

Bacterial profiles and risk factors for neonatal sepsis in a rural tertiary care hospital in north India

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Abstract

Objectives: To study, the bacterial profile in cases of neonatal sepsis admitted to the neonatal nursery or neonatal intensive care unit (NICU) and to identify the risk factors for early-onset neonatal sepsis. **Design:** Retrospective survey of hospital records from January 2012 to December 2012. **Setting:** A neonatal unit of a rural medical college hospital. **Subjects:** All inborn and outborn neonates who either had clinical signs of sepsis or were born to mothers with risk factors for sepsis and underwent a sepsis screen. Neonatal sepsis was defined as positive blood culture in babies younger than 1 month of age who had clinical signs of sepsis or had maternal risk factors for sepsis. **Results:** 396 neonates were screened for sepsis during the study period, of which 64 (16%) were culture positive. Of these, 42 (65.6%) had early-onset sepsis while 22 (34.3%) had late-onset sepsis (LOS). There were 6 deaths among those who had sepsis (9.3%). The predominant organisms in both early and LOS were *Klebsiella* and *Staphylococcus aureus* followed by *Escherichia coli*. **Conclusion:** The pattern of isolates is more or less similar to that seen in other NICU across the country. *Klebsiella* and *S. aureus* were two of the commonest organisms isolated in our study.

Key words: Bacterial profile, Neonate, Risk factors, Sepsis

Neonatal mortality in India continues to remain a major public health problem. According to the 2010 census, the neonatal mortality rate in our country is 33/1000 live births [1]. Neonatal infections are one of the three major contributors to neonatal mortality causing about one-quarter of the deaths [2]. The signs of neonatal sepsis may be non-specific and easily missed, especially in the early stages. A high index of suspicion and identification of both maternal and neonatal risk factors is an important measure in early identification and prompt treatment. Of necessity, many more babies are evaluated and treated for sepsis than those who actually have the condition [3]. Etiological causes also vary with a wide variety of aerobic and anaerobic bacteria implicated in neonatal sepsis.

Various risk factors for neonatal sepsis, such as prolonged rupture of membrane (PROM), prematurity, low birth weight (LBW), male sex, instrumental deliveries, and birth asphyxia, have been identified, but the relative importance of these risk factors in the etiology varies across different study populations [4-6]. Studies from the Indian subcontinent have demonstrated different causative organisms as compared to Western studies [6-8]. A large number of studies have been conducted in different parts of the country, and there is no dearth of data in this regard.

However, no etiological survey has previously been done in our institution, and there was a perception that a large number of patients with culture-positive neonatal sepsis were being admitted to the neonatal intensive care unit (NICU). There was also a felt need to look at the risk factors prevalent in our patient population to design effective infection control practices. This study was, therefore, undertaken to determine the bacterial profile patterns of aerobic isolates from blood cultures of neonates in our rural tertiary care hospital in north India and to identify the risk factors for early-onset sepsis (EOS) prevalent in our study population.

MATERIALS AND METHODS

A retrospective study of hospital records over a period of 1-year from 1st January 2012 to 31st December 2012 was done to look at all neonates screened for sepsis during that period. The neonatal nursery and NICU at our rural medical college and hospital caters to babies born at this hospital as well as outborns from the surrounding areas with a total capacity of 9 intensive care beds and 10 nursery beds. All inborn and outborn neonates who either had clinical signs of sepsis or born to mothers with risk factors for sepsis and underwent a sepsis screen were included in the study.

Data for the study were collected from patient files and microbiology records. The protocols for sepsis screening in neonates are already in place in the institution and study subjects were chosen accordingly. EOS was defined as the presence of positive blood culture in neonates <72 h of age who had clinical signs or risk factors for sepsis. Late-onset sepsis (LOS) was defined as a positive blood culture in neonates more than 72 h of age who had risk factors or clinical signs of sepsis [9].

As per hospital policy, all neonates admitted with maternal risk factors for sepsis or clinical signs of sepsis undergo a septic screen and blood culture. Septic screen consisted of total leucocyte counts, absolute neutrophil count, the ratio of immature neutrophils to total neutrophils, and a qualitative c-reactive protein. The septic screen was regarded as positive when two out of four parameters were positive [9]. Blood culture and the septic screen were done in the following settings.

At Birth

All neonates (i) born to mothers with maternal fever, PROM for more than 24 h, foul smelling or meconium stained liquor (MSL), or frequent (>3) unclean vaginal examinations, and/or (ii) having severe prematurity, or birth asphyxia necessitating active resuscitation.

After Birth

All newborns with lethargy, refusal to feed, abdominal distension, respiratory distress, temperature instability, pathological jaundice, convulsions, autonomic disturbances, and bleeding manifestations with constitutional symptoms [10].

The data regarding blood cultures was procured from the microbiology department records. The procedure adopted for blood cultures in the microbiology laboratory was as follows: Minimum 1 ml of blood from specimen received is inoculated into Trypticase soya broth medium and incubated at 37°C. After 24 h, subcultures were performed on sheep blood agar, MacConkey's agar, and nutrient agar. Subcultures were repeated at 48 h and 5 days intervals after which the subcultures were declared negative. If any growth was identified in any subculture, it was confirmed by standard bacteriological techniques, which include Gram staining, biochemical reactions and slide agglutination with specific antisera where appropriate. Aerobic spore bearers wherever grown were regarded as contaminants.

Statistical analysis was done using IBM SPSS statistical version 22. Chi-square and unpaired *t*-tests were used for comparison between groups.

RESULTS

During the 1-year study period, there were a total of 728 admissions in the NICU, 510 of these were intramural births

(70.05%), and remaining cases were outborn. Total 396 neonates were screened for sepsis and of these, 64 (16%) had culture proven sepsis with 40 (62.5%) of them being intramural births. The mean birth weight of the culture positive neonates was 2044.64 ± 0.548 g and mean age at presentation was 47 ± 5.45 h.

Among culture positive neonates, *Klebsiella* was the most common isolated organism in early as well as LOS. *Staphylococcus aureus* was the most common isolated Gram-positive bacterium (Table 1). In EOS, *Klebsiella* species were isolated in 41.46% of the cases. The second most frequent organism was *S. aureus* followed by *Escherichia coli*. The other commonly isolated organisms were *Acinetobacter*, coagulase-negative staphylococci, and *Enterobacter*. Enterococci were isolated in one case.

In LOS, the profile was slightly different. *Klebsiella* species were again the most common organisms (39.13%) followed by *S. aureus*. However, the other common isolated organisms were *Citrobacter* species and Enterococci. *E. coli* was much less common in LOS, being isolated in only one case. *Enterobacter*, non-fermenting Gram-negative bacilli, and coagulase-positive staphylococci were also isolated in one case each. Table 1 compares the distribution frequency of organisms in EOS and LOS.

An analysis of the perinatal risk factors showed that except postnatal age at the time of presentation the differences between the EOS and LOS groups were not statistically significant (Table 2). Backward regression analysis model showed that meconium aspiration and birth asphyxia were the common predictors of neonatal sepsis; although, the association was not significant ($p=0.309$ and 0.212 , respectively). There were a total of 6 sepsis-related deaths (9.4%); 4 of which were due to EOS and two were due to LOS. In the EOS group, two deaths were due to *Klebsiella* species, one each was due to *S. aureus* and *E. coli* sepsis while *S. aureus* and non-fermenting Gram-negative bacilli were the causative organisms in LOS group. Seven patients (10.9%) were either referred or left against medical advice.

DISCUSSION

Our study documented a culture positivity rate of 16% (64/396). This is similar to that reported in previous studies done in India and Mexico [11,12]. However, others have documented a higher culture positivity rate of 26.6-46.2% [8,13]. A low rate of culture positives may be due to the fact that screening for sepsis was done in all high-risk neonates as well as those with clinical features suggestive of sepsis. Second, anaerobic cultures were not done in this cohort of the patients. It has been documented that up to 26% cases of neonatal sepsis may be caused by anaerobes [14].

In developing countries, pathogens isolated are different from those seen in developed nations. In our study, *Klebsiella*

Table 1: Distribution frequency of bacterial isolates (n=64) from newborns with clinically suspected septicemia

Isolate	Distribution frequency (%)		
	Total cases (n=64)	EOS (n=41)	LOS (n=23)
Gram-negative bacilli (n=41)			
<i>Klebsiella</i> species	26 (40.63)	17 (41.46)	9 (39.13)
<i>E. coli</i>	7 (10.94)	6 (14.63)	1 (4.35)
<i>Enterobacter</i>	3 (4.69)	2 (4.9)	1 (4.35)
<i>Acinetobacter</i>	2 (3.13)	2 (4.9)	0
<i>Citrobacter</i> species	2 (3.13)	0	2 (8.69)
Non fermenting Gram-negative bacilli	1 (1.56)	0	1 (4.35)
Gram-positive cocci (n=23)			
<i>S. aureus</i>	17 (26.56)	11 (26.83)	6 (26.09)
Enterococci	3 (4.69)	1 (2.43)	2 (8.69)
Coagulase-negative staphylococci	2 (3.13)	2 (4.9)	0
Coagulase-positive staphylococci	1 (1.56)	0	1 (4.39)

E. coli: *Escherichia coli*, *S. aureus*: *Staphylococcus aureus*, EOS: Early-onset sepsis, LOS: Late-onset sepsis

Table 2: Comparison of perinatal factors for early and LOS

Perinatal factors	Total (n=64)	EOS (n=41)	LOS (n=23)	p value
Neonatal factors				
Mean postnatal age (days)	5.30±7.17	1.58±0.80	11.90±8.64	<0.001
Mean birth weight (g)	2044.64±0.548	2119.87±633.87	1910.52±762.73	0.243
Mean GA (weeks)	34.78±3.46	35.21±3.42	34.34±3.54	0.337
Male sex	39 (60.9%)	25 (61%)	14 (61%)	1.000
Preterm	39 (60.9%)	24 (58.5%)	15 (65%)	0.599
Maternal risk factors				
PROM>24 h	13 (20.31%)	9 (22%)	4 (19%)	0.664
Maternal pyrexia	1 (1.56%)	1 (2.4%)	0	0.450
Chorioamnionitis	1 (1.56%)	1 (2.4%)	0	0.450
Birth asphyxia	7 (10.93%)	6 (14.6%)	1 (4.3%)	0.206
Meconium liquor	6 (9.38%)	5 (12.2%)	1 (4.3%)	0.301
Multiple vaginal examinations	0	0	0	-
UTI	0	0	0	-
Mode of delivery (%)				
Normal	46 (71.8%)	30 (73.2%)	16 (69.6%)	0.758
LSCS	18 (28.2%)	11 (26.8%)	7 (30.4%)	

PROM: Prolonged rupture of membrane, EOS: Early-onset sepsis, LOS: Late-onset sepsis, GA: Gestational age, UTI: Urinary tract infection, LSCS: Lower segment cesarean section

species were the most common isolated organisms in both early and LOS. This is similar to the findings reported in earlier studies and those reported in the National Neonatal Perinatal Database [11,15]. In contrast, a study from Sikkim found *Pseudomonas* and *Enterobacter* species to be the predominant pathogens among Gram-negative organisms [16]. Among the Gram-positive organisms, *S. aureus* was the most common isolated organism. Group B streptococcus, which is common in the west, is infrequent in India [17] and was not isolated at our center in any case.

It is difficult to comment on the clinical significance of low virulence isolates such as coagulase-negative *staphylococcus*,

enterococci, and non-fermenting Gram-negative bacilli. However, in the clinical setting of sepsis, especially in small preterm neonates, it would not be wise to dismiss these isolates as contaminants. Babies with such isolates were treated for sepsis according to protocol, and we have reported these isolates in our study.

We looked at the risk factors for EOS in this study. Previous studies have shown an association between neonatal sepsis and factors such as prematurity, birth asphyxia, LBW, PROM, MSL, multiple vaginal examinations, chorioamnionitis, and urinary tract infections [7,18]. In a recent study by Sharma et al., the main risk factors for neonatal sepsis were PROM and maternal

exposure to antibiotics [6]. However, we could not demonstrate any statistically significant relation between any of the above risk factors and EOS as compared to LOS. It is possible that the numbers may be relatively small, and the study was not powered to look at individual risk factors. Furthermore, being a retrospective study, the data collection may not have been adequate.

However, it is significant that the majority of neonates with sepsis in our study were preterm (60.93%), and the average birth weight of patients was 2044.6 g. During a similar period, the average birth weight of infants born at the hospital was 2719±490 g and preterm LBW babies constituted 10% of the total live births [19]. This underlines the importance of the extra care that these infants need to prevent sepsis and sepsis-related mortality and morbidity.

Moreover, although it did not form a part of this study, our data showed that there is an increase in the drug resistance among the organisms. There is an urgent need for designing nationwide strategies to address the increasing prevalence of antibiotic-resistant organisms. The key to address this problem lies in a closer look at the risk factors for sepsis in this population so that optimum care strategies can be planned, and the risk for sepsis can be minimized.

The main limitation of our study was that it was retrospective in nature. Therefore, data regarding some of the risk factors might have been missed due to incomplete records.

CONCLUSION

Our study looked at bacterial isolates common in this area of Punjab. The pattern of isolates is more or less similar to that seen in other NICUs across the country. *Klebsiella* and *S. aureus* were two of the commonest organisms isolated all over the country, as was the case in our study.

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