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Original Research Article

Assessment of the prevalence of meningitis in clinically suspected cases of early and late onset neonatal sepsis

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ABSTRACT

Background: Meningitis is more common in the neonatal period than any other time in life and is an important cause of morbidity and mortality globally. In India, rate of neonatal sepsis is reported 0.5 per 1000 live births. The major burden of neonatal sepsis and meningitis occurs in the developing world. According to WHO estimates there are approximately 5 million neonatal deaths in a year. The objective of the study is to assess the prevalence of meningitis in neonates with clinical suspicion of sepsis.
Methods: The study was conducted among suspected cases of neonatal septicemia in neonatal intensive care unit (NICU), department of pediatrics, VPIMS, Lucknow. It is a prospective observational study. A total of 180 neonates were included in the study.
Results: Out of 180 neonates, CSF examination of 131 (72.78%) neonates was normal, of 37 (20.56%) was suggestive of meningitis. Prevalence of meningitis in neonatal sepsis was 20.0%. It was 18.0% in early neonatal sepsis and 32.6% in late neonatal sepsis cases.
Conclusions: The findings of present study suggested that there is a high risk of meningitis among neonatal sepsis cases. Cases with risk factors like twin birth, anemia, low TLC, low platelet count, acid-base imbalance and X-ray findings suggestive of pneumonitis should be kept in a high-risk category.

Keywords: CSF, Meningitis, Pneumonitis, TLC

INTRODUCTION

Meningitis is more common in the neonatal period and is an important cause of morbidity and mortality globally Furyk et al.[1] 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.[2] In India, rate of neonatal sepsis is reported 0.5 per 1000 live births.[1] According to an estimate globally there are 126,000 cases of neonatal meningitis annually, and more than 50,000 deaths Daoud et al.[3] Mortality rates vary by region, e.g. 0.7-1.9⁄1000 live births in Sub-Saharan Africa, 0.33-1.5 in the Middle East and North Africa and 0.4-2.8 in the America and Caribbean.[5]

The major burden of neonatal sepsis and meningitis occurs in the developing world. According to WHO estimates there are approximately 5 million neonatal deaths in a year. The overwhelming majority (98%) occur in developing countries Weber.[5,6] Neonatal meningitis contributes significantly to the burden of neonatal morbidity and mortality, and other causes include other infection, prematurity and birth asphyxia. The true incidence of neonatal bacterial meningitis may be underestimated, particularly in resource-poor settings for multiple reasons. These include difficulty in diagnosing neonatal meningitis, differences between hospital-based and community studies, regional differences and unregistered deaths in areas where access to health care is poor Osrin et al.[7]

The relationship between bacterial sepsis and meningitis is well established. Owing to this empirical relationship, neonates with sepsis are at a higher risk of meningitis. It is estimated that nearly 20% of early-onset sepsis and 10% of late-onset sepsis is complicated by meningitis Isaacs et al.[8] The risk increases with decreasing gestational age, Preterm neonates carry two to three times higher risk than term neonates and account for greater majority of the late-onset cases Hristeva et al [9]

No doubt meningitis is more common in the neonatal period than at any other time Delouvois et al.[10] Neonates with sepsis are at a higher risk of meningitis. The newborn is particularly susceptible to infection as the immature immune system is deficient in humoral and cellular immune responses in phagocytic and in complement functions Pong et al.[11] Neonatal meningitis is associated with a high burden of morbidity and mortality. In developing countries, mortality rates among neonates with meningitis are reported to be as high as 40-58%.[12] Morbidity is under reported but thought to be considerable Furyk et al.[1] Survivors remain at high risk for neurological sequelae and lifelong impairment as a result of infectious insult to their developing brain De Louvois, Libster et al.[14,15]

Aims and objectives

The present study shall be carried out with the aim to assess the prevalence of meningitis in neonates with clinical suspicion of sepsis. This aim shall be achieved with the help of following objective-to assess and compare the prevalence of meningitis in clinically suspected cases of early and late onset neonatal sepsis.

METHODS

Diagnostic tests for suspected meningitis in neonates

In most cases

Lumbar puncture to obtain CSF for: cell count with differential, gram stain, glucose level, protein level, bacterial cultures-Blood cultures for bacteria, serum glucose level and urine culture.

Consider

Latex antigen test of CSF and urine for *Haemophilus influenzae, Streptococcus pneumoniae, Neisseria meningitidis, group B streptococcus.*

Polymerase chain reaction test of CSF for viruses (HSV, CMV, HIV, Enterovirus), viral cultures of CSF, urine, stool, nasopharynx.

Serology for infectious etiologies as indicated by history or physical examination (maternal or infant), stain for acid-fast bacillus, CT scan of the brain with and without contrast, or MRI.

Table 1: Typical cerebrospinal fluid values in newborns and young infants.

Values	Normal term newborns	Normal infant	Bacterial meningitis	Viral meningitis
White blood cells	<30 per mL	< 10 per mL	200 to 100,000 per mL	25 to 1,000 per mL
Neutrophils	<60%	<10%	80 to 100%	<50%
Glucose	>60% of serum	>50% of serum	<40% of serum	>40% of serum
Protein	<70 mg per dl (0.7 g per L)	<40 mg per dl (0.4 g per L)	100 to 500 mg per dl (1 to 5 g per L)	50 to 100 mg per dl (0.5 to 1 g per L)

Study design

The present was conducted among suspected cases of neonatal septicemia in neonatal intensive care unit (NICU), department of pediatrics, VPIMS, Lucknow.

Study population

Samples were collected from the neonates in intensive care unit diagnosed as neonatal septicemia.

The sampling frame was bound by following inclusion and exclusion

Inclusion criteria

New born babies who had clinical features of sepsis, viz., lethargy/hypotonia, tachycardia, fever, abdominal distension, increased aspirates, retractions, grunting, hypotension/delayed capillary refill, pallor, jaundice, hepatomegaly, apnea, abnormal skin color, bradycardia and increased ventilator requirements and sclerema, shock, features of disseminated intravascular coagulation, pulmonary hemorrhage were included.

In absence of clinical features, the babies had risk factors (one major or two minor).

Major

Prolonged rupture of membranes (>24 hours) and evidence of chorioamnionitis-intrapartum fever >100.4^0 F, foul smelling liquor were major factors.

Minor risk factors

Febrile illness in the mother within 2 weeks prior to delivery, meconium stained liquor amnio, more than 3

vaginal examinations during labor, low birth weight (<2500 gm) or prematurity, prolonged labor (sum of first and second stage >24 hours) and Apgar score at 1 minute <4 were minor risk factors.

Exclusion criteria

Neonates with shock and severe cardiorespiratory instability and neonates in whom LP is contraindicated or the consent for LP is not given were excluded from the study.

Sample size calculation

As in a previous study by Hoque et al, prevalence of meningitis in clinically suspect cases of neonatal sepsis was 26.3%. We also targeted a similar prevalence in the targeted population. The sample size was calculated using the following formula:

$N=C^2P(1-P)/e^2$

Where "p" is the proposed prevalence (26.3% or 0.263), C^2 is a constant at a certain confidence level (its value at 95% confidence limit and 80% power is1.96) while e is the error allowance (taken as 10% or 0.1). Now putting these values in the above equation:

$n=1.96^2\times0.263\times (1-0.263)/0.1^2$

$=3.84\times0.194/ 0.01$

$=0.745/ 0.01$

$=74.5\sim75$

Thus at 95% confidence and 80% power, the calculated sample size shall be 75. After adding for a contingency of 20%, the projected sample size comes out to be 90. The study shall target at 100 cases.

Permissions and approvals

Ethical approval was sought from the institutional ethical committee of Vivekananda polyclinic and institute of medical sciences, Lucknow. Informed consent was obtained from guardians of all the patients enrolled in the study.

The study was conducted among suspected cases of neonatal septicemia in NICU, department of pediatrics, VPIMS, Lucknow from July 2005 to August 2012.

It is a prospective observational study. Statistical package for the social sciences (SPSS) software was used analyze data.

Parents/guardians of all the neonates falling in sampling frame were invited to participate in the study. Only those providing consent to participate in the study shall be enrolled in the study. From all the patients consenting to participate in study, demographic information, detailed maternal medical and obstetric history was obtained.

Details of gestation including complications during pregnancy, gestational age at delivery, mode of delivery and birth weight was noted. A thorough clinical examination was carried out.

RESULTS

The present was conducted among suspected cases of neonatal septicemia in NICU, department of pediatrics, VPIMS, Lucknow to compare the outcome of neonates with meningitis to those not having meningitis among neonates clinically suspected for sepsis. A total of 180 neonates were included in the study, findings of CSF examinations were as under:

Table 2: Distribution of study population according to findings of CSF examination of neonate.

CSF examination	N	Percentage (%)
Normal	131	72.78
Meningitis	37	20.56
Traumatic	12	6.67

Out of 180 neonates, CSF examination of 131 (72.78%) neonates was normal, of 37 (20.56%) was suggestive of meningitis, CSF specimen of 12 (6.67%) was traumatic and findings were inconclusive, hence these patients were excluded from assessment.

Comparison of clinical and general profile of patients according CSF findings was thus made in two groups only: (1) group I-normal CSF findings (n=131) and (2) group II-CSF suggestive of meningitis (n=37), (Table 3).

Table 3: Association of general and clinical profile with CSF findings.

Variables	Overall, (n=168)		Group I, (n=131)		Group II, (n=37)		Statistical significance	
	N	%	N	%	N	%	χ^2	P
Gender								
Male	130	77.38	101	77.10	29	78.38	0.027	0.870
Female	38	22.62	30	22.90	8	21.62		
Place of birth								
Inborn	51	30.36	43	32.82	8	21.62	1.713	0.191
Out born	117	69.64	88	67.18	29	78.38		

Continued.

Variables	Overall (n=168)		Group I (n=131)		Group II (n=37)		Statistical significance	
	N	%	N	%		N	%	N
Birth weight (kg)								
>2.5	93	55.36	72	54.96	21	56.76	5.143	0.162
1.5-2.5	61	36.31	47	35.88	14	37.84		
1-1.49	13	7.74	12	9.16	1	2.70		
<1	1	0.60	0	0.00	1	2.70		
Gestational age								
Term	114	67.86	87	66.41	27	72.97	0.569	0.451
Pre-term	54	32.14	44	33.59	10	27.03		
Appropriate for gestational age								
AGA	132	78.57	101	77.10	31	83.78	1.295	0.523
SGA	33	19.64	27	20.61	6	16.22		
LGA	3	1.79	3	2.29	0	0.00		
Multiple birth								
Single	163	97.02	130	99.24	33	89.19	10.086	0.001
Twin	5	2.98	1	0.76	4	10.81		

In meningitis group, the pathogens isolated were *S. epidermidis* (5.4%), *S. hominis* (2.7%), other CONS (8.1%), *Enterococcus* (5.4%) and group B *Streptococcus* (2.7%) as the gram-positive pathogens and *Klebsiella pneumoniae* (5.4%) and *P. aeruginosa* (2.7%) as the gram-negative pathogens.

DISCUSSION

This study has revealed some important trends and characteristics of neonatal meningitis. Prevalence of meningitis in neonatal sepsis was 22.0%. It was 18.0% in early neonatal sepsis and 32.6% in late neonatal sepsis cases. In early neonatal-twin birth, PROM, inadequate ANC visits and Acid-base imbalance were associated with significantly higher risk of meningitis. In late neonatal sepsis cases- low platelet count and chest X-ray findings suggestive of pneumonitis were associated with significantly higher risk of meningitis.

As per Furyk et al neonatal meningitis in the developing world neonatal risk factors for developing meningitis include low birth weight and prematurity; maternal risk factors include premature ruptures of membranes, prolonged rupture of membranes (>18 h), maternal colonization with group B *Streptococcus* (GBS), maternal chorioamnionitis and low socioeconomic status.[1]

The higher overall incidence of neonatal meningitis may relate to the prevailing high rate of infection or bacteremia in the developing world, as previously documented Airede et al.[3]

As per study done in Australia by Isaacs et al, there were 320 episodes of sepsis in Australian units affecting 294 babies.[2] One hundred of these episodes (31%) were early-onset; 3.0% of babies admitted to six tertiary care neonatal units attached to maternity hospitals developed late sepsis. Coagulase negative *Staphylococci* were the commonest cause of late-onset sepsis. There were 26 episodes of the *S. aureus* septicaemia. Of which only one was due to MRSA. Meningitis occurred in 13 babies (5.9%) with late-onset sepsis. The mortality from late-onset sepsis was 7.7%.

As per an Indian study in 2001 by Aggarwal et al, in situations of early onset sepsis, a lumbar puncture is indicated in the presence of either a positive blood culture or presence of clinical picture of septicemia.[4] In situations of late onset sepsis, a lumbar puncture should be done in all infants with signs and symptoms prior to starting antibiotics.

Our review documented three cases (13%) of bacterial meningitis (one probable early group B *Streptococcal*, one definite early *S. mitis*, and one probable lateK oxytoca) with positive CSF culture and negative blood cultures. The results of lumbar puncture directed the choice of antibiotic treatment and its duration. All these babies had a good outcome with no neurodevelopmental impairment Hristeva et al.[9]

As per a study done by Pong et al the diagnosis of meningitis in neonates requires sampling of CSF.[11] The bacterial culture remains the gold standard for diagnosis of meningitis. The gram-stained smear can also give an early clue to the bacterial agent. Of neonates with gram-negative bacterial meningitis evaluated by gram-stained smear, 61% were positive.

Limitations

Gaps in knowledge, the role of adjuvant antibiotic therapies and future directions for research are needed to be explored. The requirement of optimum empirical antibiotic therapy for resource-poor environments couldn't be assessed in this study.

CONCLUSION

On the basis of observations made in present study, we could find that the prevalence of meningitis in neonatal

sepsis was 22.0%. It was 18.0% in early neonatal sepsis and 32.6% in late neonatal sepsis cases. In early neonatal sepsis cases- twin birth, PROM, inadequate ANC visits and acid-base imbalance were associated with significantly higher risk of meningitis and in late neonatal sepsis cases- low platelet count and chest X-ray findings suggestive of pneumonitis were associated with significantly higher risk of meningitis. For early onset group, the morality/referral rates in sepsis alone and sepsis with meningitis cases were 25% and 18.2% respectively. For late onset group, the morality/referral rates in sepsis alone and sepsis with meningitis cases were 12.9% and 40% respectively. Blood culture positivity rate was 28.2% in sepsis alone and 32.4% in sepsis with meningitis cases. In both the groups majority of isolates were Gram positive (16.8% and 24.3% respectively). The findings of present study suggested that there is a high risk of meningitis among neonatal sepsis cases. Neonatal bacterial meningitis is found to be a major cause of morbidity and mortality in the developing countries like India. Important differences in etiology have been identified. Early and focused treatment of established disease is essential. On basis of this study, we finally concluded that meningitis is also prevalent in early onset sepsis. So doing prompt lumbar puncture in early onset sepsis should also be considered to rule out meningitis in cases of EONS.

Recommendations

Newborns with symptomatic sepsis should undergo lumbar puncture, to identify cases with meningitis. Prompt institution of antibiotics in correct dose and duration is important for preventing complications and improving survival and prognosis. Further studies are needed to assess prevalence of meningitis in different clinical subgroups and settings to formulae recommendations for lumbar puncture in neonatal sepsis in Indian context.

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REFERENCES

1. Furyk JS, Swann O, Molyneux E. Systematic review: neonatal meningitis in the developing world. Trop Med Int Health. 2011;16(6):672-9.
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;32(2):158-61.
3. Daoud AS, al-Sheyyab M, Abu-Ekteish F, Obeidat A, Ali AA, El-Shanti H. Neonatal meningitis in northern Jordan. J Trop Pediatr. 1996;42(5):267-70.
4. Aggarwal R, Sarkar N, Deorari AK, Paul VK. Sepsis in the newborn. Indian J Pediatr. 2001;68(12):1143-7.
5. Stoll BJ. The global impact of neonatal infection. Clin Perinatol. 1997;24(1):1-21.
6. 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;22(8):711-7.
7. Osrin D, Vergnano S, Costello A. Serious bacterial infections in newborn infants in developing countries. Curr Opin Infect Dis. 2004;17(3):217-24.
8. 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;32(2):158-61.
9. Hristeva L, Booy R, Bowler I, Wilkinson AR. Prospective surveillance of neonatal meningitis. Arch Dis Child. 1993;69(1):14-8.
10. De Louvois J, Blackbourn J, Hurley R, Harvey D. Infantile meningitis in England and Wales: a two year study. Arch Dis Child. 1991;66(5):603-7.
11. Pong A, Bradley JS. Bacterial meningitis and the newborn infant. Infect Dis Clin North Am. 1999;13(3):711-33.
12. Campagne G, Schuchat A, Djibo S, Ousséini A, Cissé L, Chippaux JP. Epidemiology of bacterial meningitis in Niamey, Niger, 1981-96. Bull World Health Organ. 1999;77(6):499-508.
13. Milledge J, Calis JCJ, Graham S, Phiri A, Wilson LK, Soko D et al. Aetiology of neonatal sepsis in Blantyre, Malawi: 1996-2001. Ann Trop Paediatr. 2005;25(2):101-10.
14. De Louvois J, Halket S, Harvey D. Neonatal meningitis in England and Wales: sequelae at 5 years of age. Eur J Pediatr. 2005;164(12):730-4.
15. Libster R, Edwards KM, Levent F, Edwards MS, Rench MA, Castagnini LA et al. Long-term outcomes of group B *Streptococcal* meningitis. Pediatrics. 2012;130(1):e8-15.

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