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A CLINICAL AND BACTERIOLOGICAL STUDY OF NEONATAL SEPTICAEMIA IN KATIHAR MEDICAL COLLEGE & HOSPITAL, KATIHAR, BIHAR.

Microbiology

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ABSTRACT

Background: Neonatal sepsis is a clinical syndrome of bacteraemia characterized by systemic signs and symptoms inthe first month of life. It is the leading causes of neonatal mortality and morbidity. Early diagnosis and treatment with appropriate antibiotics is important to improve the prognosis of neonatal sepsis. Our objectives were to study the organisms causing neonatal septicaemia, associated risk factors, to correlate CRP with blood culture and to study mortality rate in neonatal septicaemia. **Methods:** The study of one year included clinically suspected cases of neonatal septicaemia admitted in NICU (KMCH, Katihar, Bihar). 566blood samples were collected, processed and isolates were identified. Maternal and neonatal risk factors were studied. CRP test was done by slide agglutination test. **Results:** Blood culture was positive in 205 (36.22%) cases. Among the culture positive cases, 128 (62.44%) weremales and 77 (37.56%) females with male to female ratio of 1.66:1. Early onset sepsis was present in 137 (66.83%) and late onset sepsis in 68 (33.17%) cases. 107 (52.20%) were low birth weight babies. The most common neonatal risk factor was prematurity 75 (36.58%) and maternal risk factor was prolonged rupture of membrane 65 (31.71%). gram negative bacilli 144 (70.24%) were found to be common cause of sepsis than gram positive cocci 61 (29.76%), Klebsiellapneumoniae54 (26.34%) being most common pathogen. Out of 566, CRP test was positive in 244(43.10%) cases. Mortality rate was 23.41%. **Conclusions:** Neonatal septicaemia is a life-threatening emergency. The study of etiological profile and CRP testplays a significant role.

KEYWORDS

INTRODUCTION

Neonatal sepsis is a clinical syndrome of systemic illness accompanied by bacteremia occurring in the first month of life. The immaturity of immune system in the neonates makes them especially susceptible to infections during the neonatal and perinatal period. Neonatal septicaemia is by far the most important and often fatal sequelae of such infection. In India it is commonest cause of neonatal mortality contributing to 38% of the neonatal deaths. For epidemiological and therapeutic purposes, neonatal septicaemia is categorised into early onset neonatal septicaemia (EONS), which presents within the first 72 hours of life and late onset neonatal septicaemia (LONS) presenting after 72 hours of life.[1] This distinction has clinical relevance, as early onset neonatal sepsis is generally acquired from pathogens of maternal genital tract, whereas late onset sepsis has its origin either from the community or from hospital.

In neonatal sepsis numerous neonatal, maternal and environmental risk factors contribute to the high morbidity and mortality. The various risk factors which are associated with EONS are low birth weight (<2500gms), preterm baby, febrile illness in the mother, foul smelling and/or meconium stained liquor amnii, prolonged rupture of membrane (>24 hours), more than 3 vaginal examinations during labor, prolonged and difficult delivery with instrumentation, perinatal asphyxia or difficult resuscitation. Whereas the risk factors for development of LONS include prolonged NICU admission, poor hygiene, low birth weight (LBW), poor cord care, prematurity, bottle feeding, invasive procedure, superficial infection (pyoderma, umbilical sepsis), prelacteal feeding, ventilation, aspiration of feeds etc.

Early diagnosis is a key to reduce morbidity and mortality of neonatal septicaemia. The gold standard for diagnosis of septicaemia is the isolation of bacterial agents from the blood culture. But definitive culture results take at least 48-72 hours resulting in treatment delays. Hence two-pronged approach is used for the evaluation of neonates with possible sepsis. Nonspecific sepsis screen tests like C-reactive protein (CRP), erythrocyte sedimentation rate, total white blood cell count and absolute neutrophil count are used to evaluate the likelihood of infection, and specific diagnostic tests are performed to confirm the presence of a specific pathogen in body fluids.

Both gram negative and gram-positive bacteria have been isolated from blood. Organisms causing sepsis and their susceptibility to different antibiotics vary from place to place. As neonatal septicaemia is life threatening emergency, early diagnosis and treatment with appropriate antibiotics is necessary. Study objective was to study the organisms causing neonatal septicaemia in our region, risk factors associated with neonatal septicaemia, to correlate CRP with blood culture and to study the mortality rate in neonatal septicaemia.

METHODS

The observational study of one year was carried out from May 2018 to April 2019, in the Department of Microbiology, Katihar Medical College, Katihar, Bihar. Clinically suspected cases of neonatal septicaemia admitted in neonatal intensive care unit (NICU) were included in the study. Prior to collection of blood sample, consent from mother was taken and detailed history of each neonate along with history of maternal risk factors, neonatal risk factors and mode of delivery etc., was recorded.

Blood culture

The skin of venepuncture site was disinfected with 70% alcohol and 1% iodine for at least 1 minute and allowed to dry. With precaution to avoid touching and contaminating venepuncture site, 2 ml of blood was withdrawn with disposable needle and syringe and inoculated into blood culture bottle containing 20 ml of trypticase soy broth. The blood and broth were mixed gently; the bottles were transported immediately to laboratory and incubated at 37°C aerobically. First subculture was done after 6-17 hours on 5% sheep blood agar and Mac Conkey agar plates. Thereafter daily subculture was done for 7 days. The isolates were identified by Gram staining, colony characteristics and biochemical properties. Cultures were labelled negative if there was no growth after 1 week of incubation. Antimicrobial susceptibility of all bacterial isolates was done by Kirby-Bauer disk diffusion technique as per CLSI 2014 guidelines.

C-Reactive protein (CRP) test

For CRP testing, 2 ml Blood samples was collected and serum was separated. Testing was done by slide agglutination test according to manufacturer's instructions (Tulip diagnostics (P) Ltd).

Statistical analysis

Statistical analysis was done by chi square test and Mc-Nemar Chi-square test. p value <0.05 was considered as statistically significant.

RESULTS

Out of total 566 blood samples subjected for culture, 205 (36.22%) were culture positive and 361 (63.78%) were culture negative. The

culture positivity rate was 36.22%. Out of total 205 culture positive cases 137 (66.83%) were of age less than 3 days belonging to early onset septicaemia, while 68 (33.17%) cases were between the age of 3 days to 28 days belonging to late onset septicaemia (Table 1). Among them 128 (62.44%) were males and 77 (37.56%) were females with male to female ratio of 1.66:1.

Table 1: Age wise distribution of culture positive cases (n=205).

Age (days)	No. of cases	Total (%)
0-3	137	137 (66.83) EONS
4-6	8	68 (33.17) LONS
7-9	4	
10-12	12	
13-15	5	
16-18	12	
19-21	8	
22-24	10	
25-28	9	
0-28	205	205 (100)

Table 2 shows birth weight wise distribution of the cases. Out of the total 205 culture positive neonates, maximum neonates 107 (52.20%) were low birth weight babies. The most common neonatal risk factor responsible for the infection was prematurity in 75 (36.58%) neonates, followed by respiratory distress in 70 (34.15%) neonates (Table 3).

Table 2: Birth weight wise distribution of culture positive cases (n=205).

Neonatal Birth Weight	No. of culture positive (%)
Normal birth weight (≥2500g)	53 (25.85)
Low birth weight (<2500g)	107 (52.20)
Very low birth weight (<1500g)	45 (21.95)
Extremely low birth weight (<1000g)	0
Total	205 (100)

Table 3: Neonatal risk factors among culture positive cases (n=205).

Risk Factors	Culturepositive cases (%)
Prematurity	75 (36.58)
Respiratory Distress	70 (34.15)
Parenteral Nutrition	57 (27.80)
Mechanical Ventilation	52 (25.36)
Birth Asphyxia	07 (03.36)

Table 4 shows maternal risk factors. Mothers of 65 (31.71%) neonates had history of prolonged rupture of membrane (PROM) and maternal fever was seen in 23 (11.22%). Of the total 205 culture positive neonates, total 105 (51.22%) were delivered in hospital while 15 (07.31%) were delivered at home by normal vaginal delivery. Lower segment caesarean section (LSCS) was the mode of delivery in 65 (31.71%) cases and instrumentation was used in mothers of 20 (09.76%) neonates (Table 5).

Table 4: Maternal risk factors among culture positive cases (n=205).

Risk Factors	Culturepositive cases (%)
Prolonged Rupture of Membrane	65 (31.71)
Maternal Fever	23 (11.22)

Table 5: Distribution of culture positive cases as per mode of delivery (n=205).

Mode and place of delivery	Culturepositive cases (%)
Normal vaginal delivery at hospital	105 (51.22)
Normal vaginal delivery at home	15 (07.31)
Lower segment caesarian section (LSCS)	65 (31.71)
Instrumentation	20 (09.76)
Total	205 (100)

Table 6 shows the isolates from blood culture of neonatal septicaemia cases. Gram negative bacilli 144 (70.24%) were common etiological agents as compared to gram positive cocci 61 (29.76%). The most common gram-negative organism causing sepsis was *Klebsiella pneumoniae* 54 (26.34%) and gram-positive organism was S. aureus 36 (17.56%).

Out of total 137 EONS cases, gram negative bacilli were 103 (75.18%) and gram-positive cocci were 34 (24.82%). Of them, Klebsiella pneumoniae 44 (32.12%) was the commonest isolate. In LONS cases (68), gram negative bacilli 41 (60.29%) predominated as compared to gram positive cocci 27 (39.71%) and the most common pathogen was *S. aureus 22* (32.35%).

Table 6: Distribution of organisms as per the onset of septicaemia.

Organisms Isolated	EONS (%)	LONS (%)	Total
Gram negative organisms	103 (75.18)	41 (60.29)	144 (70.24)
Klebsiella pneumonia	44 (32.12)	10 (14.71)	54 (26.34)
Pseudomonas aeruginosa	11 (08.03)	16 (23.53)	27 (13.17)
Escherichia coli	20 (14.59)	03 (04.41)	23 (11.22)
Acinetobacterbaumannii	04 (02.92)	10 (14.71)	14 (06.83)
Enterobacterspp	08 (05.84)	00(0)	08 (03.90)
Citrobacterspp	08 (05.84)	00 (0)	08 (03.90)
Klebsiellaoxytoca	06 (04.38)	00 (0)	06 (02.93)
Acinetobacterlwoffii	02 (01.46)	02 (02.94)	04 (01.95)
Gram positive organisms	34 (24.82)	27 (39.71)	61 (29.76)
Staphylococcus aureus	14 (10.22)	22 (32.35)	36 (17.56)
CONS	14 (10.22)	04 (05.88)	18 (08.78)
Enterococcus faecalis	04 (02.92)	01 (01.47)	05 (02.44)
Streptococcus pneumonia	02 (01.46)	00 (0)	02 (00.98)
Total	137 (100)	68 (100)	205 (100)

Selection of antibiotics and study of sensitivity pattern of the isolates was done as per CLSI guidelines.[9] The most predominant isolate *Klebsiella pneumoniae* was 54 (100%) resistant to Ampicillin and Cefazolin, while they were sensitive to Imipenem 52 (96.30%) and Amikacin 45 (83.34%). All 27 (100%) isolates of *P. aeruginosa* were sensitive to Polymyxin B and *Colistin. Acinetobacter spp* (n=18) showed least resistance to Imipenem (27.78%) and Amikacin (33.33%).

Amongst gram positive organisms, *S. aureus* showed resistance to Penicillin, Cefoxitin, Erythromycin, Gentamycin and Amikacin (94.44%, 52.78%, 41.67%, 33.33% and 16.67% respectively). 52.78% of the Staphylococcus aureus were methicillin-resistant *S. aureus* (MRSA). All the 36 isolates of *S. aureus* and 18 isolates of CONS were 100% sensitive to Vancomycin and Linezolid. Among *Enterococcus faecalis* (n=05), maximum resistance of 60% was seen to Penicillin and Ampicillin and were 100% sensitive to high level Gentamycin, Vancomycin and Linezolid.

CRP test was performed in all 566 clinically suspected cases of septicaemia and its correlation with blood culture was studied. Out of 566 cases, CRP was positive in 244 (43.10%) and negative in 322 (56.90%) cases. Table 7 shows, out of 205 culture positive cases, 198(96.59%) were CRP positive and 07 (3.41%) were CRP negative while out of 361 culture negative cases, 46 (12.74%) were CRP positive and 315 (87.26%) were CRP negative, with a significant p value. Sensitivity and specificity of the CRP test was 96.59% and 87.26% respectively.

Table 7: Correlation of CRP with blood culture positivity (n=566).

CRP Test	Blood Culture		Total
	Culture Positive	Culture Negative	
Positive	198 (96.59%)	46 (12.74%)	244
Negative	07 (3.41%)	315 (87.26%)	322
Total	205 (100%)	361 (100%)	566

Mc-Nemar Chi square test used, p=8.46×10-8 (p=0.000).

Table 8 shows the mortality of neonates with respect to onset of septicaemia. Out of 137 EONS cases 35 (25.54%) and 68 LONS cases 13 (19.11%) were died of septicaemia. Overall mortality rate was 23.41%. The statistical difference in the mortality rates between two types of septicaemia was not significant.

Table 8: Mortality of culture positive cases as per the onset.

Onset	Culture Positive Cases	Mortality (%)
Early onset neonatal septicemia	137	35 (25.54)
Late onset neonatal septicemia	68	13 (19.11)
Total	205	48 (23.41)

CONCLUSION

Gram negative bacilli were found to be commonest cause of neonatal septicaemia in our setup. Male neonates were more prone to infection.

Incidence of EONS was common as compared to LONS. Various neonatal and maternal risk factors were found to be associated with neonatal septicaemia. The prematurity and low birth weight neonates were at an increased risk of developing sepsis. Blood culture should be done in all suspected cases. The most common pathogen isolated in EONS cases was *K. pneumoniae* and in LONS cases was *S. aureus*. A good correlation between blood culture positivity and CRP was found in the present study. So, CRP testing may prove helpful marker to improve diagnostic accuracy in resource limited situations. Neonatal septicaemia is important cause of morbidity and mortality among the neonates. Early diagnosis, specific treatment and strict infection control practices in neonatal units can reduce neonatal mortality and morbidity.

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