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Research Article

Neonatal sepsis: epidemiology, clinical spectrum, recent antimicrobial agents and their antibiotic susceptibility pattern

Pradeep Verma, Pramod Kumar Berwal, Niranjan Nagaraj*, Sarika Swami, Prathusha Jivaji, Satya Narayan

Department of Peadiatrics, SP Medical College, Bikaner, Rajasthan, India

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***Correspondence:**
Dr. Niranjan Nagaraj,
E-mail: getniranjan806@yahoo.com

ABSTRACT

Background: Neonatal sepsis is one of the most common causes of neonatal mortality in the developing world. This study aims to determine the incidence, the bacteriological profile of neonatal septicaemia, their antibacterial susceptibility pattern.
Methods: It is a prospective study, carried out in the tertiary care NICU of S.P. Medical College, Bikaner, Rajasthan, from January 2014 to October 2014. Blood culture specimens were collected from neonates, identification of organisms, their antibiotic susceptibility pattern detection was done.
Results: Gram negative organisms were more common (71.42%) than gram positive (28.57%). Klebsiella was the most common pathogen (48.21%) in both early and late onset septicemia. In third generation cephalosporins, only one organism (Strept. faecalis) is sensitive to ceftriaxone but cefoperazone and cefotaxim both have activity against Klebseilla and coagulase negative Staphylococcus. Ceftazidime showed better results and active against Klebseilla, E. coli, pseudomonas and unidentified gram negative bacilli. In aminoglycosides amikacin has much better results than gentamicin. Piperacillin had advantage over ampicillin. All organisms except E. coli showed sensitivity to cefotaxime. Vancomycin had good activity against gram positive organisms (enterococcus, CONS, MRSA). Neonatal mortality rate was 23.43%.
Conclusions: Neonatal sepsis is one of the major causes of morbidity and mortality in the newborns. Prematurity, low birth weight, prolonged rupture of membranes are major risk factors predisposing neonate to sepsis. This study, showed alarming results of antibiotic sensitivity patterns. The antibiotics which are routinely used like ampicillin and ceftriaxone showed poor activity against most of the organisms.

Keywords: Neonatal sepsis, Antibiotic susceptibility pattern, Microorganisms, Klebsiella, Bikaner city

INTRODUCTION

Sepsis is the commonest cause of neonatal mortality; it is responsible for about 30-50% of the total neonatal deaths in developing countries.[1,2] It is estimated that up to 20% of neonates develop sepsis and approximately 1% die of sepsis related causes.[2] Sepsis related mortality is largely preventable with prevention of sepsis itself. This includes timely recognition, rational antimicrobial therapy and aggressive supportive care. The incidence of neonatal sepsis according to the data from National Neonatal Perinatal Database (NNPD, 2002-03) is 30 per 1000 live births. The NNPD network comprising of 18 tertiary care neonatal units across India found sepsis to be one of the commonest causes of neonatal mortality contributing to 19% of all neonatal deaths.[3]

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. It

encompasses various systemic infections of the newborn such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections. Superficial infections like conjunctivitis and oral thrush are usually not included under neonatal sepsis. Among intramural births, Klebsiella pneumoniae is the most frequently isolated pathogen (32.5%), followed by Staphylococcus aureus (13.6%). Among extramural neonates (referred from community/other hospitals), Klebsiella pneumoniae is the commonest organism (27%), followed by Staphylococcus aureus (15%) and Pseudomonas (13%).[3]

Neonatal sepsis can be classified into two major categories depending on the onset of symptoms,[4] Early Onset Sepsis (EOS):It presents within the first 72 hours of life; Late Onset Sepsis (LOS): It usually presents after 72 hours of age. The ability of the new born to respond to an infection is limited to identical stereotype response to a variety of insults, thus producing identical clinical picture in a variety of conditions. The new born infant especially preterm as compared to the older children and adults has markedly decreased IgM and IgA level at birth. Although IgG may be normal in term infant but it is low in preterm infant. The percentage of CD-8 positive T-Lymphocyte (Suppressor) and cytotoxic cells in adults is actually lower in new born infant. The new born infant especially preterm have markedly decreased level of C3, C5a and properdin and all key element in alternate pathway of complement. Because of low level of antibodies and complements there is defective generation of chemotactic factors and abnormalities of opsonisation leading to life threatening bacterial infections. Considering the meagre resources available in the developing countries a reduction in sepsis related mortality may be possible by identifying high risk neonates and targeting them for intensive care and immunotherapy. The purpose of this study is to identify the most common symptoms and signs of neonatal septicaemia in our NICU and the organisms causing these infections along with their antibiotic sensitivity profiles.

METHODS

It is a prospective study, carried out in the tertiary care NICU of S.P. Medical College, Bikaner, Rajasthan, from January 2014 to October 2014.The study included all babies who were born in Women's hospital, S.P. Medical College Bikaner, and presented with clinical features suggestive of neonatal sepsis. Detailed history including history regarding maternal risk factors were taken in this study. Thorough physical examinations were conducted with special emphasis on features suggestive of neonatal sepsis. All the babies were examined twice daily to access the progress of disease and development of any new finding till the baby was discharged or expired. All those babies presenting with clinical sepsis were thoroughly investigated for any evidence of bacterial sepsis and all laboratory investigations were sent within 24 hour of admission. The babies had clinical features of neonatal sepsis and two or more laboratory criteria or culture positive were included in the study: Clinical features: Fever, cold extremities, refusal to feed, sluggish activity, vomiting, abdominal distension, bleeding, respiratory distress, grunting, apnea, cyanosis, jaundice, pallor, lethargy, excessive cry, convulsion, buldging anterior fontanalle, rash, diarrhea, umbilical discharge, pyoderma, oral thrush etc.

Laboratory criteria: 1) Total leucocyte counts (<5000 or >20000/mm^3) 2) Band cell count more than 20% 3) Band cell/Absolute neutrophil counts ratio (>0.2%) 4) Elevated C-reactive protein (>6 mg/l) 5) Micro ESR (>10 mm in 1st hour) 6) Blood culture positive. All data were tabulated and statistically analyzed and appropriate software was used for the analysis of the data.

RESULTS

In this study, incidence of neonatal septicemia was found to be 7.6%.In our study, Klebseilla pneumoniae was the commonest pathogens, documented in 48.21%, most of them present with early onset sepsis. Amongst the gram positive organisms, Enterococci (16.67%), coagulase negative Staphylococcus (8.92%) were recovered. Micro-ESR was of limited value in the diagnosis of sepsis. It revealed positive results (>10 mm in 1 hour) only in 35.5% cases. Total leukocyte counts revealed better results, being positive in 43.09% cases. Band cell:ANC ratio also showed similar significances (41.4%). However C-Reactive Protein (CRP) positive in 56.9% of suspected sepsis cases. Blood culture was positive in 45.2% of septicemic neonates. Only one organism (Strept. faecalis) was found to be sensitive to third generation cephalosporin namely ceftriaxone, the other agents like cefoperazone and cefotaxim were sensitive against Klebseilla and coagulase negative Staphylococcus.

Table 1: Distribution of screening positive cases.

Maturity	Total No. of live births			Screening positive cases		
	Male	Female	Total	Male	Female	Total
Pre term	618	412	1030	94	45	139 (13.49%)
Full term	1365	735	2100	62	38	100 (4.76%)
Total	1983	1147	3130	156 (65.27%)	83 (34.72%)	239 (7.6%)

Table 2: Spectrum of clinical features in suspected cases of neonatal septicemia.

Clinical features	Age at onset		Total
	Early	Late	
Refusal to feed	58	50	108
Lethargy	38	53	91
Respiratory distress	76	10	86
Vomiting	43	17	60
Hypothermia	39	13	52
Excessive cry	17	20	37
Fever	20	32	52
Abdominal distension	29	5	34
Circumoral hue	10	7	17
Jaundice	15	8	23
Pallor	16	9	25
Convulsion	21	21	42
Diarrhoea	10	12	22
Apnea	9	2	11
Sclerema	0	6	6

Ceftazidime showed better results and found to be sensitive to Klebseilla, E. coli, Pseudomonas and unidentified gram negative bacilli. Piperacillin had advantage over ampicillin. All organisms except E. coli showed sensitivity to cefotaxime. Out of 27 Klebseilla isolates six were resistant to all antibiotics. Citrobactor was only sensitive to cefotaxim. Vancomycin had good activity against gram positive organisms (Enterococcus, CONS, MRSA). Amongst the aminoglycosides, amikacin showed better results than gentamicin.

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

Organisms	Early onset	Late onset	Total & %
Klebsiella	18	9	27 (48.21%)
Enterococcus, Streptococcus fecalis	7	2	9 (16.07%)
Coagulase negative Staph. aureus	3	2	5 (8.92%)
Citrobactor	3	2	5 (8.92%)
E. coli	1	1	2 (3.57%)
Gram negative bacilli	0	3	3 (5.35%)
MRSA	0	3	3 (5.35%)
Pseudomonas	0	1	1 (1.78%)
Klebsiella & E. coli	0	1	1 (1.78%)

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

Organism	No. of cases	Peperacillin	Gentamicin	Ceftazidine	Ceftriaxone	Cefotaxime	Clavulanate	Vancomycin	Netilmicin	Ciproflox	Linezolid	Ampicillin	Amikacin	Erythromycin	Cefoperazone	Resistant to all antibiotics
Klebsiella	27	-	+	+	-	+	+	-	+	+	-	-	+	-	+	6
Streptfaecalis	9	+	-	-	+	+	-	+	-	_	+	+	-	+	-	-
Coagulase -ve Staph.	5	+	-	-	-	+	-	+	-	+	-	+	+	+	+	-
E. coli	2	-	-	+	-	-	+	-	-	-	+	-	+	-	+	-
Citrobactor	5	-	-	-	-	+	-	-	-	-	-	-	-	-	-	-
Gram -ve bacilli	3	-	+	+	-	+	-	-	-	-	+	-	+	-	-	-
MRSA	3	-	-	-	-	-	-	+	-	-	+	-	-	-	-	-
Psudomonas	1	+	-	+	-	-	-	-	-	-	+	-	-	-	-	-
Kleb. + E. coli	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

DISCUSSION

Out of 3130 live born babies delivered at Women's Hospital, PBM and Associated Group of Hospitals, Bikaner, Rajasthan, from January 2014 to October 2014, a total of 239 babies developed clinical features suggestive of neonatal septicemia were enrolled. The incidence of neonatal septicemia was found to be 7.6%. Joseph et al.[5] observed 7.8% incidence which is almost comparable to our study incidence 7.6%. The incidence was found to be low when compared to study conducted by Choudhary et al.[6] which reported a much higher incidence of neonatal septicemia of 11.2% in live births. The higher incidence of neonatal sepsis was due to the fact that their diagnosis of neonatal sepsis was based on clinical features alone. The incidence of male:female was 65.27%:34.72%; male:female ratio was 1.87:1. Neonatal septicemia was found to be more common in males. The 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.[9] In our study, pre term babies had more sepsis (58.15%) than term babies (41.8%). Khatua et al.[7] observed 63% pre term and 37% term babies. LBW infants (both preterm and tern SFD) have low IgG and more susceptible to infections. The placental transport of IgG from maternal to fetal circulation increases with maturity, this transport is hampered in SFD infants who are often the products of placental insufficiency. In our study 60.94% neonates in study group were less than 2.5 kg. Shitaye et al.[8] observed 60% neonates were LBW, is almost similar to our study. The incidence of early onset and late onset sepsis was 69.03% and 30.96% respectively. Our findings were consistent with that of Choudhary et al.[6] In our study most common presenting features in early onset sepsis were respiratory distress (46.06%), vomiting (26%), hypothermia (23.6%), abdominal distension (17.5%), while in late onset sepsis most common clinical features were lethargy (71.6%), refusal to feed (67.5%), fever (43.2%). Convulsion, diarrhea and excessive cry found in almost equal number of neonates in both early and late onset sepsis. The chances of sepsis depend upon the number of maternal risk factors present in any given neonate. As the risk factors increase susceptibility to sepsis increase. Out of 239 newborns suspected of sepsis PROM was observed in 146 babies, out of them (38.3%) were proved as sepsis. The other important factors predisposing to sepsis were frequent vaginal examination (23.25%), fever in mother (33.33%), and history of foul smelling liquor (24.72%).

Micro-ESR was of limited value in the diagnosis of sepsis. It revealed positive results (>10 mm in 1 hour.) only in 35.5% cases. Total leukocyte counts revealed better results, being positive in 43.09% cases. Band cell:ANC ratio also showed similar significances (41.4%). However C-Reactive Protein (CRP) positive in 56.9% of suspected sepsis cases. Blood culture was positive in 45.2% of septicemic neonates, which is comparable to Shrestha et al.[1,9] who observed 42.7% blood culture positive cases.

In our study, Klebseilla pneumoniae were the commonest pathogens, documented in 48.21%, most of them present with early onset sepsis. The other gram negative bacilli recovered were Citrobactor, E. coli, while few remained unlabeled. Amongst the Gram positive organisms, coagulase negative Staphylococcus (8.92%), Enterococci (16.67%), were recovered. While MRSA was documented in three cases and Pseudomonas in single new born. Lancefield grouping is not done in our institution. Similar to our study Klebseilla is found most common organism in study done by Desai et al.[9] (47.14%), Rathore et al.[10] (55.14%), West Peterside et al.[11] (58.2%). In study in third generation cephalosporins only one organism (Strept. faecalis) is sensitive to ceftriaxone but cefoperazone and cefotaxim both have activity against Klebseilla and coagulase negative staphylococcus. Ceftazidime shown better results and active against Klebseilla, E. coli, Pseudomonas and unidentified Gram negative bacilli. In aminoglycosides, amikacin has much better results than gentamicin. Piperacillin had advantage over ampicillin. All organisms except E. coli showed sensitivity to cefotaxime. Out of 27 Klebseilla isolates six were resistant to all antibiotics. Citrobactor was only sensitive to cefotaxim. Vancomycin had good activity against gram positive organisms (Enterococcus, CONS, MRSA). The indiscriminate use of antibiotics with consequent development of resistant strain is cause of drug resistance. Another mechanism postulated for antibiotic resistance is plasmid theory. The common principle that antibiotics must be used only when indicated cannot be over emphasized. It may also be necessary to rotate the common combinations and first choice of antibiotics in NICU, so as to change the resistance patterns. The unnecessary use of strong antibiotics for minor infections and for prophylaxis should be discouraged. In India, sepsis accounts for one fourth to nearly half of neonatal deaths with a case mortality ranging from 24-69%. The case fatality rate due to neonatal sepsis in our study was 23.43% (56 deaths in 239 cases). In our observation mortality in early onset septicemia was more (27.77%) while in late onset septicemia was 14.86%. In our study, we observed higher mortality rates with culture positive cases (35.71%) than culture negative cases (19.67%), though the difference was not statistically significant. Higher mortality in culture positive group was due to invasion of blood stream by larger number of bacteria. In our study, the mortality with Klebsiella was 33.33% and followed by Streptococcus faecalis (Enterococcus), coagulase negative Staph., Citrobactor and MRSA & pseudomonas. Thus, this study identifies neonatal septicemia, its risk factors, incidence, outcome, causative agents and their antimicrobial sensitivity. The results obtained were comparable to other studies conducted in our country in respect to the higher incidence, mortality in pre-term and low birth weight babies and causative organisms of sepsis. While it differed in overall incidence, pattern and mortality which was low as compared to other studies.

CONCLUSION

Septicemia is most frequent and severe disease which threatens survival during first few weeks of life. Considering the meager resources available in developing countries a reduction in sepsis related mortality may be possible by using hygienic measures during and after delivery and identifying high risk neonates and targeting them for intensive care and therapy. The changing pattern and frequent emergence of resistant bacteria make the problem more difficult. For best results in infection management, nurseries should periodically review their bacterial sensitivity pattern and the antibiotic policy.

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