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Profile of Neonates with Early Onset Neonatal Sepsis in A Level Three Neonatal Intensive Care Unit of Developing Country

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Abstract:
Introduction: *Neonatal infections are the commonest cause of neonatal mortality along with prematurity in India. (1) Early onset sepsis (EOS) is neonatal sepsis occurring within the first 3 days of birth and constitutes a formidable cohort to address as it is more fulminant and has a higher mortality than late onset sepsis (LOS). We decided to conduct a study to quantify the burden, profile of neonates with EONS in our unit.*
Methods: *A prospective observational study was conducted on term and preterm neonates with birth weight more than 1200 grams admitted to the nursery with symptoms of EONS or at risk for EONS for 1 year. Primary objectives of the study were to determine the incidence, and profile of bacteria causing EONS. Secondary objectives were to find role of sepsis screen (SS) and risk factors (maternal and neonatal) in EOS.*
Results: *Out of 1328 neonates admitted in the NICU, 330 cases were enrolled. Of 321 neonates with suspected sepsis 291 had probable sepsis and 227 (70.7%) had focal infection in the form of pneumonia in 79 (34.8 %) and meningitis in 170 (74.9%). Of the 21 culture positive neonates 15 (71.4%) had meningitis and 5 (23.8%) had pneumonia (4 had both meningitis and pneumonia) and 5 (23.8%) had only bacteremia. E coli and S aureus accounted for 28.5% pathogens each, Enterococcus fecalis for 19.0 %, Acinetobacter andPseudomonas for 9.5 % each and Citrobacter for 4.7%. Of the maternal risk factors Premature rupture of membrane and unclean PV examination were more likely to have meningitis as compared to those who did not (Fisher p= 0.046, OR 13.75, CI 1.207-156.56 for both).*
Conclusion: *EOS makes up about one fourth of the total patient burden in our NICU. Incidence of culture positive EOS was 1.6 % NICU admissions and 6.5 % (21/321) in those suspected to have sepsis. The occurrence of gram positive and negative sepsis was almost equal. E. coli and S. aureus were the commonest organisms cultured.*
Keywords: *EONS, incidence, bacteria profile, risk factors, sepsis screen*

I. Introduction

Neonatal infections are the commonest cause of neonatal mortality along with prematurity in India. (1)EOS is much more fulminant than late onset sepsis (LOS). Moreover, the maternal profile has a strong bearing on its occurrence and therefore it can be anticipated to occur in many cases, giving us an opportunity to catch them early and treat them vigorously if we are vigilant. The four modalities that we have to meet these challenges are looking for presence of risk factors (maternal and neonatal), closely monitoring all neonates with risk factors for clinical signs of sepsis, doing the sepsis screen and getting a blood culture (and CSF where pertinent) done. The problems faced are that most neonates with EOS present within the first 24 hours of birth and have non specific symptoms such as tachypnoea which is not specific for sepsis and can occur in conditions like transient tachypnoea of the newborn, asphyxia or difficulty in transition. Also the sepsis screen (SS) has low positive predictive value and cultures take time to be reported and may be falsely negative if mothers or neonates have been previously exposed to antibiotics. It is therefore difficult to decide whom to treat on the basis of symptoms and the SS alone and inadvertently a large number of neonates receive unnecessary antibiotics.The latest report on management of neonates with early onset sepsis issued by the American Academy of Paediatrics (AAP) gives weight age to maternal and neonatal risk factors and the sepsis screen. It is clear that we cannot follow these guidelines blindly. (2)We decided to conduct this prospective observational study to quantify the burden of EOS, the pathogens implicated, the baseline and clinical profile and the outcome of these neonates being treated in our unit according to our protocol.

II. Methods

This was a prospective observational cohort study done in a tertiary level neonatal unit of North India. The study was done over a period of 1 year after taking ethical approval from Ethics committee of the university. All consecutive neonates (term as well as preterm) admitted in NICU with clinical features suggestive of EOS or "at risk" for EOS formed the study subjects.Neonates withBirth weight less than 1200g, major congenital anomaly, severe asphyxia (Apgar <4 at 5 minutes or HIE stage 3), hyaline membrane disease and whose parent did not give consent were excluded. All the neonates suspected of having EOS on the basis of clinical signs and symptoms were considered for inclusion in the study. Those having any exclusion criteria or leaving the NICU before being investigated for EOS or dying within 24 hrs.ofadmission were excluded. A detailed history was taken including that of maternal and neonatal risk factors for EOS, antibiotic exposure of mother and neonate prior to admission, details of antenatal, peripartum events including delivery, demography and baseline characteristics. Neonates were meticulously examined and then divided in to two groups on the basis of their clinical profile and maternal risk factors -High suspicion of EOS (HS-EOS), Low suspicion of EOS (LS-EOS)

Those with at least one remarkable clinical feature or one remarkable maternal risk factor grouped as HS-EOS and rest as LS-EOS. Remarkable maternal risk factors considered were maternal fever within two weeks of delivery, Foul smelling liquor, Leaking per vaginum > 24 hrs, Prolonged labour > 24 hr, Unclean per vaginum examinations. Remarkable clinical features taken were- Hemodynamic instability (CRT> 3 sec, hypotension), Pneumonia (NNPD definition), Encephalopathy not explained by asphyxia or metabolic dysfunction or clinical features suggestive of pyogenic meningitis (fever with seizure) or bulging fontanelle. All symptomatic neonates had a sepsis screen and a blood culture. Neonates with respiratory distress, crepitations or diminished air entry suggesting pneumonia underwent a chest X-ray. All symptomatic neonates except those whose symptoms could be attributed to hyaline membrane disease or a metabolic derangement like hypoglycaemia had a LP to rule out meningitis.Neonates in "high suspicion of EOS" group were started on IV antibiotics in addition to standard supportive care of a sick neonate.Neonates in low suspicion of EOS group were given supportive care and were closely monitored for the next 6-12 hrs to decide if their symptoms and signs were consistent with sepsis. If they were consistent with sepsis they too were started on IV antibiotics."At risk" neonates were also watched closely for signs and symptoms of sepsis .If they developed these they were shifted in to one of the groups described above and managed accordingly.

Duration of antibiotics was according to the unit protocol based on the nature of disease eg pneumonia, meningitis or bacteraemia. The duration was also longer if the sepsis screen was positive (5-7 days) or the clinical picture was grave. Outcome variables seen were- Culture positive EOS (Blood/CSF), Clinical EOS (sepsis screen positive in the absence of positive cultures) or having pneumonia or meningitis, Proportion of neonates with high suspicion of EOS and low suspicion of EOS having a positive sepsis screen.

All data were entered in a excel file. Analysis was done by SPSS software version 15.0and Epi-info software. Expecting 50% of neonates with "high suspicion of EOS "to have a positive sepsis screen and 20% of "low suspicion of EOS "to have a positive sepsis screen the sample size was 37 for each group.

III. Results

Out of 1328 neonates admitted in the NICU during the study period, 532 were either suspected to have EOS or were at risk of EOS. Of these 182 did not fulfil our inclusion criteria and 20 became asymptomatic after supportive care within in 6-8 hrs, so finally 330 cases were enrolled. Out of these 321 neonates were symptomatic and suspected to have EOS. Out of these 21 had positive culture and 263 had positive sepsis screen. Table 1 gives the baseline characteristics of study patients.Incidence of culture positive EOS was 21/1328 i.e. 15.8/1000 NICU admissions. Incidence of most probable EOS was 263+ 45 /1328 i.e. 231.9 /1000 NICU admissions. Incidence of culture positive EOS in those suspected to have sepsis 21/321 ie 6.5%. Incidence of most probable EOS in those suspected to have sepsis was 263+45 / 321 i.e. 98.7 %.

Table 1 Profile of neonates with EOS

Base Line Characteristics	**No. of Neonates**		p value
	CULTURE PROVEN(n=21)	MOST PROBABLE (n=263)	
Male	15 (71.4%)	198 (76.1%)	0.6949
Birth Weight < 1500 gm	2 (9.5%)	26 (10.3%)	0.9595
Birth asphyxia	2 (9.5%)	58 (18.7%)	0.1922
Meconium stained liquor	1 (4.3%)	17 (6.4%)	0.7590
PROM> 24 hrs	12 (57.1%)	160 (60.6%)	0.7391
Maternal Fever	7 (13.3%)	36 (13.5%)	0.2563
Foul Smelling Liquor	4 (19%)	20 (6.7%)	0.0812
Prolonged Labour	2 (9.5%)	20 (6.7%)	0.7131

Unclean Pv Examination	12 (57.1%)	156 (59.6%)	0.8465
Mean weight in gm (SD)	2417.14(718.75)	2389(602.67)	0.9765
Mean gestation in weeks (SD)	36.4 wks(1.8)	37.6 (2.3)	0.8765

Male gender, PROM>24 hrs and unclean PV examination were the most common baseline neonatal and maternal characteristics responsible for both culture positive and most probable sepsis. Rate of sepsis screen positivity in high suspicion group was higher (88.3%) as compared to low suspicion group (63.9%). Statistically, this difference was also significant ($p<0.001$). Rate of sepsis screen positivity in high suspicion group was higher (93.2%) as compared to low suspicion group (40%)Statistically, this difference was also significant ($p<0.05$).

Table 2 shows the bacteriological profile of organisms isolated from patients of EONS.

Table 2: Profile of isolates in neonates with EOS

Specimen	Number Of Isolates	Names Of Isolates
Blood	6	*E. coli*
	6	*Staph. Aureus*
	4	*Enterococcus faecalis*
	2	*Pseudomans*
	2	*Acinetobacter*
CSF	2	Enterococcus faecalis
	1	Staph aureus
	1	E coli
	1	Citrobacter

Out of total 330 enrolled patients, 13 patients left against medical advice due to financial constraints, 5 patients were expired. Among 21 culture positive cases, only 1 (4.8%) expired while others (94.5%) were discharged.

IV. Discussion

In our study, incidence of suspected EOS was 241.7/ 1000 NICU admissions, culture proven EOS was 15.8/ 1000 admissions and most probable EOS was 231.9 /1000 NICU admissions. Among neonates suspected to have EOS, incidence of culture proven EOS was 6.5% and that of most probable EOS was 98.7%. Sepsis screen was positive in 81.9% (263/321). This is similar a recent Indian study(3) who reported the incidence of suspected EOS for outborn babies as 190 /1000 admissions. However sepsis screen and cultures were positive in 57% and 18% (n=15) of suspected EOS respectively in their study. Our culture positivity rate was much less than that of other studies from India and other developingcountries positivity in 17.8-51.38% of suspected sepsis. (4, 5, 6)This may be because we are having most of our out born patients who come with IV antibiotics.
Twenty neonates in our study had 25 positive cultures (20 in blood + 5 in CSF). Four neonates had the same organism isolated from blood and CSF. The proportion of Gram negative and Gram positive sepsis was similar (52.3% Gram negative and 47.6% Gram positive) *E. coli* (6) and *S. aureus* (6) were the commonest organisms isolated. Both together made up 57.1% of the isolates. *Acinetobacter* and *Pseudomonas* had equal occurrence (10% each). *Enterococci* made up 20% of all isolates. There was one *Citrobacter* (5%). We did not isolate any *Klebsiella* in our study unlike many other studies from India where it was found to be the commonest pathogen. Our results were similar to those from other units in India. (3, 5, 6)

Our data is different from that in developed countries while the use of intrapartum maternal prophylaxis for GBS has reduced the incidence of early-onset GBS disease by at least 80%; however, GBS remains one of the leading causes of EOS . Current epidemiological trends are showing a decrease in the frequency of early-onset GBS disease related directly to prenatal screening and treatment with intrapartum antibiotic. (7, 8, 9, 10)The change in pathogens over time from predominantly Gram-positive to predominantly Gram-negative requires confirmation by ongoing surveillance. In our study Imipenem and levofloxacin worked best for Gram negative bacteria (about 70% sensitivity) while piperacillin and cefepime were the second best (about 50% sensitivity). Our antibiotic susceptibility was very similar to that of others from developing countries with high resistance to Ampicillin, Betalactams and even Aminoglycosides. Sameh Samir (6) reported *E. coli* sepsis to be resistant to ampicillin but best susceptible to imipenem. High susceptibility to imipenem (91%) was also found by Macharashvili*et al*. (11).According to the results of Sameh Samir (6) it seems that piperacillin is the best effective agent against Pseudomonas. In contrast, Bhat et al (12) found that only 24% of *Pseudomonas* isolates were susceptible to piperacillin in our study only 50% pseudomonas were sensitive to piperacillin.

Of the maternal risk factors our results revealed that neonates whose mothers had PROM and unclean PV examination were more likely to have meningitis as compared to those who did not (Fisher p= 0.046, OR 13.75, CI 1.207-156.56 for both). There was a significant correlation between the sepsis screen and the clinical groups (high and low suspicion of EOS) we make in our unit when treating EOS. Sepsis screen positivity in high suspicion group was higher (88.3%) as compared to low suspicion group (63.9%, p<0.001). However without the sepsis screen the decision of when to stop the antibiotics would be difficult. In our study sepsis screen did not show a significant correlation with positive cultures. This could primarily be because more than 80% of our admissions are out born neonates and in many of them there is exposure to antibiotics in the mother or the neonate prior to admission. Presence of two abnormal parameters in a screen is associated with a sensitivity of 93%, specificity of 83%, positive and negative predictive values of 27% and 100% respectively in detecting sepsis. Escobar et al (13) reported that population based studies showed only moderate sensitivity and specificity for sepsis, using an upper limit of 0.25 to 0.30, MamtaJajoo (3) reported that the sensitivity and specificity of sepsis screen were 71% and 47%, respectively, while positive and negative predictive values were 22% and 89% respectively.

The mortality rate for culture positive EOS in our unit was 4.7% (1/ 21) and for most probable and culture positive EOS combined it was 16.2% (5/308). Of the 5 neonates with EOS who died 3 (60%) were males and 3(60%) had maternal risk factors for EOS. Three (60%) neonates died in the second week of life while the rest died in the first week itself. Twenty percent of those who died had culture proven sepsis and only twenty percent had focal infection in the form of meningitis. Out of 21 neonates with culture proven sepsis the one who died had *E coli*bacteremia without pneumonia or meningitis.Multi-centric data from India have revealed 17% mortality among out born neonates with 19.3% mortality in preterm neonates due to sepsis (14).Betty Chacko et al (5) working on inborn neonates reported that 7 neonates with EOS died, with case fatality rate of 19.4% while among the culture positive cases, 2 died, the mortality rate being 13.3%. MamtaJajoo (3) reported a case fatality rate of 14%, which is comparable to other studies done in out born newborns. They found mortality rates among preterm, 8 (57%) neonates was significantly higher than the term 6 (43%) neonates.

Our study has revealed the profile of EOS in our unit to us. EOS makes up about one fourth of the total patient burden in our NICU. The occurrence of gram positive and negative sepsis is almost equal. E coli and S aureus being the commonest organisms cultured. This audit will help us to choose empirical antibiotics judiciously.The current management policy of our unit of segregating patients with EOS into 2 groups (high and low suspicion groups) on the basis of their clinical profile (symtomps and signs and maternal risk factors) at admission seems rational (even though the details of the maternal risk factors are often sketchy as our babies are mostly out-born) as the groups correlated well with the results of the sepsis screen that came in later.

References

[1]. Aggarwal R, Sarkar N, Deorari AK, Paul VK. Sepsis in the newborn.Indian J Pediatr. 2001;68(12):1143-7.
[2]. Richard A. Polin, MD and the COMMITTEE ON FETUS AND NEWBORN (AAP Guidelines 2012).
[3]. Jajoo M, Kapoor K, Garg LK, Manchanda V, Mittal SK. To study the incidence and risk factors of early onset neonatal sepsis in an outborn neonatal intensive care unit of India. J Clin Neonatal 2015;4;91-5.
[4]. Bhat Y R, Lewis LE, K E V. Bacterial isolates of early-onset neonatal sepsis and their antibiotic susceptibility pattern between 1998 and 2004: an audit from a center in India.˜Ital J Pediatr.˜2011;37:32.˜[PMC free article
[5]. Chacko B, Sohi I. Early onset neonatal sepsis.Indian J Pediatr. 2005;72(1):23-6.
[6]. Sameh Samir Fahmey, Early-onset sepsis in a neonatal intensive care unit in BeniSuef, Egypt: bacterial isolates and antibiotic resistance pattern.
[7]. Stoll BJ, Hansen N, Fanaroff AA, et al. Changes in pathogens causing early-onset sepsis in verylow- birth-weight infants. N Engl J Med. 2002; 347:240-247.
[8]. Bauserman MS, Laughon MM, Hornik CP, Smith PB, Benjamin DK, Jr, Clark RH, Engmann C, Cohen-Wolkowiez M. 2013. Group B Streptococcus and Escherichia coli infections in the intensive care nursery in the era of intrapartum antibiotic prophylaxis.Pediatr. Infect. Dis. J. 32:208–212 .
[9]. Puopolo KM, Madoff LC, Eichenwald EC. Early-onset group B streptococcal disease in the era of maternal screening.Pediatrics.2005; 115:1240-1246.
[10]. Phares CR, Lynfield R, Farley MM, et al. .Epidemiology of Invasive Group B Streptococcal Disease in the United States, 1999-2005.JAMA.2008; 299:2056-2065. [PubMed: 18460666].
[11]. Macharashvili N, Kourbatova E, Butsashvili M, Tsertsvadze T McNutt LA, Leonard MK. Etiologyofneonatal blood stream infections in Tbilisi of Georgia. Int J Infect Dis2009;13:499- 505.
[12]. Bhat Y R, Lewis LE, K E V. Bacterial isolates of early-onset neonatal sepsis and their antibiotic susceptibility pattern between 1998 and 2004: an audit from a center in India.˜Ital J Pediatr.˜2011;37:32.˜[PMC free article].
[13]. Escobar GJ. The neonatal -sepsis work-up-: Personal reflections on the development of an evidence-based approach toward newborn infections in a managed care organization. Pediatrics 1999;103 1 Suppl E: 360-73.
[14]. National Neonatal Perinatal Database2002-2003 .NNPD Network. www.newbornwhocc.org/pdf/HRRC-Report_2002-03.pdf.

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