

AN OBSERVATIONAL STUDY TO EVALUATE THE INCIDENCE OF MENINGITIS IN NEONATES WITH LATE-ONSET SEPSIS

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Abstract

Introduction: Bacterial sepsis and meningitis continue to be major causes of morbidity and mortality in newborns, particularly in premature infants. The present study was undertaken to know the incidence of meningitis in neonates with late onset sepsis.

Material and Methods: Hospital based observational study, conducted in department of Pediatrics, Shri Krishna Medical College and Hospital Muzaffarpur Bihar India, conducted for a period of one year. 324 patients fulfilling the inclusion criteria were included and subjected to detailed history, clinical examination followed by investigations.

Results: The annual incidence of meningitis in LOS was 15. The majority of patients (44.44%) presented in the age group of 3-7 days. In meningitis cases 100% cases were lethargic; seizures in 89%, fever in 53%. Blood culture was positive in 33.92% cases of meningitis. Meningitis was seen in 66.66% of proven gram negative sepsis as against 33.34 cases of proven gram positive sepsis and 14.28% expired with meningitis and 4.10% expired with no meningitis.

Conclusions: Meningitis is common in late onset sepsis, associated with high mortality.

Keywords: Meningitis, Preterm, LBW, Lumber puncture

Introduction

Neonatal sepsis is one of the most common causes of neonatal mortality.¹ Worldwide, neonatal mortality accounts for approximately 5 million deaths each year, 96% of which occurs in developing countries.^{2,3} In developing countries, sepsis is responsible for approximately 30%–50% of the total neonatal deaths.² According to the data from the National Neonatal-Perinatal Database (NNPD), incidence of neonatal sepsis is 30/1000 live births.⁴

Neonatal sepsis is mainly categorized as early onset sepsis and late onset sepsis (LOS). LOS presents after 72 h of age with septicaemia, pneumonia, or meningitis.¹ Neonatal meningitis is a serious consequence of LOS with a mortality of 33%–48% in developing countries.² NNPD reported the incidence of meningitis 3/1000 live births.¹ Incidence of LOS associated meningitis ranges from 3% to 30%.⁵⁻⁷ Studies in the UK have found that the incidence of meningitis varies from 1.3% to 3.5% in neonates with LOS.⁵ Kaul et al. reported 22.5% incidence of meningitis in neonates with suspected clinical sepsis in a tertiary care referral neonatal unit in North India.⁸

Two other studies from North India⁹ and Central India¹⁰ reported approximately 17% incidence of meningitis in neonates with LOS. However, there is a paucity of data

from West India. Hence, this study was planned to evaluate the incidence of meningitis in LOS.

Material and methods

The study was a hospital based observational study, conducted in department of Paediatrics, Shri Krishna Medical College and Hospital Muzaffarpur Bihar India. The hospital is the referral hospital housing the department of Paediatrics. The study was conducted on the neonates admitted in the division of neonatology, department of paediatrics, from 1st January, 2019 to 31st December 2019 for a period of one year.

Inclusion criteria

- Neonates older than 72 hours with signs and symptoms suggestive of sepsis viz:
- Clinical features of sepsis i.e. physical examination—demonstrating either circulatory, respiratory, CNS dysfunction or other features of sepsis.
- CVS signs— & symptoms as evident by the presence of tachycardia (heart rate more than 160/min) or bradycardia (heart rate less than 100/min) or capillary refill time more than 3 seconds.
- Respiratory signs— & symptoms as evidenced by the presence of grunting, flaring, retractions, tachypnea (respiratory rate more than 60/min) or apnea lasting more than 20 seconds.

- CNS signs→ & symptoms as evidenced by the presence of excessive crying, high pitched cry, bulging fontanelle and/or occurrence of/or history of convulsions.
- Other symptoms/signs of sepsis included will be;→ Lethargy, reduced feeding ability, no spontaneous movement, temperature more than 38°C, hypothermia, cyanosis, abdominal distension, increased pre feed aspirates in pre terms/LBW's, pustular lesions, umbilical sepsis.
- Positive C-reactive protein.

Exclusion criteria

- Patients with spina bifida (e.g. meningocoele, myelomeningocoele, lipomeningocoele).
- Anencephaly, other neural tube defects.

Methodology

In very sick neonates, after initial stabilisation. In each neonate with clinical features of sepsis, a detailed history and examination was done. Neonates with features of sepsis and positive CRP (was done as a qualitative estimation as positive/negative with the help of latex slide agglutination test) were subjected to the following investigations:

- 1) Blood culture (1 ml sample of blood was collected under all aseptic precautions by veni-puncture and placed in a pediatric blood culture bottle containing tryptic soya broth).
- 2) Lumber Puncture after informed consent taken from parents of neonate (Included CSF cytology, biochemistry and culture).
- 3) Complete blood count.
- 4) Blood sugar.
- 5) Serum bilirubin.
- 6) Renal function tests.
- 7) USG head was done in all patients with meningitis.
- 8) Chest X-ray.

Meningitis was labelled in a neonate whose CSF• findings satisfied all the following criteria (NNF Guidelines 2010):

- 1) CSF glucose less than the plasma glucose (sample to be taken prior to LP) by $\geq 50\%$.
- 2) CSF white cell count $>10/\text{cumm}$.
- 3) CSF protein $>80 \text{ mg/dl}$
- 4) With/without CSF culture positive. Other investigations like, Arterial blood gas analysis,• CT/MRI brain was done when required.

Statistical analysis

The recorded data was compiled entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations were calculated.

Results

A total of 2645 neonates were admitted during the study for various indications. Out of these 2645 neonates, 345 neonates were presented with LOS. A total of 324 neonates were eligible for the study after exclusion.

Table 1: Showing gender, gestation, weight distribution of cases.

Gender	No.	% age
Males	182	56.17
Term	141	77.47
Preterm	41	22.40
Females	142	43.82
Term	82	57.74
Preterm	60	41.95
Weight (kg)		
1.5	24	7.40
1.5-2.499	127	39.07
2.5	173	53.06

The annual incidence of meningitis in late onset was 15%

Table 2: Age of presentation of study group (n=324)

Age of presentation	No.	% age
3-7 days	144	44.44
8-12 days	58	17.84
13-17 days	53	16.25
18-22 days	44	13.45
23-27 days	25	7.62

The mean age of presentation was 10.3 ± 7.55 days

Table 3: showing the signs/symptoms in cases with meningitis.

Symptom/sign	No.
Lethargy	100
Seizures	89
Fever	53
Refusal/dec feeding	48
Respiratory signs	27
Abdomen distension	23
Shock/sclerema	14

Table 4: Showing the occurrence of meningitis in males vs. females, according to weight and according to gestation.

Variables	Meningitis		No meningitis	
	N=56	%	N=268	%
Gender				
Males	36	64.28	142	52.98
female	20	35.08	126	47.01
Weight				
1.5 kg	3	63.79	26	9.70
1.5-2.499 kg	34	32.20	98	36.56
2.5 kg	19	5	144	53.73
Gestation				
Preterm	37	66.07	100	37.31
Term	19	33.33	168	62.68

Table 5: Showing the microorganisms isolated from the blood cultures of septic neonates

Organisms	No.	% age
MRSA	19	42.22
Klebsiella	8	17.77
E.coli	7	15.55
Enterobacter	4	8.88
Acnitobacter	3	6.66
CoNS	2	4.44
Pseudomonas	2	4.44
total	45	100.0

Table 6: Showing the microorganisms isolates in the study group.

Organisms	No	% age
MRSA	19	90.47
CoNS	2	9.52
Total	21	100
Klebsiella	8	33.33
E.coli	7	29.16
Enterobacter	4	16.66
Acnitobacter	3	12.5
Pseudomonas	2	8.33
Total	24	100

Table 7: Showing the microorganisms isolated from the blood cultures of meningitis neonates.

Organisms	No	% age
MRSA	9	40.90
Klebsiella	6	27.27
E.coli	4	18.18
Enterobacter	1	4.54
Acnitobacter	1	4.54
CoNS	1	4.54
Total	22	100.0

Table 8: Showing Blood culture positivity in meningitis and non-meningitis patient.

Blood culture	Meningitis		No meningitis	
	No	% age	No	% age
Positive	19	33.92	19	7.08
Negative	37	66.07	251	93.65
Total	56	100.0	268	100.0

Above Table 8 shows blood culture was positive in 33.92% cases of meningitis vs. 7.08% cases that had sepsis only but no meningitis.

Table 9: Showing the risk of meningitis in gram positive vs. gram negative sepsis.

Groups	Gram negative		Gram positive	
	No	% age	No	% age
Meningitis	14	66.66	7	29.17
No meningitis	7	43.34	17	70.83
Total	21	100.0	24	100.0

The above Table 9 gives us the values of presence or absence of meningitis in the cases with proven gram positive versus gram negative septicaemia. Meningitis was

seen in 66.66% (14/21) cases of proven gram negative sepsis and 29.17% (7/24) cases of proven gram positive sepsis.

Table 10: Showing the outcome of meningitis vs. non meningitis cases.

Outcome	Meningitis		No meningitis	
	No	% age	No	% age
Expired	8	14.28	11	4.10
Recovered	48	85.71	257	95.89

The above Table 10 shows the outcome of meningitis versus no meningitis in LOS cases in the study group in terms of recovery and death of the case. The death in the meningitis cases were 14.28 % while the same figure for non-meningitis cases was 4.10%.

Discussion

Neonatal sepsis is one of the commonest causes of neonatal morbidity and mortality. Near about 0.3-3% of neonates with sepsis do have meningitis but in case of LOS, the incidence of meningitis is higher, even upto 30%. The overlapping clinical manifestations of septicaemia and meningitis make it very difficult to differentiate a neonate with meningitis from the one with septicaemia alone as meningitis is associated with much more mortality and morbidity, it is always better to have a high suspicion for meningitis while treating neonates with septicaemia. The incidence of meningitis in LOS in our study was 15%. Similar observation was reported by Visser and Hall where 24% septic neonates with LOS had meningitis.¹¹ Other studies reported prevalence of meningitis in neonates with late onset sepsis as 17.9%, 17% and 17.2% respectively.¹²⁻¹⁴

The neonates with meningitis in the present study had diverse signs and symptoms with lethargy predominating in 100% cases followed by seizures, fever, and refusal/decreased feeding and respiratory sign/symptoms in 89%, 53%, 48% and 27%, respectively. Abdominal distension and shock/sclerema was noticed in 23% and 14% cases respectively. Similar to these observations another study also reported feed intolerance and lethargy as most common clinical features in meningitis, present in 73.3% and 60% cases respectively¹², while Hoque MM et al.¹⁵ observed no difference in the clinical features in cases with meningitis and septicaemia alone. The patients who were diagnosed with only septicaemia and no meningitis had lethargy and other general symptom including refusal of feed/decreased feeding in 100%, respiratory signs, gastrointestinal sign/symptoms, seizures in 58.5%, 31.7% and 13.4% respectively while shock was observed in only 1.2%. Karthikayen and Premkumar observed that in cases with culture proven sepsis, lethargy with refusal of feeds (28%), fever (28%) and respiratory distress (31.3%) were the major presenting features.¹⁶

Blood culture was positive in 45 (12.7%) septic neonates with Gram positive organisms comprising 46.66% (21/45) and Gram negative organisms comprising 53.34% (24/45). Studies from the literature^{14,17,18} reported that Gram positive organisms contributed to the culture positive isolates in 39%, 41% and 53.4% respectively whereas Gram negative organisms contributed to the same in 61%, 59% and 46.6% respectively.

Among the meningitic group blood culture was positive in 19 (33.92%) cases. Meningitis was seen in 66.66% cases of proven gram negative sepsis and 33.34% cases of proven gram positive sepsis. The overall mortality was 5.86% (19/324) which included preterms who accounted for 47.36% (9/19) of total deaths.

Out of the neonates having meningitis, 14.28% expired (8/56) in the present study which is similar to the previous study¹⁴ which observed that meningitis was associated with a mortality of 20% in his study. Two studies reported a much higher mortality rate in the meningitis group i.e. 37.7% and 37.5% respectively but in both these studies EOS group was also included along with LOS group.^{15,19} Al Harithi et al.²⁰ had observed a mortality of 48% in neonatal meningitis but they included EOS cases also and meningitis was documented only on CSF culture positivity.

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