Original Research Article

Clinical investigative profile of Neonatal septicemia and outcome at tertiary care teaching center

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Abstract

Introduction: Neonatal sepsis remains a substantial cause of morbidity and mortality at a global level. Precise estimates of neonatal sepsis burden vary by setting. Its causative bacteria and their respective sensitivity patterns are different in each hospital and region. Septicemia indicates bacteria are present in the blood, producing an infection and reproducing within the bloodstream. Neonatal septicemia is defined as infection in the first 28 days of life. **Material and Methods**: This is a prospective and observational study was conducted in the Department of Microbiology, Tertiary care teaching hospital. Blood Samples from suspected patients of neonatal septicemia admitted in NICU of our hospital over a period of 1 year. All clinically suspected patients of neonatal septicemia admitted in NICU of our hospital. **Result:** Out of 138 cultures positive neonatal septicemia patients 76 (55.07%) were male and 62 (44.93%) were female. Out of 412 clinically suspected neonatal septicemia patients 138 (33.49%) were found culture positive. Out of 138 culture positive samples the Gram-negative bacteria were 94 (68.12%) and Gram-positive bacteria were 44 (31.88%) found. Klebsiella pneumoniais found to be most common isolate38 (27.54%) followed by Escherichia coli35 (25.36%) and Staphylococcus aureus 28 (20.29%). **Conclusion:** The clinical features of neonatal sepsis being non-specific, pose a great challenge for prompt diagnosis. Lethargy, refusal of feeds and apnoea were the most common clinical features in this study. Klebsiella was the predominant gram-negative organism and Staphylococcus aureus and CONS were the predominant gram-positive isolates from blood culture in EOS and LOS.

Keywords: Neonatal sepsis, Klebsiella pneumoniais, Staphylococcus aureus

Introduction

Neonatal sepsis remains a substantial cause of morbidity and mortality at a global level[1]. Precise estimates of neonatal sepsis burden vary by setting. Its causative bacteria and their respective sensitivity patterns are different in each hospital and region[2]. Septicemia indicates bacteria are present in the blood, producing an infection and reproducing within the bloodstream. Neonatal septicemia is defined as infection in the first 28 days of life[3].

National Neonatal Forum of India has defined neonatal sepsis as follows:

Probable (Clinical) Sepsis: In an infant having clinical picture suggestive of septicaemia, if there is the presence of any one of the following criteria: Existence of predisposing factors: maternal fever or foul-smelling liquor or prolonged rupture of membranes (>24 hrs) or gastric polymorphs (>5 per high power field)[4].

Positive septic screen - presence of two of the four parameters namely, TLC (< 5000/mm), band to total polymorphonuclear cells ratio of>0.2, absolute neutrophil count < 1800/cumm, C-reactive protein (CRP) >1mg/dl and microESR > 10 mm-first hour. Radiological evidence of pneumonia[5].

Culture Positive Sepsis: In an infant having clinical picture suggestive of septicemia, pneumonia or meningitis, if there is presence of either of the following: Isolation of pathogens from blood or CSF or urine or abscess (es) and Pathological evidence of sepsis on autopsy[6].

We live in world which is heavily populated by microorganisms of astonishing diversity. In this environment, the pediatrics group populations are commonly affected by various infectious diseases[7]. Judicious choice of empiric antibiotics, antibiotic stewardship and alternate modalities should be considered for the management or prevention of neonatal sepsis in India. Though various international and Indian studies on neonatal septicemia are available, the present study was carried out to study blood culture isolates of neonatal septicemia in our institute. Also, to determine their susceptibility patterns among the patients admitted in our institute so that the emergence of neonatal septicemia and drug resistance in bacteria could be controlled effectively. Thus, this study is small step from our department on pathway towards neonatal care.

Hence it is very much essential that local microbiological data should be prepared including information regarding the common isolates and their susceptibility patterns. This data should be monitored and reviewed regularly to provide updated information to clinicians so as to form an effective empirical therapy guideline for management of neonatal septicaemia[8].

Material and Methods

This is a prospective and observational study was conducted in the Department of Microbiology, Tertiary care teaching hospital. Blood Samples from suspected patients of neonatal septicemia admitted in NICU of our hospital over a period of 1 year

Inclusion Criteria

1. All clinically suspected patients of neonatal septicemia admitted in NICU of our hospital.

Exclusion Criteria

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1. Parents of neonate not willing to participate in this study.
2. Patients who underwent surgery.
3. Neonates with lethal congenital anomalies

Blood Sample Collection

About 3 ml of blood was withdrawn using sterile syringe. Two ml of blood was inoculated aseptically into blood culture bottles containing 10 ml Brain Heart Infusion broth (BHI) achieving dilution of 1 in 5 to nullify the natural bacteriostatic/bacteriocidal activity of blood. Remaining 1 ml of blood was allowed to clot in sterile bottle for separation of serum. This serum was used to test CRP.

Processing of Samples

The inoculated blood culture bottles were incubated at 37ºC under aerobic condition for 7 days. The first subculture was done after 24 hours of incubation, the second subculture done on third day and final subculture was done on seventh day.

Culture

Subcultures were done on Nutrient agar, Blood agar, and MacConkey agar.

Results

This study was conducted in Department of Microbiology of tertiary care hospital. A Total of 412 blood samples from clinically suspected neonates from NICU were processed. The result of the study is illustrated as follows.

Table 1: Age and sex distribution in culture positive neonatal septicemia patients (n=138)

Age group (Day)	Male (%)	Female (%)	Total (%)
1-3	50(65.79)	38(61.29)	88(63.77)
4-7	5(06.58)	5(08.06)	10(07.25)
8-14	16(21.05)	16(25.81)	32(21.74)
15-28	05(06.58)	3(04.84)	08(5.78)
Total	**76 (55.07)**	**62 (44.93)**	**138 (100)**

Neonate is considered from day 1 of birth to day 28. Out of 138 culture positive neonatal septicemia patients 76 (55.07%) were male and 62 (44.93%) were female. Male:Female ratio in culture positive patients is 1.23 : 1

Out of 138 culture positive patients 88(63.77%) were from day 1-3, 10(07.25%) from day 4-7,32(21.74%) from day 8-14,08(5.78%) day 15-28. Maximum 88 (63.77%) patients were seen from age group of day 1-3. Maximum male 50 (65.79%) and Maximum female 38 (61.29%) were from same age group of day 1-3.

Table 2: Distribution of organisms according to onset of septicemia in culture positive neonatal septicemia patients (n=138):

Organism	Early-onset n=88 (%)	Late-onset n=50 (%)	Total n=138 (%)
Klebsiella pneumonia	29 (32.96)	9 (18.00)	38 (27.54)
Escherichia coli	27 (30.68)	8 (16.00)	35 (25.36)
Staphylococcus aureus	22 (25.00)	6 (12.00)	28 (20.29)
CoNS	02 (2.27)	11 (22.00)	13 (09.42)
Pseudomonas aeruginosa	02 (2.27)	10 (20.00)	12 (08.70)
Citrobacter species	02 (2.27)	02 (04.00)	04 (02.90)
Enterobacter species	01 (1.14)	02 (04.00)	03 (02.17)
Enterococcus species	02 (2.27)	01 (02.00)	03 (02.17)
Acinetobacter species	01 (1.14)	01 (02.00)	02 (01.45)

Out of 412 clinically suspected neonatal septicemia patients 138 (33.49%) were found culture positive. Out of 138 culture positive samples the Gram-negative bacteria were 94 (68.12%) and Gram-positive bacteria were 44 (31.88%) found.

Klebsiella pneumoniais found to be most common isolate38 (27.54%) followed by Escherichia coli35 (25.36%) and Staphylococcus aureus28 (20.29%). In early onset, neonatal septicemia most common pathogen was found to be Klebsiella pneumonia29 (32.96%), Escherichia coli27 (30.68%)and Staphylococcus aureus22 (25.00%). In late onset neonatal septicemia most common pathogen was found to be Klebsiella pneumonia 9 (18.00%), Escherichia coli 8 (16.00%)and Staphylococcus aureus6 (12.00%)

Table 3: Antimicrobial susceptibility pattern of enterobacteriaceae isolates in culture positive neonatal septicemia patients (n=80)

Antibiotic	*K. pneumoniae* n=38 (%)	*E. coli* n=35 (%)	*Citrobacter*n = 4(%)	*Enterobacter*n= 3(%)
Ampicillin (10µg)	00 (00.00)	00 (00.00)	00 (00.00)	00 (00.00)
Piperacillin (100µg)	12 (31.57)	12 (34.28)	01 (25.00)	01 (33.33)
Cefazolin (30µg)	12 (31.57)	15 (42.85)	02 (50.00)	01 (33.33)
Cefepime (30µg)	12 (31.57)	14 (40.00)	02 (50.00)	02 (66.66)
Cefuroxime (30µg)	14 (36.84)	15 (42.85)	03 (75.00)	02 (66.66)
Ceftriaxone (30µg)	14 (36.84)	14 (40.00)	03 (75.00)	02 (66.66)
Ceftazidime (30µg)	16 (42.10)	14 (40.00)	03 (75.00)	02 (66.66)
Cefpodoxime (10 µg)	15 (39.47)	14 (40.00)	03 (75.00)	02 (66.66)
Aztreonam (10µg)	25 (65.78)	30 (85.71)	03 (75.00)	02 (66.66)
Imipenem (10µg)	30 (78.94)	31 (88.57)	04 (100)	03 (100)
Gentamicin (10µg)	25 (65.78)	12 (34.28)	03 (75.00)	00 (00.00)
Tobramycin (10µg)	12 (31.57)	14 (40.00)	02 (50.00)	01 (33.33)
Amikacin (30µg)	26 (68.42)	24 (68.57)	03 (75.00)	03 (75.00)
Tetracycline **(30µg)**	14 (36.84)	13 (37.14)	01 (25.00)	01 (33.33)
Ciprofloxacin (30µg)	26 (68.42)	15 (42.85)	03 (75.00)	03 (75.00)
Cotrimoxazole Trimethoprim /sulfamethoxazole (1.25/23.75)	16 (42.10)	20 (57.14)	04 (100)	02 (66.66)

All Gram negative isolates are 100% resistance to Ampicilin.all Gram negative isolates are more commonly susceptible to Imipenem with varying percentage. After Imipenem Klebsiella pneumoniae is moderately sensitive to Aztreonam 25 (65.78%) and Ceftazidime 16 (42.10%). Klebsiella pneumoniae is resistant to Ampicillin, Piperacillin and most of third generation cephalosporin.

After Imipenem E.coliis highly sensitive to Aztreonam 30 (85.71%) but moderately sensitive to Amikacin and Cotrimoxazole. E. coli is resistant to Ampicillin, Piperacillin and most of third generation cephalosporin.Citrobacteris moderately sensitive (75.00%) sensitivity to Aztreonam, Cefuroxime, Ceftriaxone, Ceftazidime and Cefpodoxime ciprofloxacin. After Ampicilin Citrobacteris most

resistant to Piperacillin 3(75.00%)Enterobacteris moderately sensitive (66.66%) to Aztreonam, Cefuroxime, Ceftriaxone, Ceftazidime, Cefpodoxime and cotrimoxazole. Enterobacter are 100% resistant to Gentamicin and Ampicilin.

Table 4: Correlation of crp with blood culture positivity in neonatal septicemia (n=412)

CRP	Blood Culture Positive (%)	Blood Culture Negative (%)	Total (%)
Positive	116 (28.16)	41 (9.95)	157
Negative	22 (5.34)	233 (56.55)	255
Total	**138**	**274**	**412**

Out of 412 samples processed both culture positive and CRP positive are 116 (28.16%), both culture negative and CRP negative are 233 (56.55%), culture positive but CRP negative are 22 (5.34%) and culture negative but CRP positive are 41 (9.95%).

Sensitivity of CRP test in blood culture positive cases was 84.06% and specificity of CRP test was 85.04%. Positive predictive value 73.89% and negative predictive value 91.37%. After applying Chi square test, statistical analysis showed CRP positivity was found to be highly significantly associated with blood culture positivity (P-value was <0.001).

Discussion

Neonatal sepsis remains a dreaded cause of neonatal mortality and morbidity. The blood culture positivity in LOS in the present study was 42.5%, while 57.5% had probable sepsis. Roy et al had a blood culture positivity of 47.5% in their study[9]. In other Indian studies, the blood culture yield has ranged from as low as 25% to as high as 64.87% in neonates with sepsis[10]. Among hospitalised neonates, an incidence of LOS varying between 0.4% to 14.2% has been reported[11]. Tallur et al in their study of neonatal sepsis reported that 16.5% had late onset sepsis[12].The commonest organism causing LOS in the present study was Klebsiella followed by Staphylococcus aureus and coagulase negative Staphylococcus. Waters et al in their review of the etiology of community acquired neonatal sepsis in low and middle income countries found Klebsiella to be highly prevalent in South-East Asia. In developing countries, they found potential similarities in major causative organisms between hospital-acquired and community acquired neonatal sepsis[13]. Tallur et al reported also reported Klebsiella species as the most common organism in their study[14]. Vishwanathan R et al in their study in a rural NICU set up, reported 46.3% blood culture positivity with predominant gram negative isolates, Klebsiella being the most common organism followed by E coli. They also noted that profile of organisms causing early and late onset sepsis was similar in their study[15].

In 2012, Hammoud MS et al in Kuwait reported CONS as the most common causative organism in 35.7% of LOS; Klebsiella was the most common gram negative organism in 18.8% of LOS[16]. Tsai MH et al reported that rates of LOS were inversely proportional to birth weight and gestational age. Increased risk of mortality and morbidity was associated with Pseudomonas and Candida SPP in LOS[17]. CONS account for 35.5% - 47.4% of LOS in some developing nations and a higher percentage in industrial countries. CONS is emerging as the most common causative organism in LOS. As the pattern of isolates in LOS changes over time and regions, this should be regularly re-evaluated to guide management[18].

In our study out of 412 samples processed, both culture positive and CRP positive are 116 (28.16%), both culture negative and CRP negative are 233 (56.55%), culture positive but CRP negative are 22 (5.34%) and culture negative but CRP positive are 41 (9.95%). In different studies sensitivity, specificity, positive predictive value and negative predictive value of CRP test in blood culture positive samples varies[18]. In our study sensitivity, specificity, positive predictive value and negative predictive value of CRP test in blood culture positive samples was 84.06%, 85.04%, 73.89% and 91.37% respectively. While study done by Prasad et al sensitivity, specificity, positive predictive value and negative predictive value of CRP test in blood culture positive cases was 87.37%, 71.43%, 73.45% and 86.21% respectively. Specificity, positive predictive value and negative predictive value of our study is nearly correlating with Prasad et al.In our study, statistical analysis showed CRP positivity was found to be highly significantly associated with blood culture positivity with P-value was <0.001. Study by Valinjkar et al also showed significant association of CRP positivity with blood culture positivity.

Conclusion

The clinical features of neonatal sepsis being non-specific, pose a great challenge for prompt diagnosis. Lethargy, refusal of feeds and apnoea were the most common clinical features in this study. Klebsiella was the predominant gram-negative organism and Staphylococcus aureus and CONS were the predominant gram-positive isolates from blood culture in EOS andLOS.

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