophil count low as per Manroe chart for term babies and Mouzinho chart for VLBW babies, Immature: total neutrophil ratio >0.2, micro ESR >10mm, CRP >1 mg/dl). It was found that though individual sepsis screen parameters showed little correlation with blood culture status, yet on combination it was found that specificity and positive predictive accuracy increased while sensitivity decreased than individual tests.[4]

The classic clinical picture of systemic fungal infection in neonates is almost indistinguishable from bacterial sepsis. The signs and symptoms are non-specific. End organ damage is more common and severe in systemic fungal infections. There is a changing trend towards increasing fungal sepsis though still fungal outbreaks are less reported because fungal etiology is usually least suspected and hence antifungal treatment are usually very delayed or seldom attempted. With increasing incidence of fungal sepsis, identification of fungal etiology as well as following sensitivity trends has become more important for appropriate management of these neonates.

METHODS

Study design and data collection

This single centre, prospective analytical study was carried out from November 1, 2016 to October 30, 2017 and included a total of 391 culture positive out-born neonates, admitted to the Neonatal Intensive Care Unit (NICU) at the Department of Paediatrics, JLN Medical College, Ajmer, Rajasthan, India.

Inclusion criteria were neonates who had positive blood culture - fungal or bacterial. Exclusion criteria were neonates who were blood culture negative or who left treatment against medical advice.

The study was approved by the Ethical Committee of the JLN Medical College, Ajmer. For each enrolled neonate the demographic variables collected included: sex, birth weight [normal birth weight >2.5 kg, low birth weight (LBW) 1.5-2.499 kg, very low birth weight (VLBW) 1.0-1.499kg, extremely low birth weight (ELBW) <1.0 kg] and place of delivery (home or hospital based).

Gestational age [term: ≥37 weeks, preterm (premature) <37 weeks, extreme preterm (extremely premature) <28 weeks] of neonates presenting less than 72 hours was determined by new Ballard scoring and those presenting after 72 hours by LMP. Maternal risk factors studied were: History of fever, number of per-vaginal examinations, mode of delivery, colour of liquor. Variables in Clinical examination of baby at the time of admission recorded were: axillary temperature using a mercury thermometer kept at axillary site for 3 minutes (hypothermia <36.5°C and hyperthermia >37.5°C), capillary refill time (>3s or <3s), respiratory rate (>60/min or ≤60/min).

Comorbidities studied were necrotizing enterocolitis (NEC), intracranial haemorrhage (ICH). Laboratory tests recorded were: TLC (Leukopenia <5000/cu mm or Normal ≥5000/cu mm), Platelet count (thrombocytopenia <1.0 lakh/cu mm or normal ≥1.0 lakh/cu mm), C reactive protein (Qualitative analysis: reactive or non-reactive), random blood sugar: using glucometer (Hypoglycemia <45 gm/dl and Hyperglycemia >125 mg/dl.), serum creatinine (raised or normal based on age specific normal values). Outcome was recorded in terms of need for mechanical ventilation, successful discharge, expiry and length of hospital stay (<7 days or 8-14 days or 15-21 days or >21 days).

Microbiological analysis

Blood culture (1-2 ml by venepuncture collected in Brain Heart Infusion Broth (BHI) incubated at 37° C subculture on Sabdraud Dextrose Agar (SDA), blood agar and McConkey agar, if broth turbid. The broth was incubated for maximum 7 days. If no turbidity was seen at the end of 7 days, sample was labelled sterile. Blood culture positive cases were then taken as subjects for this study. Individuals were divided into two groups of bacterial culture positive cases and fungal culture positive cases.

Tabulation of data and statistical analysis

The data was recorded in a pre-structured performa and then tabulated and analysed. The two groups bacterial culture positive and fungal culture positive cases of neonatal sepsis were compared under clinical history, clinical features, laboratory findings and outcome. The culture positive cases of bacterial and fungal sepsis were analysed for spectrum of bacteria and fungi respectively. Data entry and statistical analysis were performed using chi square test, mean and percentage.

All data were entered into a spreadsheet and analysed using SPSS. A P-value of 0.05 or less was considered statistically significant.

RESULTS

Incidence

During the study period 2190 neonates were admitted in the NICU, of which 406 cases showed positive blood culture reports. Fifteen cases (1 fungal and 14 bacterial) left against medical advice (LAMA), therefore were excluded from the study. Hence, 391 cases were included in the study. The incidence of neonatal sepsis in our NICU was therefore 17.85%.

Categorisation of cases

Out of the total 391 cases of neonatal sepsis 15.09% (59/391) were fungal and 84.91% (332/391) were bacterial (Table 1). EOS and LOS cases in bacterial sepsis were 30.12% (100/332) and 69.88% (232/332) respectively. While in fungal sepsis EOS and LOS were 33.90% (20/59) and 66.10% (39/59) respectively (Table 1). There were 120 cases of early onset neonatal sepsis, out of which 83.33% (100/120) were bacterial while only 16.67% (20/120) cases were fungal (Table 1). There were total 271 cases of late onset neonatal sepsis, of which 85.61% (232/271) were bacterial and 14.39% (39/271) were fungal (Table 1).

Table 1: Categorisation of sepsis cases.

Type	EOS	LOS	Total cases
Bacterial	100 (83.33%)	232 (85.61%)	332 (84.91%)
Fungal	20 (16.67%)	39 (14.39%)	59 (15.09%)
Total	120	271	391

Table 2: Analysis of variables.

Factor		Bacterial (n = 332)	Fungal (n = 59)	P value
Sex	M	202	35	NS
	F	130	24	
GA	Extreme preterm <28 weeks	6	4	0.0014
	Preterm 28 to <37 weeks	98	29	
	Term ≥37 weeks	228	26	
Gestational age	< 28 weeks	6	4	0.0258
	< 37 weeks	104	33	0.00003
Birth weight	ELBW	3	3	0.004
	VLBW	44	15	
	LBW	162	27	
	Normal	123	14	
Birth weight	<1000 gram	3	3	0.016
	<1500 gram	47	18	0.0018
	<2500 gram	209	45	0.048
Maternal factors	Meconium stained liquor	39	3	NS
	Per vaginal examinations >3	25	4	NS
	Maternal fever present	27	6	NS
Mode of delivery	NVD	230	45	NS
	LSCS	102	14	
Clinical signs	Tachypnoea (RR >60)	118	21	NS
	CRT prolonged (≥3sec)	108	24	NS
	Hypothermia	251	39	NS
	Hyperthermia	37	6	NS
Laboratory features	TLC <5000	168	20	NS
	Thrombocytopenia (Plt <1.0lac)	171	54	<0.001
	Qualitative CRP reactive	196	50	0.0002
	S. Creatinine raised	52	12	NS
	Hypoglycaemia present	216	32	NS
	Hyperglycaemia present	36	14	0.006
Comorbidities	ICH	8	3	NS
	NEC	40	14	0.017
	Ventilation	104	28	0.016
Length of stay	<7 days	140	33	NS
	8-14 days	104	17	
	15-21 days	42	5	
	>21 days	46	4	
Outcome	Successful discharge	215	29	NS
	Mortality	65	24	0.0004

Demographic variables

Sex

In the present study out of total cases, 60.61% were males while 39.39% were females. Males and females having bacterial sepsis were 60.84% and 39.16%, respectively. While in fungal sepsis distribution of males and females was 59.32% and 40.68% respectively**.** The difference between the two groups was insignificant (p-value 0.825) (Table 2).

Gestational age

Amongst 59 cases of fungal sepsis 4 (6.8%) were extreme preterms, 29 (49.15%) were preterms, 26 cases (44.06%) were term while out of 332 cases of bacterial sepsis 6 (1.8%) were extreme preterms, 98 (29.51%) were preterms, 228 (68.37%) were terms. The difference was statistically significant (p-value:0.0014). (Table 2) Extreme preterm versus preterm and term: the incidence of bacterial and fungal sepsis in extreme preterms of gestational age <28 weeks was 6/332 cases (1.81%) and 4/59 cases (6.78%) respectively. This difference was statistically significant (p-value: 0.0258) (Table 2). Preterm (gestational age <37 weeks) versus term. Out of the fungal sepsis cases, 55.93% were of gestational age <37 weeks. On the other hand, in the bacterial group, 31.32% cases were preterms. The difference was statistically significant (p-value: 0.0003) (Table 2).

Birth weight

Out of 59 cases of fungal sepsis 5.08% were ELBW, 25.42% were VLBW, 45.76% were LBW, and 23.72% were normal birth weight. While out of the 332 cases of bacterial sepsis, 0.90% cases were ELBW, 13.25% VLBW, 48.79% LBW, 37.04%were of normal birth weight. The difference was statistically significant (p-value: 0.004) (Table 2). In the present study extremely, low birth weight neonates (<1000 gm birth weight) were 5.08% and 0.90% in fungal and bacterial sepsis respectively. This difference was significant (p-value = 0.016) (Table 2). 30.50% fungal sepsis cases and 14.15% bacterial sepsis cases of were very low birth weight (<1500 gm). This difference was significant (p-value =0.0018) (Table 2). 62.95% bacterial cases and 76.27% fungal cases were of low birth weight (< 2500 gm). This difference was also significant (p-value = 0.048) (Table 2).

Maternal Factors

Meconium stained liquor was found in 3 (5.08%) cases of fungal sepsis and 39 (11.78%) cases of bacterial sepsis. The difference was statistically insignificant (p-value = 0.126) (Table 2). History of >3 pervaginal examinations was found in 4 (6.78%) cases of fungal sepsis and 25 (7.53%) cases of bacterial sepsis. The difference was not statistically significant (p-value = 0.839) (Table 2).

Maternal fever during antenatal period was found in 6 (10.17%) cases of fungal sepsis and 27 (8.13%) cases of bacterial sepsis. The p-value is 0.604. So, there was no significant difference (Table 2).

Mode of delivery: out of the 59 fungal sepsis cases 45 (76.27%) cases were vaginally delivered and 14 (23.73%) cases were delivered by LSCS. In bacterial sepsis out of the total 332 cases 230 (69.28%) cases were vaginally delivered and 102 (30.72%) cases were delivered by LSCS. The difference was not significant (p-value = 0.28) (Table 2).

Clinical features

35.59% cases of the fungal sepsis had tachypnoea (respiratory rate of >60) at the time of admission while 35.54% cases of bacterial sepsis had tachypnoea at the time of admission. There was no significant difference in the finding (p - value = 0.999) (Table 2).

Prolonged Capillary Refill Time (CRT) of >3 sec at the time of admission was found in 40.68% of fungal cases and in 32.53% of bacterial cases. There was no significant difference in the finding of prolonged CRT between the two groups (P-value = 0.22) (Table 2).

Hypothermia at admission was present in 66.10% of fungal cases and 75.60% of bacterial cases. The difference was insignificant (p-value = 0.124) (Table 2). Hyperthermia at admission was found in 10.17% of fungal cases while it was found in 11.14% of bacterial cases. There was no significant difference (P- value = 0.82) (Table 2).

Laboratory features

A Total Leucocyte Count (TLC) of less than 5000 was found in 66.10% of fungal sepsis cases and 49.40% of bacterial sepsis cases. The difference was significant (P-value = 0.018) (Table 2).

Majority of cases of fungal sepsis (84.75%) had thrombocytopenia while it was much lesser in the bacterial cases (59.04%). The difference was statistically highly significant (p value <0.001) (Table 2).

Reactive C-reactive protein was found in more cases of fungal sepsis (84.75%) as compared to bacterial sepsis (59.04%). There was a statistically highly significant difference between the two groups (p value = 0.0002) (Table 2). Incidence of raised S. creatinine was 15.66% and 20.34% in the bacterial and fungal groups respectively. The difference was statistically insignificant (p value = 0.37) (Table 2).

Hypoglycemia was seen at admission in 54.24% of fungal cases and 65.06% of bacterial cases. There was no significant difference (P value = 0.11) (Table 2).

Hyperglycemia at admission was found more in fungal sepsis (23.73%) as compared to bacterial sepsis (10.84%) The difference was statistically significant (p value = 0.006) (Table 2).

Intracranial haemorrhage (ICH) was found in 5.08% cases of fungal sepsis and 2.41% cases of bacterial sepsis. There was no statistically significant difference (p value = 0.25) (Table 2).

23.73% of fungal cases and 12.05% of bacterial cases developed Necrotizing enterocolitis (NEC). The difference was found to be statistically significant (p value = 0.017) (Table 2).

Outcome

Mechanical ventilation done seen more in cases with fungal sepsis (47.6%) than bacterial cases (31.33%). The difference was statistically significant with the p value of 0.016 (Table 2).

Length of stay

Of the total cases of fungal sepsis 55.93% stayed for <7 days, 28.81% for 8-14 days, 8.47% for 15-21 days and 6.78% for >21 days. While out of the bacterial sepsis cases 42.17% stayed for <7 days, 31.33% for 8-14 days, 12.65% for 15-21 days and 13.86% for >21 days. The difference was not significant (p-value = 0.18) (Table 2).

About half (49.15%) of the fungal sepsis cases and 215 (64.76%) cases of bacterial sepsis were successfully discharged. The difference was statistically significant (p-value = 0.022) (Table 2). Of the 59 cases of fungal sepsis 24 (40.67%) cases expired. On the other hand, out of 332 bacterial sepsis cases 65 (19.57%) cases had fatal outcome. The difference was statistically significant (p-value = 0.0004) (Table 2).

Table 3: Bacterial sepsis species spectrum.

Bacterial Species	Number	Percentage
CONS	133	40.06
Klebsiella	90	27.11
Enterococcus	43	12.95
COPS	21	6.325
Pseudomonas	20	6.024
E. *coli*	18	5.422
Citrobacter	5	1.506
Streptococcus	1	0.301
Proteus mirabilis	1	0.301
Total	332	100

Bacterial spectrum

There were 332 cases of bacterial sepsis, out of which majority of cases were CONS (40.06%), *Klebsiella* (27.11%), *Enterococcus* (12.95%), followed by COPS (6.325%), *Pseudomonas* (6.024%), *E. coli* (5.42%), while 7 cases were of *Citrobacter* (1.506%), *Proteus mirabilis* (0.3%) and *Streptococcus* (0.3%) combined altogether (Table 3). Incidence of Gram positive bacterial sepsis (59.64%) was more than Gram negative bacterial sepsis (40.36%).

Table 4: fungal sepsis species spectrum.

Fungal Species	Number	Percentage
Non albicans candida	30	50.84
Candida albicans	16	27.11
Aspergillus flavus	6	10.17
Aspergillus fumigatus	4	6.78
Aspergillus niger	2	3.39
Aspergillus terreus	1	1.70
Total	59	100

Fungal spectrum

In our study, maximum cases in fungal sepsis were of Non albicans candida (50.84%) followed by Candida albicans (27.11%). Other organisms found were *A. flavus* (10.17%), *A. fumigatus* (6.78%), *A. niger* (3.39%) and *A. terreus* (1.70%) (Table 4).

DISCUSSION

The aim of this prospective study was to identify possible risk factors for fungal sepsis allowing discrimination from bacterial sepsis. The identification of such factors would enable a more effective choice for empirical therapy in order to reduce the morbidity and mortality. Similarly, a knowledge of the prevailing species spectrum of bacterial and fungal sepsis is also important so that empirical therapy can be given accordingly. The incidence of sepsis in our study was thus, 17.8%. It is in accordance with the finding by Bhat S et al and Girma et al who have reported incidence of 25% and 14.4% respectively.[5,6] Some studies gave a lesser incidence like Sanghvi et al 3.8% and Yelda et al 4.3%.[7,8] Higher incidence reported in the present study could be due to many reasons. Ours being a tertiary hospital receives sick patients from other peripheral centres. Babies in the present study were outborn and were referred in an already sick condition.

In the present study we found that bacterial cases were 84.91% and fungal cases were 15.09%. Similar results were found by Chib R et al with bacterial cases 84.5% and fungal cases 15.5%.[9] Also, Rabindran et al notes 88.47% bacterial cases and 11.53% fungal cases.[10] Also, Yunus M et al noted 15.7% incidence of Candidial sepsis.[11] A lower incidence of fungal sepsis was noted by Ho Lim W et al and Bhat S et al, who recorded 3.8% and 6.25% fungal cases respectively.[12,5] The lower incidence of fungal sepsis in these studies may be explained by difference in study populations. In the present study we got a higher percentage of late onset sepsis (LOS) cases

(69.31%). While early onset sepsis (EOS) cases were 30.69%. Similar results were found by Softic I et al who noted 71.3% LOS, 28.7% EOS and also Lebea M et al with 83.7% LOS and 16.3% EOS.[13,14] Similarly higher incidence of LOS as compared to EOS was noted by Isaacs D et al, Ballot D et al, Ho Lim W et al, Emam M et al, Thakur S et al and Motara F et al.[15,16,12,17-19] Higher incidence of late onset sepsis in our study can be because of outborn admissions, longer hospital stays and increased invasive procedures and device usage.

In the present study, we got 332 cases of bacterial sepsis, out of which majority of cases were CONS (40.06%), *Klebsiella* (27.11%), *Enterococcus* (12.95%), followed by COPS (6.325%), *Pseudomonas* (6.024%), *E. Coli* (5.42%), while less common were *Citrobacter* (1.506%), Proteus mirabilis (0.3%) and *Streptococcus* (0.3%).

Coagulase Negative Staphylococcus (CONS) was the commonest organism as in the present study, in some other studies like, Dawudo et al, Ho Lim W et al, Yelda et al and Eman M et al.[20,12,8,17] Commonest organisms vary across various studies.

Present study revealed a greater percentage of fungal sepsis caused by *Non albicans candida* (NAC) (50.84%) as compared to *Candida albicans* (27.11%), followed by *A.flavus* (10.17%), *A.fumigatus* (6.78%), *A. niger* (3.39%) and *A. terreus* (1.70%). Many other studies show a shift from *Candida albicans* to *Non-Candida albicans* with current changing trends seen both in India and across the world. This has immense epidemiological importance, since it is known that certain strains of *Non-albicans Candida* exhibit varying degree of resistance, both innate and acquired to currently used common antifungal agents.[21]

In the present study, difference in distribution of males and females between bacterial and fungal sepsis cases was insignificant. Similarly, Ho Lim W et al and Chib R et al also showed no significant difference with respect to sex of neonate.[12,9]

In present study there was higher incidence of fungal sepsis compared with bacterial sepsis with decreasing gestational age. Extreme prematurity (<28 weeks) was found to be an independent risk factor. This could be because of longer hospital stay of these babies, thinner skin, decreased immunity and more interventional and procedural care. Some studies on fungal sepsis by Swanson JR et al, Clerihew et al, Sil A et al and Yunus M et al show increased incidence of fungal sepsis with lesser gestational age.[21,22,23,11]

Out of 59 cases of fungal sepsis 5.08% were ELBW, 25.42% were VLBW, 45.76% were LBW, and 23.72% were normal birth weight. While out of the 332 cases of bacterial sepsis, 0.90% cases were ELBW, 13.25% VLBW, 48.79% LBW, 37.04%were of normal birth weight. The incidence of fungal sepsis as significantly more in ELBW, VLBW and LBW cases compared to bacterial cases. Rabindran et al also found that risk of fungal sepsis was significantly higher in lower birth weight babies as compared to bacterial sepsis (p value = 0.014).[10]

In the present study, majority of the maternal factors were found insignificant like meconium stained liquor (MSL), per vaginal examinations >3 and maternal fever and mode of delivery. Similar result for mode of delivery was found by Ho Lim W et al, Chib R et al.[12,9] There were some studies on risk factors for fungal sepsis which showed insignificance of mode of delivery like Chaurasia D et al and Yunus M et al.[24,11] On the other hand, Swanson JR et al found caesarean section as a significant risk factor for Candidial sepsis (p value <0.0001).[21]

In the present study, all the clinical factors were found to be insignificant in differentiating bacterial from fungal sepsis. These were tachypnoea (respiratory rate >60) (p value = 0.999), prolonged capillary refill time (CRT) (p value = 0.22) and temperature (hypothermia and hyperthermia with p value = 0.124 and 0.82, respectively). Ho Lim W et al similarly found temperature as an insignificant risk factor in comparison of bacterial and fungal sepsis.[12] But they also found that increased respiratory effort was significantly more in fungal cases as compared to bacterial cases.

In the present study, total leukocyte count of less than 5000 was more common in bacterial sepsis (50.60%) than fungal sepsis (33.90%), the difference being statistically significant (p value = 0.018). In another study, Warris et al found this difference to be insignificant.[25]

In the present study, thrombocytopenia (platelet count <1.0 lac) occurred significantly more in fungal sepsis as compared to bacterial ones, 91.53% versus 51.51% (p value ≤0.001). Warris et al gave similar results (100% versus 50%), so did, Rabindran et al, Charoo et al, and Ho Lim W et al.[25,10,26,12] While Manzoni P et al found no significant difference (19.6% versus 16.4%).[27]

This study revealed that C-reactive protein (CRP) was reactive in 84.75% cases of fungal sepsis while it was reactive in only 59.04% cases of bacterial sepsis. The difference was statistically significant (p value = 0.0002). Corroborating with the present findings, Rabindran et al found higher incidence of reactive CRP (p value = 0.003) in fungal sepsis as compared to bacterial sepsis.[10] Study by Ho Lim W et al also showed similar result (100% versus 83.5%, p value = 0.009).[12] In systemic fungal infections, CRP levels are high as compared to superficial fungal infections like acute fungal stomatitis.

Warris et al however, got insignificant difference between the two groups (100% fungal vs 75% bacterial).[25] In present study, biochemical derangements that did not show significant difference were raised S. creatinine (20.34% fungal versus 15.66% bacterial, p

value = 0.37) and hypoglycaemia (63.43% bacterial versus 54.24% fungal, p value = 0.11).

While hyperglycaemia was found in 23.73% fungal cases and 10.84% bacterial cases. The difference was statistically significant (p value = 0.006). Though Ho Lim W et al found hyperglycemia more (37.17%) in bacterial sepsis than fungal sepsis (16.7%).[12] However, the difference was insignificant.

Amongst the comorbidities intra cranial haemorrhage (ICH) was found in 5.08% fungal cases and 2.41% bacterial cases. The difference was statistically insignificant (p value = 0.25). While necrotizing enterocolitis (NEC) was found significantly more in fungal cases (23.73% versus 12.05%, p value = 0.017). This could be because of the fungal infection per se or because fungal sepsis occurred more in premature babies which itself is a risk factor for NEC.

In the present study, 47.46% cases of fungal sepsis were ventilated as compared to only 31.33% of bacterial cases. The difference was statistically significant (p value = 0.02). In another study by Warris et al artificial ventilation was given to 88% fungal cases and 25% bacterial cases (p value = 0.022).[25] Whether intubation in itself is a causal factor in development of fungal sepsis or merely reflects more vulnerable neonates in NICU setting is difficult to discern. As the fungal cases are more preterm they frequently require mechanical ventilation, this could be another cause for this difference. Yunus M et al in their study on fungal sepsis in neonates revealed mechanical ventilation as a risk factor for fungal sepsis.[24] Ho Lim W et al (2012)[73] however found no significant difference (64.1% bacterial versus 50% fungal).[12]

This study shows no statistically significant difference in the length of stay in the hospital between bacterial and fungal sepsis (p value = 0.18). Similar observation was made by Ho Lim W et al and Chib R et al in their respective studies.[12,9] Warris et al however found longer stay in fungal sepsis cases.[25] Their result can be explained by the fact that they included only preterms <34 weeks in their study who required longer stay in hospital and incidence of fungal sepsis was inversely related to the gestational age.

In the present study, mortality was significantly higher in fungal sepsis as compared to bacterial sepsis (40.67% versus 19.57%, p value = 0.0004). Similarly, Ho Lim W et al also found significant (p value <0.01) difference in mortality.[12] On the contrary, some studies do not agree with our result like Warris et al (p value = 0.164) and Chib R et al (p value >0.05).[25,9]

Higher mortality in fungal sepsis can be attributed to lesser clinical suspicion and delay in administration of antifungal drugs. Also affected babies were majorly premature in our study, which in itself is a risk factor for increased mortality.

CONCLUSION

Incidence of bacterial and fungal sepsis in the form of early onset and late onset forms along with the spectrum of organisms involved has been found. The greater association with risk factors like lower gestational ages, lower birth weight, hyperglycaemia, leucopenia, thrombocytopenia and CRP positivity for fungal sepsis compared to bacterial sepsis has been found. Also, greater association of fungal sepsis with comorbidities like NEC and outcomes like need for mechanical ventilation and mortality has been found. We conclude that fungal sepsis is an important and major cause of sepsis and related morbidity and mortality in NICU. For early and appropriate treatment, it is necessary to suspect and differentiate between fungal and bacterial sepsis and commence appropriate empiric therapy before blood culture reports are available. This study is a step in this direction.

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