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Original Research Article

Incidence and clinico-demographic characteristics of neonatal meningitis in clinically suspected sepsis: an observational study

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ABSTRACT

Background: Authors objective was to study the incidence and risk factors for meningitis in neonates with clinical suspicion of sepsis in Neonatal Intensive Care Unit (NICU) of tertiary care hospital of Mumbai, India.
Methods: This descriptive observational study enrolled Consecutive 92 patients of either sex with suspected neonatal sepsis admitted in NICU of Tertiary Care Hospital. All neonates admitted to NICU with clinical suspicion of sepsis or developing signs of sepsis during NICU stay were included in study. Exclusion criteria were 1.Neonates with hemodynamic instability 2.major congenital malformations 3.contraindication or no willingness for Lumber puncture (LP) 4.neonates who have received intravenous antibiotics for more than 24 hours elsewhere.
Standard data collection form was used to collect all demographic data and clinical characteristics of neonates.
Results: Incidence of meningitis in study population was 7.6%. Cases of meningitis in study population had mean birth weight 1.91 kg, 71.43% were preterm, 57.14% vaginaly delivered, 42.86% by LSCS, Premature rupture of membrane (PROM) observed in 28.57% cases. Meconium stained liquor in 42.86% cases and foul smelling liquor in 28.57% cases observed. 42.86% cases required resuscitation and 28.57% received surfactant therapy. Poor feeding (100%), lethargy (85.71%), weak cry (85.71%) and tachypnea (50.58%). Retractions (85.71%), Grunting (57.14%) and Nasal flaring (42.86%) were clinical presentation. Lab findings in a case of meningitis: mean Hemoglobin (Hb) 15.22 gm%, Leukopenia (28.57%), Leukocytosis 28.57%, Absolute Neutrophil count (ANC) <1800 (28.57%), Thrombocytopenia 42.85%, blood culture positive (28.57%) hypoglycemia (28.57%), CSF white cell count (124.57cells/ml.), mean CSF protein level (60 mg/dl.) Mean CSF glucose level (40.86 mg/dl.) CSF culture was positive in two cases of meningitis.
Conclusions: Authors study highlights the diagnostic utility of routine lumbar puncture in neonates with clinically suspected sepsis.

Keywords: Cerebrospinal Fluid, Cerebrospinal Fluid culture, Clinically Suspected sepsis, Lumber puncture, Meningitis, Neonate

INTRODUCTION

Bacterial sepsis and meningitis continue to be major cause of morbidity and mortality in neonates. WHO estimates that there are approximately 5 million neonatal deaths per year. The overwhelming majority (98%) occur in developing countries.[1] Meningitis occurs more commonly during the first month of life than during any other subsequent period and it is associated with high morbidity and mortality.[2,3] Meningitis complicates 20% cases of early-onset and 10% cases of late-onset sepsis.[4] The incidence of neonatal meningitis in western countries varies from 0.2-0.5 cases per thousand live births but

much higher rates of 1.1-1.9 per 1000 have been reported from developing countries.[5]

The case fatality rates (CFRs) in bacterial meningitis was 26% in developed countries even with antimicrobial therapy and availability of advanced intensive care, which were higher ranging from 16-32% in developing countries.[6]

Permanent neurological sequelae such as hearing loss, mental retardation, seizures and behavioral changes may occur in up to 50% of survivors even having antimicrobial therapy.[7]

Because of the high mortality and morbidity resulting from bacterial meningitis, rapid and accurate diagnosis is needed to increase the survival rate and decrease complications. Therefore delay in diagnosis and initiation of proper antimicrobial therapy can result a poor outcome. Bacterial meningitis cannot always be diagnosed on the basis of clinical sign and symptoms. So laboratory support is essential for the rapid diagnosis of meningitis.[8] Conventional methods for diagnosis of bacterial meningitis is based on examination of CSF including physical, biochemical, cytological, Gram staining and culture.[9] The early signs and symptoms of neonatal meningitis are very non-specific and indistinguishable from those of septicemia and other non-infective causes such as birth asphyxia, respiratory distress syndrome and hypoglycemia amongst others.[3,10] A high index of suspicion is therefore necessary and laboratory support essential to make a diagnosis and offer appropriate treatment. It is also important to look at commonest clinical features which can guide us in undertaking invasive investigations.

It is important that neonatal meningitis must be diagnosed as early as possible on the basis of the 'soft' signs of early neonatal infection such as temperature changes, jaundice, apnea, tachypnea, tachycardia and CSF studies.[11]

In our hospital, we have a large number of neonates with sepsis. The high index of suspicion and laboratory support essential for early diagnosis of those with meningitis and it is of great significance for early institution of appropriate and adequate management. Hence this study is undertaken to determine the number of neonates with meningitis in clinically suspected cases of neonatal sepsis.

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.[12] Two other studies from North India and Central India reported approximately 17% incidence of meningitis in neonates with late onset sepsis.[9,10] However, there is a paucity of data from West India. Hence, this study was planned to evaluate the incidence of meningitis and associated risk factor in clinically suspected sepsis.

METHODS

This descriptive observational study was conducted at a tertiary care hospital in neonatal intensive care unit (NICU), Mumbai, West India. Ethical Committee of the Institute approved the study protocol. Neonates, who were born in our hospital or transferred to the NICU from March 2014 to February 2015. Neonates admitted to NICU, with clinical suspicion of sepsis were enrolled in the study. History included maternal fever (>38.5°C), prolonged mature rupture of membranes (>18hours), type of delivery, surfactant therapy, meconium stained liquor, birth weight, gestational age and any resuscitative procedures done. Sign and symptoms of sepsis were defined as the following: hypothermia, poor feeding, apnea, tachypnea, heart rate abnormalities, capillary refilling time, icterus, cyanosis, foul smelling umbilical discharge, nasal flaring, grunt, retractions, respiratory distress, abdominal distension, irritability, lethargy and weak cry. Neonates with cardiorespiratory instability, major congenital malformations, LP contraindicated or consent for LP is not given.

And who have received intravenous antibiotics for >24 hours were excluded from study. Meningitis diagnosed as per the following criteria: a. CSF cytology showing leukocyte count 11+10 with 90th percentile being 22. Proportion of polymorphonuclear leukocyte is 2.2+3.8% with 90th being 6. b. CSF glucose 46+10mg/dl or <50% of blood glucose (Blood glucose done simultaneously). c. CSF protein 84+45 mg/dl. d. CSF positive for bacterial pathogens by Gram stain or positive CSF culture. Neonates with clinical suspicion of sepsis were undergone following investigations Hemoglobin, Total White Blood Cell (WBC) count, Differential WBC count and Absolute Neutrophil count (ANC), Blood glucose level, C - reactive protein (CRP),Blood culture and sensitivity, Arterial blood gas (in selected cases),CSF biochemical, pathological and microbiological analysis, CSF culture and sensitivity, Chest X ray. Baseline characteristics of the study population were recorded in predesigned pro forma.

Study outcome

- Incidence of meningitis in clinically suspected sepsis.
- Maternal and neonatal risk factors for meningitis in clinically suspected sepsis.

Statistical methods

Statistical analysis of data was carried out using the SPSS 16.0 program. Means of quantitative data were compared using the student's t-test and Mann Whitney U-test where applicable while the Chi-square and Fisher's exact tests were used for qualitative data. A p-value of less than 0.05 was considered significant.

RESULTS

Statistically 92 patients that satisfied the inclusion criteria included in this study. Seven of the 92 patients studied had meningitis as per the case definition, giving an overall incidence rate of 7.6%.

The clinic-demographic profile of neonates with clinically suspected sepsis is summarized in (Table 1).

Early onset sepsis (EOS) found in 44(47.83%) cases (included 4(57.14%) of meningitis and 40 (47.06%) of non-meningitis. Late onset sepsis were found in 48 (52.17%) cases, (3 (42.86%) of meningitis and 45(52.94%) cases of no meningitis) (P =0.70).

In all mentioned maternal factors, difference between meningitis and no meningitis cases was statistically insignificant (Table 1).

Table 1: Clinico-demographic characteristics of study population (n=92).

Sex	All cases (n=92	Meningitis (n=7)	No Meningitis (n=85)	p- value
Male	51(55.43%)	4(57.14%)	47(55.29%)	0.376
Female	41(44.56%)	3(42.86%)	38(44.7%)	
Mean Birth weight (kg)	1.97(1.25-2.69)	1.91(1.36-2.72)	1.87(1.24-2.7)	0.81
Mean Gestational age (weeks)	34.5(30.62-37.84)	33.2(29.82-38.5)	35.6(30.66-37.82)	0.96
Preterm	72	5	67	0.76
Term	20	2	18	
Maternal Risk factors				
Maternal fever	11(11.96%)	0(0%)	11(12.94%)	0.84
PROM	20(21.74%)	2(28.57%)	18(21.18%)	0.64
Meconium stained Liquor	34(36.96%)	3(42.86%)	31(36.47%)	0.73
Foul smelling Liquor	29(31.52%)	2(28.57%)	27(31.76%)	0.86
Prolonged Labour	2(2.17%)	0(0%)	2(2.35%)	0.68
Clinical parameters				
Poor feeding	87(94.57%)	7(100%)	80(94.11%)	0.50
Weak Cry	57(61.96%)	6(85.71%)	51(60%)	0.08
Lethargy	51(55.43%)	6(85.71%)	45(52.94%)	0.09
Tachypnea	49(53.26%)	6(85.71%)	43(50.58%)	0.07
Retractions	66(71.73%)	6(85.71%)	60(70.59%)	0.39
Grunting	50(54.34%)	4(57.14%)	46(54.11%)	0.87
Nasal Flaring	60(65.21%)	3(42.86%)	57(67.06%)	0.19

Resuscitation was done in total 34(36.96%) cases. Three (42.86%) cases among meningitis and 31(36.45%) cases among no meningitis required resuscitation at birth. Surfactant therapy was given to 29(31.52%) cases. Two (28.57%) among meningitis and 27(31.76%) among no meningitis required surfactant therapy.

In above clinical symptoms Tachypnea, Weak cry and Lethargy were more common in meningitis (Table 1).

Most common signs observed were Retractions (71.73%), Nasal flaring (65.21%) and Grunting (54.34%) (Table 1).In cases with meningitis, leukopenia was present in 28.57%. Leukocytosis was present in 28.57%.Absolute Neutrophil count (ANC) <1500 observed in 28.57% of cases.

Thrombocytopenia was observed in 42.85% patients with meningitis and in 65.89% patients without meningitis. Blood culture was positive in 28.57% of cases.

Hypoglycemia (blood glucose level ≤40 mg/dl) was observed in 28.57% of cases with meningitis and 23.53% cases without meningitis. CSF white cell count in patients with meningitis was 124.57cells/ mL and in patients without meningitis were one cell/ mL. Mean CSF protein level in meningitis patients was 60 mg/dl and in patients without meningitis was 40.01 mg/dl. Mean CSF glucose level in meningitis patients was 40.86 mg/dl and in patients without meningitis was 53.29 mg/dl. CSF culture was positive in two cases of meningitis. (Table 2 and 3).

DISCUSSION

Neonates are extremely vulnerable to infections in the first 28 days of life. Death and morbidity during this period are very high. Sepsis accounts for 25-40% of all neonatal death, meningitis can occur alone or as a part of sepsis in neonatal period. Meningitis in newborn has varied clinical presentation and a rapid and often fatal

course. Hence early diagnosis of meningitis is important to influence the outcome.

Table 2: Blood investigations.

WBC count	All (n=92)	Meningitis (n=7)	No meningitis (n=85)	p- value
Leukopenia (< 5000)	44 (47.82%)	2 (28.57%)	42 (49.41%)	0.03
Leucocytosis (>30000)	4 (4.34%)	2 (28.57%)	2 (2.35%)	
ANC <1800	42	2	40	0.77
Percentage (%)	45.65	28.57	47.05	
Thrombocytopenia	59	3	56	0.22
Percentage (%)	64.13	42.85	65.89	
Blood culture Positive	12	2	10	0.22
Percentage (%)	13	28.57	11.76	
Mean Blood Glucose level (mg/dl)	82.7	77.7	83.1	0.76
Hypoglycemia (≤ 40 mg/dl)	22(23.91%)	2 (28.57%)	20 (23.53%)	

Table 3: CSF studies.

CSF studies	All mean (95%CI)	Meningitis mean (95%CI)	No meningitis mean (95%CI)	p- value
CSF Protein (mg/dl)	41.53(29.23-53.83)	60.00(35.46-84.34)	40.01(30.52-49.5)	0.07
CSF Glucose (mg/dl)	52.34(27.7-78.3)	40.86(20.72-61)	53.29(27.74-78.84)	0.16
CSF white cell count (cells/mL)	10.40(-31.16-51.56)	124.57(26.09-223.05)	1(-0.81-2.81)	0.01
CSF Culture	No. of cases	Percentage (%)		P- value
Positive	2	28.57		0.001
Negative	5	71.43		

In our study incidence rate was 7.6%. It is in accordance with the study done by Shiva F et al, Greenberg et al and Kumar P et al. [13-15] Higher incidence rates of neonatal meningitis reported from developing countries as compared to developed country.[16,17]

The Male: female ratio amongst our study patients with meningitis was 1.3:1, comparing well with the slight male preponderance noticed by Dr L. Kalpana.[18]

Mean birth weight in study population with meningitis was 1.91 kg and without meningitis was 1.87 kg. Low birth weight (LBW) was almost equally prevalent amongst neonates with and without meningitis. Over all 71.74% patients were LBW, Similar observation noted in study by Groover et al, Berman P.H. et al, and Laving et al .[19-21]

Similarly as LBW, prematurity was also almost equally prevalent in both population with (71.43%) and without meningitis (78.82%). Similar observation noted by Groover et al, Berman P.H. et al, Laving et al.[19-21] Mode delivery was not significantly different in both population with and without meningitis.

Onset of illness was observed on average on 3rd day in patients with meningitis and on 5.35th day in patients without meningitis. Although onset of illness was slightly early in patients with meningitis, it was not statistically significant (p value=0.7). This observation is comparable with study done by Shiva F et al.[13]

Maternal risk factors were not much prevalent in patients with meningitis. PROM observed in 28.57% cases, Meconium stained liquor observed in 42.86% cases and foul smelling liquor observed in 28.57 cases similar finding observed by Laving et al.[21]

We did not find any significant association between interventions (resuscitation or surfactant therapy) and incidence of meningitis.

The most common presenting clinical symptoms in meningitis patients were poor feeding (100%), lethargy (85.71%), weak cry (85.71%) and tachypnea (50.58%). This finding was comparable with study done by Dr L. Kalpanaa and Laving et al.[18, 21]

The most common clinical signs which observed in meningitis include Retractions (85.71%), Grunting (57.14%) and Nasal flaring (42.86%). These symptoms were also seen commonly in sepsis patients.

Leukopenia (WBC count <5000) was present in 28.57% cases with meningitis and 49.41% cases without meningitis. Leukocytosis (WBC count >30000) was

present in 28.57% cases with meningitis and 2.35% cases without meningitis. Presence of leukopenia or leukocytosis was statistically significant (p =0.03). Dr L Kalpana et al, had shown that presence of Leukopenia is significantly associated with mortality.[18]

Absolute Neutrophil count (ANC) <1800 observed in 28.57% of cases with meningitis and 47.05% in cases without meningitis (p = 0.77).

Thrombocytopenia was observed in 42.85% patients with meningitis and in 65.89% patients without meningitis (p value=0.22).

In our study blood culture was positive in 13% of study population with Klebsiella spp. being the most common pathogen identified. There were 28.57% cases culture positive meningitis. There was no significant association between blood culture positivity and case of meningitis (p=0.22). The observation is in accordance with study done by Laving et al.[21]

Blood cultures were negative in 71.43% of neonates with meningitis, comparable to the 52% negative blood culture rate by Shattuck et al, and 46.7% negative blood culture rate by Laving et al, and there was no correlation between blood culture positivity and cases of meningitis.[21,22] The results further reemphasize the importance of not relying solely on blood cultures nor neglecting to perform lumbar punctures on neonates with suspected sepsis, as otherwise nearly half the babies with meningitis would remain undetected.

Mean CSF glucose level in meningitis patients was 40.86 mg/dl and in patients without meningitis was 53.29 mg/dl. Observation made in CSF parameters is comparable with study done by Laving et al.[21]

CSF culture was positive in two cases of meningitis. In one case we isolated Gr B Streptococci and in other Klebsiella spp. CSF culture is diagnostic of meningitis (p=0.001) but CSF cell counts and CSF biochemical parameters are useful guides as to the presence of disease, especially if CSF cultures are non-yielding.[21]

CONCLUSION

Authors study highlights the importance of routine lumbar puncture in neonatal sepsis evaluation. CSF cell counts and CSF biochemical parameters are useful guide for diagnosis especially when CSF cultures are negative. As there is variable incidence rate of neonatal meningitis in different studies, we recommend large multicentric studies in future to evaluate this hypothesis.

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REFERENCES

1. Weber MW, Carlin JB, Gatchalian S, Lehmann D, Muhe L, Mulholland EK, WHO Young Infants Study Group. Predictors of neonatal sepsis in developing countries. Pediatr Infect Dis J. 2003 Aug 1;22(8):711-7.
2. Isaacs D, Barfield C, Clothier T, Darlow B, Diplock R, Ehrlich J, et al. Late-onset infections of infants in neonatal units. J Paediatr Child Health. 1996 Apr;32(2):158-61.
3. Hristeva L, Booy R, Bowler I, Wilkinson AR. Prospective surveillance of neonatal meningitis. Archives Dis Child. 1993 Jul 1;69(1 Spec No):14-8.
4. 4. Airede AI. Neonatal bacterial meningitis in the middle belt of Nigeria. Develop Med Child Neurol. 1993; 35:424-30.
5. McCracken Jr GH. Management of bacterial meningitis current status and future prospects. Am J Med. 1984 May 15;76(5):215-23.
6. Afifi S, Wasfy MO, Azab MA, Youssef FG, Pimentel G, Graham TW, et al. Laboratory-based surveillance of patients with bacterial meningitis in Egypt (1998-2004). Europ J Clini Microbiol Infect Dis. 2007 May 1;26(5):331-40.
7. Welinder-Olsson C, Dotevall L, Hogevik H, Jungnelius R, Trollfors B, Wahl M, et al. Comparison of broad-range bacterial PCR and culture of cerebrospinal fluid for diagnosis of community-acquired bacterial meningitis. Clini Microbiol Infect. 2007 Sep 1;13(9):879-86.
8. Mani R, Pradhan S, Nagarathna S, Wasiulla R, Chandramuki A. Bacteriological profile of community acquired acute bacterial meningitis: a ten-year retrospective study in a tertiary neurocare centre in South India. Ind J Med Microbiol. 2007 Apr 1;25(2):108-114.
9. Mishra OP, Batra P, Ali Z, Anupurba S, Das BK. Cerebrospinal fluid lysozyme level for the diagnosis of tuberculous meningitis in children. J Tropic Pediatr. 2003 Feb 1;49(1):13-6.
10. Wiswell TE, Baumgart S, Gannon CM, Spitzer AR. No lumbar puncture in the evaluation for early neonatal sepsis: will meningitis be missed?. Pediatr. 1995 Jun 1;95(6):803-6.
11. Holt DE, Halket S, De Louvois J, Harvey D. Neonatal meningitis in England and Wales: 10 years on. Archi Dis Childhood-Fetal Neonatal Edition. 2001 Mar 1;84(2):F85-9.
12. Sáez-Llorens X, McCracken Jr GH. Bacterial meningitis in children. Lancet. 2003 Jun 21;361(9375):2139-48.
13. Shiva F, Mosaffa N, Khabbaz R, Padyab M. Lumbar puncture in neonates under and over 72 hours of age. J Coll Physicians Surgeons-Pakistan: JCPSP. 2006 Aug;16(8):525-8.
14. Greenberg D, Shinwell ES, Yagupsky P, Greenberg S, Leibovitz E, Mazor M, et al. A prospective study of neonatal sepsis and meningitis in southern Israel. Pediatric Infect Dis J. 1997 Aug 1;16(8):768-73.

15. Kumar P, Sarkar S, Narang A. Role of routine lumbar puncture in neonatal sepsis. J Paediatr Child Health. 1995 Feb;31(1):8-10.
16. Johnson CE, Whitwell JK, Pethe K, Saxena K, Super DM. Term newborns who are at risk for sepsis: are lumbar punctures necessary?. Pediatr. 1997 Apr 1;99(4):e10.
17. Haque, K.H. (2003): Infection and immunity in the newborn. In: Forfar and Ameil's Textbook of Pediatrics. By: Campbell AGM, Mcintosh N (edrs) 5th ed. Churchill Livingstone. London:273-289.
18. Kalpana L. Clinical Profile of Neonatal Meningitis and Analysis of Various Factors for Prognostic Significance. IOSR J Dental Med Sci (JDMS). 2012 (Nov-Dec);2(5):01-7
19. Overall JC. Neonatal bacterial meningitis: analysis of predisposing factors and outcome compared with matched control subjects. J Pediatr. 1970 Apr 1;76(4):499-511.
20. Groover RV, Sutherland JM, Landing BH. Purulent meningitis of newborn infants: eleven-year experience in the antibiotic era. N Eng J Med. 1961 Jun 1;264(22):1115-21.
21. Berman PH, Banker BQ. Neonatal meningitis: a clinical and pathological study of 29 cases. Pediatr. 1966 Jul 1;38(1):6-24.
22. Shattuck KE, Chonmaitree T. The changing spectrum of neonatal meningitis over a fifteen-year period. Clini Pediatr. 1992 Mar;31(3):130-6.

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