

Original Research Article

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## Neonatal Sepsis, Recent Microbiological Agents and their Antibiotic Susceptibility Pattern, Elevated CRP and Other Laboratory Parameter Association

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### ABSTRACT

Bacterial infections remain an important cause of paediatric mortality and morbidity. It might be possible to reduce these factors by early diagnosis and proper management. The aim of the study was to analyze the bacteriological profiles with their antibiogram, and to register the risk factors for septicemia in neonates and infants. Setting and design: This study was conducted in a tertiary care teaching hospital at S.P. Medical College, Bikaner, India, and included clinically suspected cases of septicemia in neonates and infants. Blood culture reports were studied in 239 cases of clinically suspected septicemia in neonates and infants, using the standard technique of Mackie and McCartney. The antibiotic sensitivity was performed by Kirby-Bauer's disc diffusion method. Risk factors for sepsis in the children were registered. Elevated CRP, TLC, Band cell count, micro ESR laboratory parameters were taken into account. Blood culture was positive in 45.25% of cases. Gram-negative septicemia was encountered in 71.42% of the culture-positive cases. *Klebsiella pneumoniae* were the predominant pathogens amongst gram-negative organisms in both early & late onset septicaemia. Amongst the Gram positive organism, Enterococci (16.67%) were predominant. Ceftriaxone, third generation cephalosporin, was sensitive only against *Enterococcus faecalis* while cefoperazone & cefotaxim both have activity against *Klebsiella* & coagulase negative *Staphylococcus*. ceftazidime was active against *Klebsiella*, *E.coli* & *Pseudomonas*. CRP levels were elevated in 136 (56.9%). The most important risk factors of septicemia in our study population were preterm birth (13.49%). As the cultures showed variable antibiogram with complicated patterns of resistance, culture and sensitivity test should be performed in all cases of septicaemia.

### Keywords

Septicaemia,  
neonates,  
Blood culture,  
antibiogram.

### Article Info

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### Introduction

Sepsis is the commonest cause of neonatal mortality, it is responsible for about 30-50% of the total neonatal deaths in developing countries (Bang *et al.*, 1999; Stoll, 1997). It

is estimated that upto 20 % of neonates develops sepsis and approximately 1% die of sepsis related causes (Baron and Finegold, 1994). The incidence of neonatal

sepsis according to data from National Neonatal Perinatal Database (NNPD, 2002-2003) is 30 per 1000 live births. The NNPD network comprising of 18 tertiary care neonatal units across India found sepsis is to be one of the commonest cause of neonatal mortality contributing to 19% of all neonatal deaths (Report of the National Neonatal Perinatal Database (National Neonatal Forum) 2002 – 03). Among intramural births, *Klebsiella pneumoniae* was the most frequently isolated pathogen (32.5%), followed by *Staphylococcus aureus* (13.6%). Among extramural neonates (referred from community/other hospitals), *Klebsiella pneumoniae* was again the commonest organism (27%), followed by *Staphylococcus aureus* (15%) and *Pseudomonas* (13%)

Neonatal sepsis is the clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in first month of life. It encompasses various systemic infections of the newborn such as septicaemia, meningitis, pneumonia, arthritis, osteomyelitis and urinary tract infections,

Neonatal sepsis can be classified into two major categories depending upon the onset of symptoms. Early onset sepsis (EOS) – it represent within 72 hrs of life. Infants with EOS usually represent with respiratory distress and pneumonia. Late onset sepsis (LOS) – usually represent after 72 hrs of age. The source of infection in LOS is either nosocomial or community- acquired and neonates usually present with sepsis, pneumonia or meningitis. The purpose of this study is to identify organism causing these infections along with their antibiotic sensitivity profiles.

The aim of this study includes that the incidence of neonatal septicaemia. And to study the risk factors responsible for

development of sepsis. Also to study the recent pattern of microbiological agents responsible for neonatal septicaemia.

## **Materials and Methods**

This prospective study was conducted on neonates born in women's hospital, S.P.Medical College, Bikaner and admitted to the N.I.C.U attached to Department of Paediatrics, S.P.Medical College and Associated Group of Hospitals, Bikaner.

## **Inclusion criteria**

239 clinically suspected cases of septicaemia in neonates and infants and two or more laboratory criteria or culture positive were included in study. Signs and symptoms of sepsis included: temperature instability, feeding difficulties, respiratory distress, jaundice, convulsions and autonomic disturbances. Laboratory criteria were : (1) Total leucocyte counts (<5000 or >20000/mm<sup>3</sup>).(2) band cell count more than 20 % (3) band cell / absolute neutrophil counts ratio (>0.2%) (4) elevated C- reactive protein (>6mg/l) (5) micro ESR (>10 mm in 1<sup>st</sup> hr) (6) Blood culture positive.

## **Sample collection and processing**

After taking permission from parents 1- 2 ml blood was collected from a peripheral vein of neonates and infants using proper aseptic precautions and inoculated immediately into 5 mL of glucose broth with 0.025% Sodium polyanethol sulfonate as anticoagulant (HiMedia Laboratories, Mumbai). Blood cultures were processed using the standard technique described by Mackie and McCartney (Collee *et al.*, 1996). The bottle was incubated at 37°C. After 24 hrs subcultures were done on blood agar and MacConkey's medium for next 24 hrs. A negative result was followed up by examining the broth daily and doing a final

subculture at the end of 7 days or at appearance of turbidity, whichever was earlier. Aerobic isolates were studied. Any growth was identified by colonial characteristics, Gram staining, and standard biochemical tests (Baron *et al.*, 1994). Antimicrobial susceptibility testing was performed by the Kirby-Bauer disc diffusion method as per the NCCLS recommendations (Performance Standards for antimicrobial susceptibility testing, Eighth Information Supplement, 2000.).

**C-reactive protein (CRP)**

Estimation was done by qualitative slide agglutination test. If CRP conc. Is greater than 6 mg/L a visible agglutination is observed and if CRP conc. less than 6 mg/L, then no agglutination is observed

Other laboratory tests were also taken into account

**Results and Discussion**

239 newborns, clinically suspected of sepsis were selected for the study. Septicaemia was suspected according to clinical feature and

proved by positive blood culture or  $\geq 2$  positive lab criterias (Table-1). The overall incidence of sepsis was higher in preterm (13.49%) as compare to full term (4.76%). The incidence was higher in males (65.27%) as compare to females (43.72%). This may be due to factors regulating the synthesis of gammaglobulin are probably situated on X chromosomes in the male infants thus confers less immunological protection compare to female counterpart(7) Early onset septicaemia was more common. it was present in 69.03% cases while late onset septicaemia was present in 30.96%.

Gram negative organism were more common (71.42%) than Gram positive (28.57%) in blood culture positive cases (Table -2). *Klebsiella* was the most common pathogen (48.21%) in both early and late onset septicaemia. Other Gram negative bacilli recovered were *Citrobacter*, *E.coli*, and others. Pseudomonas was recovered in single case. Amongst the Gram positive organism, enterococci (16.67%), coagulase negative staphylococcus (8.92%) were recovered. MRSA was documented in three cases ( Table-3).

**Table.1** Correlation of blood culture sensitivity with laboratory criterias

Laboratory Criteria $\geq 2$			Laboratory criteria < 2		
Blood culture positive	Blood culture negative	Total	Blood culture positive	Blood culture negative	Total
52 (45.21%)	63	115	4(3.22%)	120	124

**Table.2** Distribution of culture positive cases according to Gram Staining

Gram staining	No. of cases	Percentage
Gram positive	16	28.57 %
Gram negative	40	71.43%
Total	56	100%

**Table.3** Distribution of etiological agents according to age of onset

Organism	Early onset	Late onset	Total &%
<i>Klebsiella</i>	18	9	27 (48.1%)
<i>Enterococcus fecalis</i>	7	2	9(16.07%)
Coagulase negative <i>Staph. Aureus</i>	3	2	5 (8.92%)
<i>Citrobacter</i>	3	2	5 (8.92%)
<i>E. coli</i>	1	1	2(3.57%)
Other gram negative bacilli	0	3	3(5.35%)
MRSA	0	3	3(5.35%)
<i>Pseudomonas</i>	0	1	1(1.78%)
<i>Klebsiella and E.coli</i>	0	1	1(1.78%)

**Table.4** Bacterial isolates and their sensitivity to various antibiotics

Micro-organism	No. of cases	Peperacillin	Gentamicin	ceftazidime	Ceftriaxone	Cefotaxime	Clavulanate	Vancomycin	Netilmicin	Ciproflo	Linezolid	Ampicillin	Amikacin	Erythromycin	Cefoperazone	Resistant to all antibiotics
<i>Klebsiella</i>	27	-	+	+	-	+	+	-	+	+	-	-	+	-	+	6
<i>Enterococcus fecalis</i>	9	+	-	-	+	+	-	+	-	-	+	+	-	+	-	-
CONS	5	+	-	-	-	+	-	+	-	+	-	+	+	+	+	-
<i>E.coli</i>	2	-	-	+	-	-	+	-	-	-	+	-	+	-	+	-
<i>Citrobacter</i>	5	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-
Other GNB	3	-	+	+	-	+	-	-	-	-	+	-	+	-	-	-
MRSA	3	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-
<i>Pseudomonas</i>	1	+	-	+	-	-	-	-	-	-	+	-	-	-	-	-
<i>Kleb. &amp; E.coli</i>	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

**Table.5** Laboratory investigation in suspected cases of neonatal septicaemia

Investigation	Present	Absent	No. of cases
TLC	103 (43.09%)	136	239
Band cell : ANC ratio	99 (41.4%)	140	239
m – ESR	85 (35.5%)	154	239
CRP	136 (56.9%)	103	239

The present study, showed alarming results of antibiotic sensitivity paterrens. The antibiotics which are commonly used like

ampicillin and ceftriaxone showed poor activity against most of the organism. Only *Streptococcus fecalis* was sensitive against

ceftriaxone. Cefoperazone and cefotaxim both have activity against Klebsiella and coagulase negative staphylococcus. Ceftazidime shown better results and active against *Klebseilla*, *E.coli*, *Pseudomonas* and other gram negative bacilli. Piperacillin had advantage over ampicillin. All organism except *E.coli* showed sensitivity to cefotaxime. Out of 27 *Klebseilla* isolate 6 were resistant to all antibiotics. Citrobactor was only sensitive to cefotaxim (Table -4) The antimicrobial sensitivity pattern differs in different studies as well as at different times in the same hospital in Indian and overseas studies. This is mainly a result of indiscriminate use of antibiotics.

In suspected cases of septicemia other deranged laboratory parameters, increased CRP (56.9%), deranged total leukocyte count (43.09%), band cell: ANC ratio (41.4%) and micro-ESR (35.5%) were present (Table-5).

In conclusions, systemic bacterial infection in the newborn creates a significant burden due to its impact on neonatal mortality and long-term morbidity. In spite of ongoing efforts in early diagnosis, treatment, and prevention, neonatal sepsis still remains an enigmatic area for neonatologists due to changes in epidemiology and the lack of ideal diagnostic markers. As the cultures showed variable antibiogram with complicated patterns of resistance, culture and sensitivity test should be performed in all cases of septicemia.

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