



EPIDEMIOLOGICAL AND CLINICOBACTERIOLOGICAL STUDY OF NEONATAL SEPSIS

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Received: 12 June 2023

Published: 01 July 2023

DOI: 10.1027/marpe.2023.0189

Abstract

Background: Neonatal mortality is still high in developing countries like India, which is mostly contributed by sepsis. In India neonatal mortality rate for the year 2002 was 32 per thousand live birth¹. 30-50% of neonatal deaths are due to sepsis². Early diagnosis and appropriate management can improve the outcome of neonatal sepsis. Diagnosis of neonatal sepsis can be difficult at times as the symptoms and signs are nonspecific. Use of early markers of neonatal sepsis along with clinical judgment makes the management of neonatal sepsis more logical. Choice of antibiotic in the management of sepsis depends on the etiological agent and their susceptibility pattern which changes from time to time.

Method: This study was conducted as a prospective study at St.John's medical college hospital, from 1st May 2011 to 30th April 2012.

Results: There were 1169 admissions to the NICU during the one year study period. 502 babies who underwent septic screen were identified and enrolled in the study. There were 238 episodes of sepsis and the incidence of sepsis in this study was 20.01% among the babies admitted during study period. The incidence was more in extreme preterm and extreme low birth weight categories. 75% of babies with extreme low birth weight and all babies with gestational age <28 weeks developed sepsis, while it was 12.19% in babies more than 2500gm and 13.45% in babies who are more than 38 weeks. Among babies with sepsis culture positive sepsis was seen in 18.45%. *E.coli* was the commonest organism in EOS and *Klebsiella* in LOS. Among the isolates 66.66% of staphylococci were methicillin resistant (MRSA) and 60% of Nonfermenting gram negative bacilli (NFGNB) were resistant to all drugs tested.

Conclusion: In this study incidence of neonatal sepsis was 20.35%. Lower the birth weight and gestational age, higher was the incidence of sepsis. PROM >18 hours, MSAF and prematurity were found to be associated with EOS while extreme prematurity, prolonged ventilation, indwelling catheters and prolonged hospital stay were found to be statistically significant in causing LOS. The number of culture positive sepsis was 18.45% among the babies with neonatal sepsis. It is alarming that most of the isolates in culture positive babies were resistant to the commonly used antibiotics.

Introduction

“Neonates constitute the nation’s foundation and Mothers are its pillars and no one can afford to neglect their needs and rights”

UNICEF

Neonatal period is considered the most important age group at all times as newborns are most vulnerable to disease and death. Historically the probability of death during neonatal period was so high that many traditional practices were postponed until after first week of life, ensuring the probability of child’s survival. Also the quality of life and health as the child grows to adult life is partly determined at this stage. Many avoidable handicaps during childhood like cerebral palsy, mental subnormality and recurrent seizures have their origin in perinatal period. Septicemia is a major cause of mortality and morbidity in neonatal period. Incidence of neonatal sepsis according to National neonatal perinatal database (NNPD) 2002 data is 32 per 1000 live births in tertiary care institutions¹.

The bacteriological profile of neonatal sepsis is constantly under change, more so with advances in early diagnosis, treatment and increased survival of preterm babies. So any protocol for sepsis management must be based on the antimicrobial sensitivity, which needs to be reviewed from time to time. Also sepsis if identified and treated appropriately in time it has very good outcome. There are many studies on bacteriological profile in Western countries, but only a few in Indian set up. This study was done to know the current incidence of sepsis among the babies admitted to NICU, the pattern of etiological agent in neonatal sepsis and the antibiotic sensitivity profile of the microorganisms isolated.

Methodology

SOURCE OF DATA:

All Newborns admitted to St. Johns medical college hospital NICU with culture positive or probable sepsis are identified and data collected using the Performa.

INCLUSION CRITERIA: Newborns with risk factors, symptoms and signs of neonatal sepsis admitted to St.John's medical college NICU.

EXCLUSION CRITERIA: Age >28 days

METHOD OF DATA COLLECTION

Study conducted prospectively in babies admitted to NICU from first May 2011 to 30th April 2012. Those with signs of sepsis or with risk factors for sepsis were identified and included in study. Data was collected using performa. Investigations including CBC, CXR, Blood culture sensitivity and CRP were done on the same day (IT ratio and micro ESR were not done). CSF study and cultures of urine, surface swab, tracheal aspirate etc done only in selected cases. The components of sepsis screening in this study are TLC <5000 or >20000, ANC based on Manroe's and Mouzino's charts, CRP >1mg/dl and thrombocytopenia <100000.

CRITERIA FOR DIAGNOSIS OF SEPSIS

1. CONFIRMED SEPSIS

Newborn with clinical features of sepsis in whom the pathogen is isolated from blood, urine or CSF

2. PROBABLE SEPSIS

Newborn with any clinical features of sepsis with culture negativity, but having two or more positive tests in sepsis screen, or with radiological evidence of pneumonia.

3. ADDITIONAL EPISODE OF SEPSIS

Neonate is considered to have additional episode of sepsis, if another organism is cultured from a subsequent culture or if the infant meets the criteria for probable sepsis again after 10 days of appropriate antibiotic therapy with a definite symptom free interval of one week.

Babies with confirmed sepsis or probable sepsis were followed up, to study the outcome. Good outcome is one in which the subject recovered completely from sepsis. Any baby who lost follow up as in case of discharge against medical advice is considered dead.

DATA ANALYSIS

Data was analyzed using SPSS. Statistical test was done using Chi squared test. Where the numbers in a cell was less than five a Fisher’s exact test was used. P value of <0.05 was considered statistically significant.

Results

Characteristic of study population

There were 1169 admissions during the 1 year study period. Among them 908 were inborn and 261 were outborns. 502 babies who underwent septic screen were identified and enrolled in the study, in whom 236 babies were diagnosed to have sepsis and the total number of episodes of sepsis were 238(20.35%). Among the 238 babies with sepsis 168(70.58%) had EOS and 70(29.42%) had LOS. 11 babies who went discharge against medical advice within 48 hours were not included in analysis.

Sepsis in inborn versus outborn

	Inborn	outborn	
Total admission	908	261	
Episodes of sepsis	137(15.08%)	101(38.69%)	
EOS	104(75.9%)	64(66.3%)	
LOS	33(24.1%)	37(33.7%)	P 0.036

Gestational age distribution of babies with sepsis

Ges.age	Babies with sepsis	NICU admissions	percentage
<28 wk	9	9	100%
28-31	40	74	54.05%
32-35	91	429	21.21%
36-37	33	161	20.49%
>38	65	483	13.45%

Sepsis in different birth weight categories

	No of sepsis	No of babies	percentage
<1000 g	15	20	75.00
1000-1499	60	124	48.38
1500-2499	95	489	19.42
>2500	68	525	12.95

Risk factors

The risk factors evaluated as cause of EOS were peripartum maternal fever, PROM

>18 hours, MSAF, prematurity, low birth weight and birth asphyxia. In this study no significant association was found in causing EOS by peripartum maternal fever (p 0.413) or birth asphyxia (p 0.15), where as PROM >18 hours and MSAF are found to be related (p 0.05, 0.04)

Risk factors for early onset sepsis

variable	no	P value	Odds ratio
Maternal fever	16	0.423	-
PROM	107	0.03	1.03
MSAF	96	0.04	1.22
Extreme low weight	15	0.001	2.71
asphyxia	85	0.15	-

PROM, MSAF and extreme low weight are found to be clinically significant in causing EOS with odds ratio 1.03, 1.22 and 2.71 respectively. Though birth asphyxia was present in many babies with EOS the association was not statistically significant. There was no statistically significant association between intrapartum maternal fever and EOS.

Risk factors for late onset sepsis

variable	no	P value	Odds ratio
Extreme low weight	15	0.001	2.71
Central line ventilation	51	0.000	2.89
Associated complications(CHD,NEC, surgical intervention)	104	0.02	1.67
TPN	62	0.008	2.35
Duration of hospital stay	125	0.45	0.38
		0.03	1.02

Risk factors evaluated for LOS were ventilation (p 0.02), central line (p 0.000), associated surgical conditions (p 0.008) and TPN (p 0.45). Logistic regression analysis used to find the association between duration of hospital stay and LOS. It was found that the longer the duration of hospital stay, the more likely to develop LOS (odds ratio 1.02). TPN did not have statistically significant association in causing LOS.

Septic screen

Among the babies with sepsis 53.19% had at least 2 positive parameters in septic work up. 31.36% had x-ray evidence of pneumonia. Positive blood culture was found in 44 neonates (18.8%) with sepsis. either had two abnormal lab features and or radiological evidence of pneumonia. Among the babies with sepsis 5.88% had meningitis confirmed by positive CSF report.

The following table shows the sensitivity and specificity of sepsis markers used in this study.

	Confirmed sepsis (no.44)	Probable sepsis (no.194)	Total sepsis (no.238)	No sepsis (264)	sensitivity	specificity
CRP	92.23%	81.9%	87.06%	2%	85%	98%
Abnormal ANC	72.6%	62.46%	67.53%	21.68%	65%	79%
thrombocytopenia	60.94%	43.47%	50.2%	11.54%	54%	87.42%

Among the babies with sepsis, 87.06% had positive CRP. Abnormal ANC and thrombocytopenia were seen in 67.53% and 50.20% respectively. The sensitivity and specificity of above lab parameters were comparable to previous in India⁵⁹.

Clinical presentation:

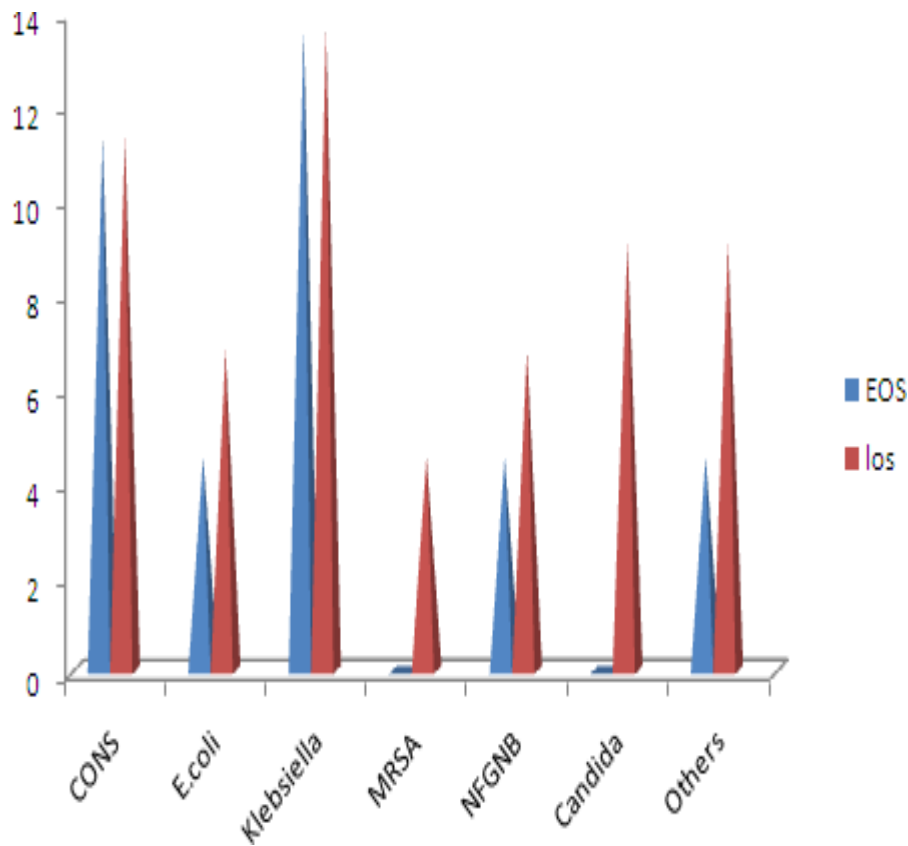
The most common presentation was respiratory distress (80.32%), followed by poor feeding(59.4%), abdominal distention(32.33), letharginess (29.42), seizures(22.7), hypoglycemia (18.93%), shock (15.38%), metabolic acidosis (9.46%), abnormal temperature (6.8%) and sclerema (0.05%).Majority of the patients had (77%) two symptoms at presentation, 12.30% had only one clinical feature and the remaining 10.7% had more than 2 clinical features. The percentage occurrence of clinical features found in this study is comparable with previous studies³¹.

Pattern of etiological agent in early and late onset sepsis

organism	EOS	LOS
CONS	5	5
E.coli	2	3
Enterobacter	-	1
GNB	-	1
Klebsiella	6	6
Salmonella	1	-
MRSA	-	2
NFGNB	2	3
Aeromonas	1	-
Staph.aureus	-	1
Strep.pneumoniae	-	1
Candida albicans	-	2
Candida nonalbicans	-	2

Klebsiella was the predominant pathogen causing both EOS and LOS in this study. Fungal sepsis noted only with LOS. 46.54% of patients with culture positive sepsis died compared to 12.22% in culture negative group with p value 0.000. Sepsis with gram negative sepsis got higher mortality compared to gram positive sepsis.

Bacteriological profile of neonatal sepsis



Both EOS and LOS had predominant gram negative septicemia. EOS had 29.42% gram positive and 70.58% gram negative isolates. LOS had 70.58% gram positive and 60.87% gram negative organism.

Antibiotic sensitivity pattern of blood culture isolates

	cephalo sporin	ciprofl ox	gent amy cin	amika cin	Netil myci	pipta z	mero pena m	MD R	meth icilli n	vanc omy cin
CONS	41.66%	75%	20.2 2%	48.34 %	83.33 %	-	-	-	-	100 %
E.coli	45%	74.56 %	8.80 %	51.5%	75%	100 %	100 %	-	-	-
Klebsiella	36.7%	45.45 %	12%	34.4%	37%	18.8 %	37.2 %	54. 5%	-	-
Staphylococ ci	29.45%	34%	-	-	-	-	-	-	44%	100 %
NFGNB	-	-	30%	40%	40%	40%	-	60 %	-	-
Enterococci	64.56%	71.38 %	30.0 3%	47.59 %	70.58 %	-	-	-	-	100 %

Outcome

The mortality (death+dama) due to sepsis in this study is 56(11.55%).Mortality (deth + dama) in culture positive group was 29.54% compared compared to 9.38% in culture negative group ($p < 0.001$). Outcome was also found to be related to the gestational age. Babies with age less than 28 weeks found to have higher percentage of mortality.

Gestational age and mortality

	Died+dama	Total no. in study	percentage
<28 week	9	18	50.00
28-31	11	64	17.18
32-35	18	166	7.83
36-38	8	70	7.14
>38	10	184	5.43

Birth weight and mortality

	Died + dama	Total no	percentage
<999 g	19	29	65.51
1000-1499	13	120	10.83
1500-2499	14	180	7.77
>2500	10	173	5.80

Lower the birth weight, greater the mortality due sepsis; p value 0.001

Discussion

This study was done in St.John's medical college hospital NICU which is a tertiary care referral centre with 35 beds including 7 ventilators. The number of deliveries during the one year study period was 2496, with 908 inborn NICU admissions and 261 out born NICU admissions. The incidence of neonatal sepsis among the neonates admitted to NICU In this study is 20.01% ,which is less compared to the reports from studies of tertiary care units in other developing countries where it was 39%⁶⁰,but higher than those reported in developed countries.

The incidence of sepsis was found to have strong association with birth weight and gestational age. 75% of babies with weight <1000 gm had developed sepsis, while it was only 12.95% in birth weight group of >2500. All babies <28 week had developed sepsis during hospital stay, while it was only 13.45% in babies more than 38 weeks.

The most common clinical presentation was respiratory distress (80%), followed by CNS symptoms of seizure poor feeding and letharginess. In babies with shock rate of mortality was high (p 0.001). This was comparable to the study conducted by Mondal et.al at Pondicherry³¹, while in another study conducted at Hubli Jaundice was the most common presentation⁶¹.

Among the risk factors evaluated for EOS PROM >18 hours, MSAF, prematurity and low birth weight were found to be statistically significant with p value 0.03, 0.04 and

0.001 respectively where as intrapartum maternal fever and asphyxia were not predictive of EOS in this study. In case of LOS prolonged ventilation, indwelling central line and associated surgical problems (PUV, NEC, PDA, CDH) were found to have statistically significant with p values 0.000, 0.02 and 0.008 respectively. A study done Kurien et.al found a statistically significant association between EOS with Meconium liquor and multiple vaginal examination. In the same study could not

Among the babies with sepsis 44 had culture positive sepsis (18.48%), which was much less compared to the existing reports, where it was 54.4% according to NNPD⁶². This could be due to prior antibiotic therapy and or lack of improvised microbiological techniques.

In this study the predominant organism both in EOS and LOS was Klebsiella, which was different from the existing reports. The most common organism of EOS in western countries is GBS. One of the studies from south India reported E.coli as the most common organism of EOS and Klebsiella in LOS⁶³. Emerging drug resistance is a concern on the basis of this study. Only 41.66% of the CONS isolate was sensitive to cephalosporins, which is the first line antibiotic in this nursery. 54.54% of the Klebsiella were multidrug resistant and among the Staphylococcal isolates 66.66% were methicillin resistant. Also 60% of the NFGNB 60% are resistant to all tested antibiotics. All the resistant organisms were isolated from babies with LOS.

The mortality due to sepsis in this study was 11.55 which is less compared to NNPD data where it is 19%. Extreme low birth weight and culture positive sepsis were the best predictors of mortality in neonatal sepsis.

Conclusion

- Neonatal sepsis is still common in our setting and continues to be a major cause of neonatal mortality.
- In this study incidence of neonatal sepsis was 20.35%. Lower the birth weight and gestational age, higher was the incidence of sepsis.
- PROM >18 hours, MSAF and prematurity were found to be associated with EOS while extreme prematurity, prolonged ventilation, indwelling catheters and associated complications were the risk factors which are found to be statistically significant in causing LOS.
- The number of culture positive sepsis was 18.48% among the babies with sepsis.
- It is alarming that most of the isolates in culture positive babies were resistant to the commonly used antibiotics. Though the first line antibiotic was second generation cephalosporin, only 50% of the organisms causing EOS were sensitive to second generation cephalosporins.
- Culture positive sepsis had a higher positive predictive value for mortality in neonatal sepsis.

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