Original Article

Diagnosis of Neonatal Meningitis with early Onset Sepsis in Pakistan Institute of Medical Sciences Islamabad

Misbah Anjum[1], Chetan Das[2] and Devedass[2]

ABSTRACT

Objective: To see frequency of neonatal Meningitis in early onset of neonatal sepsis.
Study Design: Descriptive study
Place and Duration of Study: This study was conducted at the Children's Hospital NICU and Neonatal Nursery of MCH Centre PIMS, Islamabad from February 2015 to August 2015
Materials and Methods: Total of 90 septic neonates were screened who fulfilled the inclusion criteria. All the information recorded in the proforma and data was entered in software SPSS version 18. The descriptive analysis were carried out and reported as mean with standard deviation for age. The level of significance was selected as 5% (p-value 0.05). The results are presented as tables and graphs.
Results: Total of 90 septic neonates were enrolled in this study. The mean (standard deviation) age of all septic neonates was 36.3 (± 20.2) hours and half of the neonates with sepsis 51 (56.7%) were preterm. The male to female ratio was 1.9 to 1 and intrapartum maternal high fever was present in only 4 (4.4%).The poor feeding which was present in 51 (57.0%) neonates with sepsis and irritability was significantly associated with septic neonates with meningitis (p-value 0.001).
Conclusion: We concluded in this study that there is low incidence of neonatal meningitis among neonates with early onset sepsis, but it is quite important to have lumbar puncture in all neonates with early onset sepsis because these 3.3 percent cases of meningitis would have been otherwise missed.

Key Words: Neonatal, meningitis, early onset, sepsis, Lumbar puncture

Citation of article: Anjum M, Das C, Devedass. Diagnosis of Neonatal Meningitis with early Onset Sepsis in Pakistan Institute of Medical Sciences Islamabad. Med Forum 2017;28(3):51-55.

INTRODUCTION

Septic neonates are defined on clinical grounds as those not doing well, with lethargy, irritability, poor feeding, temperature instability, respiratory distress, apnea, abdominal distension, vomiting or poor perfusion. Laboratory investigations shows Leukopenia <5000 white blood cell (WBC) per mm3 or leukocytosis >20,000 WBC per mm3or positive C-reactive protein and/ or Positive blood culture.[1]

Early onset neonatal sepsis is defined as presentation of neonates with sepsis in the first 72 hours of life. Late onset neonatal sepsis is defined as presentation of neonates with sepsis after 72 hours of life. Neonatal meningitis is defined as: Positive cerebrospinal fluid (CSF) culture (Gold Standard) or Negative CSF culture but raised CSF WBC count >25 WBC per mm3 of an atraumatic tap with Red Blood cells (RBC) count <1000 RBC per mm3. [2]

1. Department of Paeds, National Institute of Child Health, Karachi.
2. Department of Paeds, LUMHS Jamshoro

Correspondence: Dr. Chetan Das, Assistant Professor of Pediatrics, Liaquat University of Medical and Health Sciences Jamshoro.
Contact No: 03332960920
Email: drchetandas@hotmail.com

Received: January 1, 2017; Accepted: February 10, 2017

MATERIALS AND METHODS

All neonates with suspected sepsis admitted at the Neonatal Intensive Care Unit (NICU), The Children's Hospital, Islamabad and Neonatal Nursery of Mother and Child Health (MCH) Centre, Pakistan Institute of Medical Sciences (PIMS), Islamabad were screened and fulfilled inclusion criteria were enrolled in the study. The study was conducted from February 2015 to August 2015. The sample size for the study was estimated by using Statcalc program of EpiInfo software. By selecting the population size as 100, (estimated admissions of suspected early onset neonatal sepsis at our setting in six months) and expected frequencies as 6% with worse expected as 3%. With the confidence level selected as 95%, the estimated sample size was 71. A convenience, non-probability, sampling technique was chosen. Inclusion criteria for enrollment were age less than 72 hours, both gender, diagnosed to have sepsis as defined above and informed consent given. The neonates who has age more than 72 hours, major congenital abnormalities such as meningomylocele, hydrocephalous, consent refused by parents and traumatic lumbar puncture were excluded from study. Parents/caretakers were informed about the nature of the study and about the association of neonatal sepsis with meningitis and consequences of delayed or missed diagnosis of meningitis. The approval from hospital ethical committee was taken.

All parents/caretakers were interviewed and detailed information regarding the maternal and neonatal risk factors was collected. General physical and systemic examination was carried out. Afterwards, a lumbar puncture was performed by keeping aseptic measures in each neonate. Samples were taken and sent for the laboratory investigations at the time of enrollment. All the information regarding history, examination and laboratory investigations was filled on a proforma, especially designed for this study. The management of neonatal sepsis was then started in all neonates.

Data Analysis: All the information recorded in the Proforma was entered by using the software SPSS version 13. Student t test and Chi-square tests were carried out. The Chi-square test values were estimated and p-values were obtained and reported. The level of significance was selected as 5% (p-value 0.05). The results are presented as tables and graphs.

RESULTS

During the study period of six months, a total of 90 septic neonates, who fulfilled the inclusion criteria were enrolled in this study. The age in hours at the time of enrollment of all the enrolled neonates with sepsis are shown in Table 1. The mean (standard deviation) age of all septic neonates was 36.3 (± 20.2) hours. The youngest neonate was only one hour old, while the oldest one was 71 hours of age. The peak age of enrollment was between 21 to 50 hours of age, as 62% (n = 56) of neonates with sepsis were aged between 21 and 50 hours.

Out of 90 neonates with sepsis, majority of neonates were male 59 (65.6%), whereas only 31 (34.4%) were neonates were females. The male to female ratio was 1.9 to 1.

The frequencies and percentages of various reported maternal risk factors are presented in Table 2. The preterm, defined as less than 37 weeks of gestational age, was identified as the most common risk factor as more than half of the neonates with sepsis 51 (56.7%) were preterm.

The history of intrapartum maternal high fever was present in only 04 (4.4%) neonates, while 18 (20.0%) neonates with sepsis had positive history of premature rupture of membrane.

Amongst the neonatal risk factors, birth weight less than 2.5 Kg was the most frequently reported risk factors among the neonates with sepsis, as 64 (71.1%) neonates had birth weight less than 2.5 Kg.

Low APGAR score, defined as less than 5 at 5 minutes, was reported in 09 (10.0%) neonates with sepsis, whereas chorioamnionitis was present in only 2 (2.2%) neonates with sepsis.

Leukopenia was present in 09 (10.0%) of neonates with sepsis, while leukocytosis was present in 19 (21.1%) neonates with sepsis. Out of 90 neonates with sepsis, 45 (50.0%) had positive C-reactive protein. Out of 90 neonates with sepsis, more than half of neonates with sepsis, 52 (57.8%) had positive blood culture, while 38 (42.2%) neonates had negative blood culture.

Amongst the 52 neonates who had positive blood culture, the most common micro-organism was Coagulase Negative Staphylococcus, which was found in 27 (51.9%) neonates with sepsis. However, cultures positive for coagulase negative staphylococci were regarded as contaminants. In remaining 25 blood culture positive cases, other micro-organisms were present and the most common organism was Enterobacter reported in 12 (48%) neonates with sepsis. Other organisms grown were Klebsiella, E-Coli and Staph Aureus present in 9 (36%), 3 (12%) and 1 (4%) respectively (Figure 1).

The frequency of meningitis among all the neonates with sepsis enrolled in this study. Out of 90 neonates with sepsis, only 3 (3.3%) neonates were declared to have neonatal meningitis. CSF culture was negative in all three neonates and these neonates were diagnosed to have neonatal meningitis on the basis of abnormal CSF pleocytosis.

The neonates diagnosed to have meningitis were slightly younger than neonates with no meningitis as the mean (standard deviation) age of all septic neonates with meningitis was 29.3 (± 16.7) hours and among septic neonates without meningitis it was 36.6 (± 20.5) hours. However, this difference was not statistically significant (p-value = 0.55).

All septic neonates with meningitis were male, while among septic neonates without meningitis, 56 (64.4%) were boys and this difference was not statistically significant (p-value = 0.20) (Table 2).

The presence of various risk factors were also compared between septic neonates with meningitis and without meningitis and shown in Table 3. No statistical significant differences were found in the presence of various risk factors between the septic neonates with meningitis and without meningitis. All septic neonates with meningitis had positive blood cultures. Out of three septic neonates with meningitis, one had Enterobacter, other had Klebsiella and the third one had E-Coli.

Table No.1: Frequency of maternal risk factors among neonates (n =90)

	No. of neonates	%age
Intrapartum maternal high fever		
Yes	04	4.4%
No	86	95.6%
PROM > 24 hours		
Yes	18	20%
No	72	80%
Preterm (< 37 weeks)		
Yes	51	56.7%
No	39	43.3%

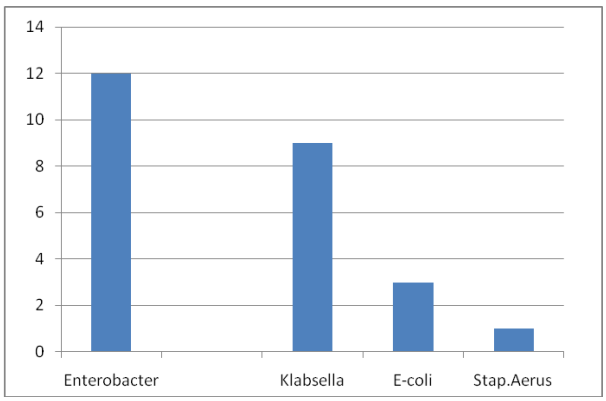

Figure No.1: Frequency of presence of various organisms among the blood culture positive septic neonates (n = 25)

Table 2: Comparison of demographic characteristics of septic neonates with meningitis versus septic neonates without meningitis (n = 90)

Demographic features	With meningitis (n = 3)	Without meningitis (n = 87)	p-value
Age (in hours)			
Mean (SD)	29.3(± 16.7)	36.6 (± 20.4)	0.55
Gender			
Male	3(100%)	56(64.4%)	0.20
Female	0 (0%)	31(35.6%)	---

Table No.3: Comparison of presence of risk factors among septic neonates with meningitis versus septic neonates without meningitis (n = 90)

Septic Neonates			
Risk factors	With meningitis (n = 3)	Without meningitis (n = 87)	p-value
Intrapartum maternal high fever	0 (0.0%)	4 (4.6%)	0.70
PROM > 24 hours	1 (33.3%)	17 (19.5%)	0.55
Preterm (< 37 Weeks)	1 (33.3%)	50 (57.5%)	0.40
Low APGAR	0 (%)	9 (10.3%)	0.71
Birth weight < 2.5 Kg	02 (66.7%)	62 (71.3%)	0.86
Chorioamnionitis	0 (0%)	2 (2.3%)	0.79
Abdominal distension	1 (33.3%)	15 (17.2%)	0.47

DISCUSSION

Early onset neonatal sepsis is usually caused by micro-organisms such as Group B Streptococcus, E-Coli, Klebsiella, Listeria or other Gram-negative organisms. These micro-organisms are usually acquired from the maternal genitourinary tract. The timing of clinical infection depends on the density of colonization of the mother, rate and density of colonization of the newborn, strain and hence the invasiveness of the micro-organism, and presence or absence of various obstetric risk factors. [3, 4,5]

Incidence of neonatal meningitis in early onset sepsis in this study is comparable with other studies. A recent study by Shiva and colleagues in Iran enrolled 380 suspected cases of neonatal sepsis. Out of 380, 248 neonates were younger than 72 hours of life. Among neonates younger than 72 hours, meningitis was diagnosed in 17 (6.9 percent) neonates. In India, Chacko and Sohi examined 36 neonates with early onset sepsis and found that meningitis was present in 3 (8.3 percent) of neonates [6, 7, 8].

A hospital based study in Nairobi, Kenya, reported a much higher rate of meningitis among neonates with sepsis 15 (17.9 percent) septic neonates had neonatal meningitis.[9]

On the other hand, several studies have reported extremely low yields from routine lumbar puncture. Walsh-Sukys and colleagues evaluated 861 neonates for sepsis within the first 72 hours of life and found only 2 (0.2 percent) cases of meningitis. Hence, the authors suggested that lumbar punctures should be reserved for infants with central nervous system signs or bacteremia.[10, 11,12]

Similarly, another study from Nigeria, examined 562 neonates and lumbar punctures were performed in all neonates less than 72 hours of age and no case of meningitis is found in neonates less than 72 hours of age. The authors suggested that meningitis is very rare in the first 72 hours of life and therefore, the expected yield of routine lumbar punctures in early onset sepsis does not justify the risks associated with the procedure. They subscribed to the view expressed in several earlier studies that routine lumbar puncture should be eliminated from early onset sepsis evaluation and reserved for bacteremiac infants, or infants with neurological signs.[13]

There are several reasons for variation like sample size, medico-legal perspective in different health settings from less than 1 percent to around 18 percent of incidence of neonatal meningitis among septic neonates. In communities with heightened awareness of medico-legal implications, there is a trend to be very stringent in the work-up of a possible septic neonate, resulting in a low yield of positive lumbar puncture. If the selection criteria for a septic work-up would have been similar in different settings then the incidence of meningitis would not have shown such diversity in different surveys. However, early recognition of neonatal meningitis is of prime concern because of the increased morbidity and mortality associated with delayed or missed diagnosis. Because neonates have a limited repertoire of responses to any stressful

condition, sepsis with or without meningitis is often invoked as a possible diagnosis in any sick infant.

In current study, out of 90 neonates with sepsis, blood culture was positive in 25 neonates with sepsis. The most common micro-organism is Enterobacter, which is reported in 12 (48 percent) septic neonates with positive blood cultures. Other micro-organisms cultured are Klebsiella, E-Coli and Staph Aureus present in 9 (36 percent), 3 (12 percent) and 1 (4 percent) septic neonates with positive blood cultures respectively. These results are comparable with other studies in this region.

In India, a study reported approximately 42 percent blood culture positive cases of early onset sepsis. In their sample, they reported pseudomonas (60 percent) as the most common micro-organism. Other micro-organisms,Klebsiella, Staph.Aures, S. Viridin and E-Coli were present in 13 percent, 13 percent, 7 percent and 7 percent respectively among the septic neonates with positive blood cultures [8].

A study from Iran reviewed 136 neonates with sepsis and found pseudomonas as the most common micro-organism, as 42 percent blood cultures were positive for this organism. Other most common organisms were Klebsiella and coagulase negative Staphylococci, as 32 percent and 15 percent respectively among the septic neonates with positive blood cultures. Other 10 percent were due to micro-organisms such as E. Coli, Enterococci, Micrococci, Citrobacter, Staph. Aureus and Streptococcus group B 13. In another study in Iran researchers reviewed 242 neonates with sepsis. The researchers found that Staph Aureus and Klebsiella were the leading etiologic micro-organisms for neonatal sepsis [14.]

From Libya, Misallati and colleagues retrospectively reviewed 36 cases of blood culture proven neonatal septicemia. Out of 36, 11 (31 percent) neonates were less than 72 hours of age at the time of presentation, and therefore diagnosed to have early onset sepsis. Among the neonates with early onset sepsis, Enterobacter (36 percent) was the most common micro-organism cultured in those neonates. Other common micro-organisms were Salmonella, Klebsiella and Pseudomonas. E-Coli were present in only one neonate with early onset sepsis [15].

Not a single case of Group B Streptococcus is found in our study. This is consistent with other studies which reported a significantly low rate of early onset Group B streptococcus sepsis and meningitis. This reduction is further evidence of the effectiveness of maternal intrapartum antibiotic prophylaxis in preterm neonates. There is a positive correlation between positive blood culture and neonatal meningitis. Johson and colleagues also reported an association of positive blood culture with the presence of meningitis in neonates [13,14,15,16].

Results of this study are quite similar with other studies, out of 25 cases of blood culture positive sepsis, 3 (12 percent) have neonatal meningitis. Hence, all septic neonates with meningitis have positive blood cultures. Out of three septic neonates with meningitis, one has Enterobacter, other has Klebsiella, while third one has E-Coli. Our results are comparable with an Indian study where researchers examined 36 neonates with early onset sepsis and found that meningitis was present in 3 cases. Similar to our study, in their study too, all meningitis cases have positive blood cultures. Therefore, some experts have pointed out that in early onset sepsis, lumbar puncture is indicated in the presence of a positive blood culture or if the clinical picture is consistent with septicemia [9].

However, it is difficult to rely on blood culture to perform lumbar puncture because the blood culture results are usually available after 48 hours. Furthermore, blood cultures are negative in 15 to 55 percent cases of neonatal meningitis. If lumbar punctures are performed only in neonates with positive blood culture, a number of neonates with meningitis will be missed [17,18].

In this study, the comparison of neonates with meningitis and without meningitis regarding their demographic features such as age and gender show no statistical difference. Moreover, there is no statistical difference regarding the maternal and neonatal risk factors between neonates with meningitis and with no meningitis. However, out of three neonates with meningitis, two have weight less than 2.5 Kg in our study. Some researchers suggest that in low birth weight babies with respiratory distress, a lumbar puncture is not necessary. On the other hand, Stoll and colleagues have shown their concerned that meningitis may be under diagnosed in very low birth weight neonates due to failure to perform lumbar puncture in these neonates. [19, 20]

Our results show that apart from irritability, there are no statistical differences regarding presence of various symptoms between the septic neonates with meningitis and without meningitis. The septic neonates with meningitis are statistically more likely to have irritability than septic neonates without meningitis. However, in our study cases, the septic neonates with meningitis also have various specific as well as non-specific symptoms for neonatal meningitis such as poor feeding, seizures, lethargy and abdominal distension but no statistical differences are seen between septic neonates with meningitis and without meningitis. Likewise, several studies have shown that neonates with meningitis have shown neurological manifestations including seizures, lethargy, stupor, irritability. However, neurological symptoms are more common in late onset sepsis; consideration of meningitis remains prudent whenever a neonate demonstrates even slight lethargy or irritability. Therefore, on the basis of symptoms in neonates with early onset sepsis, it is difficult to distinguish to

perform a lumbar puncture to rule out meningitis and hence, lumbar puncture should be carried out in all neonates with early onset sepsis, regardless of their symptoms. [7,16]

CONCLUSION

Although a low incidence of neonatal meningitis with early onset sepsis, but it is quite important to have lumbar puncture in all neonates with early onset sepsis because these 3.3 percent cases of meningitis would have been otherwise missed. All neonates with early onset sepsis diagnosed to have meningitis have positive blood cultures. Apart from, irritability, there are no statistical differences regarding the fetal and maternal risk factors and symptoms between septic neonates with meningitis and with no meningitis. Hence, we suggest that the lumbar puncture should be a part of routine septic work up in all neonates less than 72 hours of age with suspected sepsis.

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Simonsen KA, Ann L, Anderson-Berry B, Shirley F, Delair A, Dele Davies H. Early-Onset Neonatal Sepsis. Clin Microbiol Rev 2014; 27(1): 21–47.
2. Singh M, Narang A, Bhakoo ON. Predictive perinatal score in the diagnosis of neonatal sepsis. J Trop Pediatr 1994; 40:365-8.
3. Ajayi OA, Mokuolu OA. Evaluation of neonates with risk for infection/suspected sepsis: is routine lumbar puncture necessary in the first 72 hours of life? Trop Med Int Health 1997; 2:284–8.
4. Hamer DH, Darmstadt GL, John BC, Anita KM, Zaidi SM. Etiology of Bacteremia in Young Infants in Six Countries Pediatr Infect Dis J 2015;34(1): e1–e8.
5. Birju A Shah, James F Padbury. Neonatal sepsis Virulence 2014; 5(1): 170–178.
6. Chacko B, Sohi I. Early Onset Neonatal Sepsis. Indian J Pediatr 2005; 72:23-6.
7. Shiva F, Mosaffa N, Khabbaz R, Padyab M. Lumbar puncture in neonates under and over 72 hours of age. JCPSP 2006; 16:525-8.
8. Eldadah M, Frenkel LD, Hiatt M, Hegyi T. Evaluation of routine lumbar punctures in newborn infants with respiratory distress syndrome. Pediatr Infect Dis J 1987;6:243–6.
9. Walsh-Sukys M, Shenker N, Boxerbaum B, Fanaroff AA. Lumbar puncture in the newborn sepsis evaluation: Another Anachronism? Pediatric Research 1992;31:228A.
10. 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.
11. Hendricks-Munoz KD, Shapiro DL. The role of the lumbar puncture in the admission sepsis evaluation of the premature infant. J Perinatol1990; 10:60-4.
12. Weiss MG, Ionides SP, Anderson CL. Meningitis in premature infants with respiratory distress: role of admission lumbar puncture. J Pediatr 1991; 19: 973– 5.
13. Rad EM, Momtazmanesh N. Neonatal Sepsis due to Klebsiella: Frequency, Outcome and Antibiotic Sensitivity. Iranian J Publ Health 2004; 33:43-8.
14. Ghadamli P. A review of bacterial pathogens of neonatal sepsis at hospitals of ShahidBeheshti University during the period between1992-1997. J Qazvin Univ Med Sci 1998; 2:53-7.
15. Misallati A, El-Bargathy S, Shembesh N. Blood-culture-proven neonatal septicemia: a review of 36 cases. East Mediterr Health 2000;2-3:483-6.
16. Johnson CE, Whitwell JK, Pethe K, Saxena K, Super DM. Term Newborns WhoAre at Risk for Sepsis: Are Lumbar Punctures Necessary? Pediatrics 1997; 99:e10.
17. Heath PT, NikYousoff NK, Baker CJ. Neonatal meningitis. Arch Dis Child Fetal Neonatal Ed 2003; 88:73-8.
18. MacMahon P, Jewes L, de Louvois J. Routine lumbar punctures in the newborn—are they justified? Eur J Pediatr 1990;149:797–9.
19. Kaftan H, Kinney JS. Early onset neonatal bacterial infections Semin Perinatol 1998; 22:15-24.
20. Stoll BJ, Hansen N, Fanaroff AA, Wright LL, Carlo WA, Ehrenkranz RA, et al. To tap or not to tap: high likelihood of meningitis without sepsis among very low birth weight infants. Pediatrics 2004;113: 1181–6.