Importance of Obtaining Lumbar Puncture in Neonates with Late Onset Septicemia a Hospital Based Observational Study from North-West India

Varun Kaul, Rekha Harish, Sandesh Ganjoo[1], Bella Mahajan[2], Sunil Kumar Raina[3], Diptiman Koul[4]

Department of Pediatrics, Government Medical College, Jammu, Jammu and Kashmir, [1]Department of Obstetrics and Gynaecology, Dr. RPGMC, Tanda, Kangra, Himachal Pradesh, [2]Department of Microbiology, Government Medical College, Jammu, Jammu and Kashmir, [3]Department of Community Medicine, Dr. RPGMC, Tanda, Kangra, Himachal Pradesh, [4]Department of Medicine, Government Medical College, Kashmir, Jammu and Kashmir, India

ABSTRACT

Objectives: The objective of this study was to estimate the prevalence of meningitis in cases with late onset septicemia (LOS). **Materials and Methods:** A prospective study was carried out for a period of 1 year in a tertiary care hospital in North West India to estimate the prevalence of meningitis in cases of LOS. In all the admitted neonates with features of sepsis with a positive C-reactive protein, a lumbar puncture (LP) was carried out and results interpreted on the basis of cerebrospinal fluid (CSF) cytology and biochemistry. Simultaneous blood and CSF cultures were also taken. All other baseline investigations were performed and in those diagnosed as meningitis an ultrasound head was carried out prior to discharge. No urine cultures were obtained. **Results:** The study showed the prevalence of meningitis as 22.5% in neonates with LOS with statistically significant implications of meningitis versus gestation, sex, acquired the place of infection, and outcome in terms of sequelae/mortality. **Conclusions:** Meningitis is commonly associated with late onset sepsis hence LP should be the standard of care in such neonates as the treatment protocol and the outcome is directly proportional to the diagnosis at initial presentation.

Key words:
Late onset septicaemia, meningitis, neonates

INTRODUCTION

Invasive neonatal infections are important causes of mortality and morbidity in newborn infants all over the world including the industrialized countries with high hygienic standards, deliveries at hospitals, access to antimicrobial agents for prophylaxis, treatment, and facilities for advanced intensive care. Most studies of incidence and etiology of neonatal sepsis and meningitis come from these countries although there is a lack of data from the developing countries where the mortality and morbidity are probably immense.

Sepsis is responsible for about 30-50% of the total neonatal deaths in developing countries.[1,2] The incidence of neonatal sepsis according to the data from National neonatal perinatal database is 30/1000 live births.[3] The database comprising 18 tertiary care neonatal units across India found sepsis to be one of the most common causes of neonatal mortality contributing to 19% of all neonatal deaths.[3,4] Septicemia was the most common clinical category with incidence of 23/1000 live births while the incidence of meningitis was reported to be 3/1000 live births.[3] Late onset septicemia (LOS) usually presents after 72 h of age.[5-10] Any newborn with bacterial sepsis is also at risk of meningitis. As such the incidence of meningitis in neonatal sepsis has varied from 0.3% to 3% in various studies, but LOS has been reported to be fairly associated with meningitis; with percentage ranging from 3% to 30%.[5,11-13] Hence, the work-up for any newborn with signs of infection should include a spinal tap.[14]

Keeping this in view a study to evaluate the Importance of obtaining lumbar puncture (LP) in neonates with LOS was planned.

MATERIALS AND METHODS

The study, observational in nature, was conducted on neonates admitted in the division of neonatology, department of pediatrics, of a tertiary care hospital in

Address for correspondence:
Dr. Sunil Kumar Raina,
Department of Community Medicine, Dr. RPGMC, Tanda, Kangra, Himachal Pradesh, India. E-mail: ojasrainasunil@yahoo.co.in

Access this article online	
Quick Response Code:	Website: www.jcnonweb.com
	DOI: 10.4103/2249-4847.116407

northwest India over a period of 1 year from November 2008 to October 2009.

Inclusion criteria

- Neonates older than 72 h with signs and symptoms suggestive of sepsis viz:
  - Clinical features of sepsis, i.e., physical examination demonstrating either circulatory, respiratory, Central Nervous System (CNS) dysfunction or other features of sepsis
  - Circulatory dysfunction was 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 s
  - Respiratory dysfunction was evidenced by the presence of grunting, flaring, retractions, tachypnea (respiratory rate more than 60/min) or apnea lasting more than 20 s
  - CNS dysfunction was evidenced by the presence of excessive crying, high pitched cry, bulging fontanels and/or occurrence of/or history of convulsions
  - Other symptoms/signs of sepsis included were; Lethargy, reduced feeding ability, no spontaneous movement, temperature more than 38°C, hypothermia, cyanosis, abdominal distension, increased pre-feed aspirates in pre-terms/Low Birth Weight, pustular lesions, umbilical sepsis.
- Positive C-reactive protein (CRP).

Exclusion criteria

- Patients with spina bifida
- Anencephaly, other neural tube defects
- In very sick neonates, after initial stabilisation.

Definitions used

Hospital acquired infection:

- Those neonates who were aseptic (CRP negative) at admission to the hospital.
- Those who developed sepsis during hospital stay/or presented within 1 week of discharge from the hospital (CRP positive).

Community acquired infection: Those neonates who reported from the community at the first visit and were having features of sepsis at presentation (CRP positive).

In each neonate with clinical features of sepsis, a detailed history and examination was carried out as per a structured performa.

Neonates with features of sepsis and positive CRP (done as a qualitative estimation as positive/negative with the help of latex slide agglutination test) were subjected to the following investigations:

- LP (included cerebrospinal fluid (CSF) cytology, biochemistry and culture)
- 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)
- Complete blood count (including band cell count)
- Blood sugar, serum bilirubin (when required on clinical suspicion), and Renal function tests
- Chest X-ray.

Meningitis was labelled in a neonate whose CSF findings satisfied all the following criteria:

- CSF glucose less than the plasma glucose (sample was taken 30 min prior to LP) by ≥50%
- CSF white cell count >10/cumm
- CSF protein >80 mg/dl.
- With/without CSF culture positive.

Other investigations such as liver function tests, Prothrombin Time Index (PTI), arterial blood gas analysis, computed tomography/magnetic resonance imaging brain were carried out as and when required.

Ultrasonography of head was carried out in all patients with meningitis, at the time of discharge.

The neonates were followed-up, to determine their final outcome.

Statistical analysis

The data were analyzed with the help of computer software Epi-Info version 6.0.1 and SPSS 10.0 for Windows. Chi-square test was used to ascertain statistical significance among the proportions. Prevalence along with 95% confidence limits was calculated to express the magnitude. Odd's ratio with 95% confidence limits was estimated vis a vis the presence or absence of meningitis in late onset neonatal sepsis. A $P<0.05$ was considered as statistically significant unless proved otherwise.

RESULTS

Mean weight was 2.515 kg with a standard deviation of 0.606 kg. Majority (51.8%) of the neonates came under the normal weight group while 41.8% constituted the low birth weight group and only 6.4% were in the Very Low Birth Weight group. The sex distribution in the study group was equal with males and females being 51 each with a sex ratio of 1. Demographic profile of cases is depicted in Table 1. The mean age of presentation of LOS in the hospital acquired group was 5.73 days with a standard deviation of 2.85 days

vis 5.73±2.85 and that in the community acquired group was 15.93±6.27 days respectively.

Out of 102, 23 were having meningitis, which corresponded to 22.5% prevalence in this study with a 95% confidence interval of 14.4-30.6. Hospital acquired versus community acquired meningitis vis a vis the age at presentation is depicted in Table 2.

Clinical presentation of neonates with meningitis is depicted in Table 3. The statistical correlation with respect to the various factors in the meningitis versus no meningitis group is depicted in Table 4. The blood culture isolates in the septic neonates is depicted in Table 5 with CSF culture being sterile in all cases with meningitis diagnosed as per the criteria mentioned above.

DISCUSSION

In the present study, 22.5% (23/102) of neonates with LOS had meningitis. Almost comparative observation was reported by Visser and Hall where in the prevalence of meningitis in septic neonates with LOS was 24%.[15] Schwersenski *et al.* and Hristeva *et al.* reported the prevalence of meningitis in LOS as 3.5% and 6.8% respectively, but the former excluded neonates more than 72 h and less than 7 days from their study and the latter delayed the LP procedure in all the babies who had respiratory distress.[11,16] Kenyan study, Brazilian study and Asian study conducted by various authors reported prevalence of meningitis in neonates as 17.9%, 17% and 17.2% respectively.[17-19] However, Brazilian study included both early and late onset cases of septicemia.[18] These variations in the prevalence could be explained on the basis of the fact that meningitis was diagnosed in all these studies on the basis of CSF culture positivity alone.

In the present study, the LBW neonates with sepsis were 45.1% and pre-terms with sepsis were 21.6%. Out of neonates having meningitis 52.2% were pre-term and 47.8% were term. This high prevalence of meningitis in LBW and especially pre-term has also been reported by various studies.[17,20,21] In the Brazilian study, it was observed that 81% of neonates with meningitis were pre-term, which appears to be due to the fact that he involved both Early Onset Septicemia (EOS) and LOS cases in his study.[18] In a study performed at Taiwan, it was observed that LOS was significantly more common in VLBW and pre-term neonates.[21]

Out of all the neonates having meningitis in the present study, 73.9% and 26.1% were males and females respectively and this difference was statistically significant. For pre-terms, the same data extrapolated wasn't statistically significant. This difference in the pattern of observance can be explained on the basis of better available neonatal intensive care set up and early initiation of the drug therapy based on the available sensitivity reports. In the present study, meningitis was more frequently observed in the hospital acquired group as compared to the community acquired group (33.9% and 10.2% respectively), the difference being statistically significant. The mean age of presentation in hospital acquired LOS was 5.73 (±2.85) days

Table 1: Profile of patients presenting with late onset septicemia

Parameter	Number (*n*=102) (%)
Weight (kg)	
<1.5	7 (6.9)
1.5-2.5	46 (45.1)
>2.5	49 (48)
Sex	
Male	
Term	41 (40.2)
Pre-term	10 (9.8)
Female	
Term	39 (38.2)
Pre-term	12 (11.8)
Age of presentation (days)	
3-7	46 (45.1)
8-12	18 (17.6)
13-17	14 (13.7)
18-22	17 (16.7)
23-27	7 (6.9)

Table 2: Age of presentation vis a vis the hospital acquired versus community acquired group and meningitis and no meningitis group

Age of presentation (days)	Hospital acquired		Community acquired	
	Meningitis *n* (%)	No meningitis *n* (%)	Meningitis *n* (%)	No meningitis *n* (%)
3-7	15 (14.8)	31 (30.4)	Nil	Nil
8-12	2 (1.9)	4 (3.9)	2 (1.9)	10 (9.8)
13-17	1 (1)	0	1 (1)	12 (11.8)
18-22	0	0	2 (1.9)	15 (14.8)
23-27	0	0	0	7 (6.8)

Table 3: The signs/symptoms in cases with meningitis

Symptom/sign	Percentage
Lethargy	100
Seizures	92
Fever	49
Refusal/decreased feeding	46.2
Respiratory signs	25
Abdominal distention	21
Shock/sclerema	11

Table 4: Various parametric differences between meningitis versus no meningitis cases with statistical interpretation

Parameter	Meningitis	No meningitis	Yate's Chi-square	Odd's ratio	95% confidence interval	*P* value
Gestation						
Preterm	12	16	7.582	4.29	1.60-11.50	0.005
Term	11	63				
Sex						
Males	17	34	5.614	3.75	1.33-10.52	0.017
Females	6	45				
Place of infection						
Hospital acquired	18	35	6.925	4.52	1.52-13.4	0.008
Community acquired	5	44				
Gram negative versus gram positive sepsis (blood culture isolates)						
Gram negative	8	4	3.094	8	1.12-56.79	0.078
Gram postive	2	8				
Outcome						
Mortality/sequelae	9	11	5.67	3.97	1.38-11.38	0.017
Recovered	14	68				

Table 5: Organisms isolated from septic neonates

MRSA	Acinetobacter	Klebsiella	Enterobacter	Pseudomonas	Coag neg staph	*Escherichia coli*
9	4	4	2	1	1	1

MRSA – Methicillin resistant Staphylococcus aureus

and that in community acquired group was 17.93 (±7.34) days. Similar observations were observed in a Chinese study for community acquired LOS (16±7 days). The mean age of presentation of cases of meningitis was 5.64 (±3.47) days in the hospital acquired group and 11.55 (±7.2) days in community acquired group with a mean age of presentation of cases of meningitis as 8.6 (±5.33) days as a whole.[22] The delayed age of presentation of community acquired meningitis was possibly due to the poor health-care seeking behavior in the community. However, in a study performed at Kenya the mean age of the presentation was 4.1 days, but their study included both EOS and LOS cases.[17]

Out of the neonates having meningitis, 26.1% expired (6/23) in the present study which lies almost in the middle of the range as compared to the observations made by Tiskumara *et al.* who observed in their study that meningitis is associated with mortality of 20% viz a viz a much higher mortality rate in the meningitis group, i.e., 37.7% and 37.5% as reported by Longe *et al.* and Hoque *et al.* respectively. However, in both these studies EOS group was also included along with LOS group.[19,20,23]

Sequelae in the form of hydrocephalus were observed in 13% (3/23) cases of meningitis cases. The combined recovery versus sequlae/death risk in cases of meningitis was 60.9% and 39.1% versus 86.1% and 13.9% in those without meningitis respectively, the comparisons being statistically significant. In the present study, the combined risk of mortality/sequeale is still high about 39.1%, whereas Bennhagen *et al.* in their study conducted in Sweden had observed that the combined mortality and handicap rates had decreased from 34% in 1976 to 15% in 1983.[24] This is probably because of their fast improving intensive care facilities. Al-Harthi *et al.* had observed mortality of 48% in neonatal meningitis, but they included EOS cases also and meningitis was documented only on CSF culture positivity.[25]

CONCLUSIONS

Meningitis is a major association with LOS cases. It is associated with significant morbidity and mortality and entails a prolonged antibiotic course. Thus, it is concluded that a LP is important in the evaluation of LOS cases and should be the standard of care in its management.

REFERENCES

1. Bang AT, Bang RA, Baitule SB, Reddy MH, Deshmukh MD. Effect of home-based neonatal care and management of sepsis on neonatal mortality: Field trial in rural India. Lancet 1999;354:1955-61.
2. Vergnano S, Sharland M, Kazembe P, Mwansambo C, Heath PT. Neonatal sepsis: An international perspective. Arch Dis Child Fetal Neonatal Ed 2005;90:F220-4.
3. NNPD, Report of the National Neonatal Perinatal Database (National Neonatology Forum) 2002-2003 http://www.newbornwhocc.org/pdf/nnpd_report_2002-03.PDF [Last accessed on 27/04/2013].
4. Sankar MJ, Agarwal R, Deorari AK, Paul VK. Sepsis in the newborn. Indian J Pediatr 2008;75:261-6.

5. Baltimore RS. Neonatal nosocomial infections. Semin Perinatol 1998;22:25-32.
6. Berger A, Salzer HR, Weninger M, Sageder B, Aspöck C. Septicaemia in an Austrian neonatal intensive care unit: A 7-year analysis. Acta Paediatr 1998;87:1066-9.
7. Gerdes JS, Polin R. Early diagnosis and treatment of neonatal sepsis. Indian J Pediatr 1998;65:63-78.
8. Tseng YC, Chiu YC, Wang JH, Lin HC, Lin HC, Su BH, *et al*. Nosocomial bloodstream infection in a neonatal intensive care unit of a medical center: A three-year review. J Microbiol Immunol Infect 2002;35:168-72.
9. Haque KN, Khan MA, Kerry S, Stephenson J, Woods G. Pattern of culture-proven neonatal sepsis in a district general hospital in the United Kingdom. Infect Control Hosp Epidemiol 2004;25:759-64.
10. Makhoul IR, Sujov P, Smolkin T, Lusky A, Reichman B. Epidemiological, clinical, and microbiological characteristics of late-onset sepsis among very low birth weight infants in Israel: A national survey. Pediatrics 2002;109:34-9.
11. Schwersenski J, McIntyre L, Bauer CR. Lumbar puncture frequency and cerebrospinal fluid analysis in the neonate. Am J Dis Child 1991;145:54-8.
12. Malbon K, Mohan R, Nicholl R. Should a neonate with possible late onset infection always have a lumbar puncture? Arch Dis Child 2006;91:75-6.
13. Townsend T. Infection. In: Seidel HM, Rosenstein BJ, Pathak A, Mckay W Primary Care of the Newborn: Mobile Medicine Series, Saunders, 4e, 2006:306.
14. Thilo EH, Adam A, Rosenberg AA. Bacterial infections. The newborn infant. In: Hay WW, Levin MJ, Sandheimer JM, Deterding RR. Current Pediatric Diagnosis and Treatment. Mc Graw Hill, 17th ed 2004 :51.
15. Visser VE, Hall RT. Lumbar puncture in the evaluation of suspected neonatal sepsis. J Pediatr 1980;96:1063-7.
16. Hristeva L, Bowler I, Booy R, King A, Wilkinson AR. Value of cerebrospinal fluid examination in the diagnosis of meningitis in the newborn. Arch Dis Child 1993;69:514-7.
17. Laving AM, Musoke RN, Wasunna AO, Revathi G. Neonatal bacterial meningitis at the newborn unit of Kenyatta National Hospital. East Afr Med J 2003;80:456-62.
18. da Silva LP, Cavalheiro LG, Queirós F, Nova CV, Lucena R. Prevalence of newborn bacterial meningitis and sepsis during the pregnancy period for public health care system participants in Salvador, Bahia, Brazil. Braz J Infect Dis 2007;11:272-6.
19. Tiskumara R, Fakharee SH, Liu CQ, Nuntnarumit P, Lui KM, Hammoud M, *et al*. Neonatal infections in Asia. Arch Dis Child Fetal Neonatal Ed 2009;94:F144-8.
20. Longe AC, Omene JA, Okolo AA. Neonatal meningitis in Nigerian infants. Acta Paediatr Scand 1984;73:477-81.
21. Jiang JH, Chiu NC, Huang FY, Kao HA, Hsu CH, Hung HY, *et al*. Neonatal sepsis in the neonatal intensive care unit: Characteristics of early versus late onset. J Microbiol Immunol Infect 2004;37:301-6.
22. Zhu ML, Zheng G, Chen JN, Lin ZL, Zhu JH, Lin J. Comparative analysis of the pathogens responsible for hospital acquired and community acquired late onset neonatal septicemia. Zhonghua Er Ke Za Zhi 2008;46:124-7.
23. Hoque MM, Ahmed AS, Chowdhury MA, Darmstadt GL, Saha SK. Septicemic neonates without lumbar puncture: What are we missing? J Trop Pediatr 2006;52:63-5.
24. Bennhagen R, Svenningsen NW, Békássy AN. Changing pattern of neonatal meningitis in Sweden. A comparative study 1976 vs. 1983. Scand J Infect Dis 1987;19:587-93.
25. Al-Harthi AA, Dagriri KA, Asindi AA, Bello CS Neonatal meningitis. Neurosciences 2000;5:162-5.

How to cite this article: Kaul V, Harish R, Ganjoo S, Mahajan B, Raina SK, Koul D. Importance of obtaining lumbar puncture in neonates with late onset septicemia a hospital based observational study from north-west India. J Clin Neonatol 2013;2:83-7.

Source of Support: Nil, **Conflict of Interest:** None declared.