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Original Research Article

Clinico-epidemiological spectrum of early onset neonatal sepsis in neonates admitted in NICU of a tertiary care institute

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ABSTRACT

Background: Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. Neonatal sepsis may be classified into two groups : early onset sepsis and late onset sepsis . Early onset neonatal sepsis is generally associated with the acquisition of microorganisms from the mother and usually presents with respiratory distress and pneumonia.
Methods: The study included one hundred term neonates with early onset neonatal sepsis. A septic screen including total leukocyte count, absolute neutrophil count, blood smear evaluation, blood cultures and C-reactive protein (CRP) were performed in all neonates with suspected sepsis to corroborate early onset sepsis diagnosis. Epidemiological parameters including gender of the neonate, mode of delivery, rural/urban residence were recorded in addition to clinical profile.
Results: Respiratory distress was the most common presentation in the form of tachypnea, seen in 63 (63.0%) neonates. In present study, Staphylococcus aureus was the most common organism isolated followed by *Staphylococcus epidermidis*, *Staphylococcus hominis*, *Acinetobacter baumannii* and *Klebsiella pneumonae*.
Conclusions: Early onset neonatal sepsis was seen more in males. Among the gram-positive *Staphylococcus aureus* and among gram negative *Acinetobacter baumannii* and *Klebsiella pneumonae* were most common organisms to be isolated.

Keywords: Blood culture, Early onset sepsis, Sensitivity, Term neonates

INTRODUCTION

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life.[1,2] Neonatal sepsis may be classified into two groups : early onset neonatal sepsis (EONS) and late onset neonatal sepsis (LONS).

The definition of early onset sepsis is variable from <3 days (American Academy of pediatrics) to <7 days (centre for disease control definition based on epidemiology studies).[2] EONS usually presents with respiratory distress.[1,3] Prematurity, low birth weight, foul smelling and meconium stained liquor, premature rupture of membranes, prolonged labour, more than three vaginal examinations during labor, and perinatal asphyxia constitute the main risk factors for EOS.[1,4] Neonate with sepsis may present with one or more of the following symptoms and signs viz. temperature instability, lethargy, poor cry, refusal to suck, poor perfusion, prolonged capillary refill time, respiratory distress, apnea, grunting, cyanosis and gasping respiration, bradycardia/tachycardia, hypoglycemia/ hyperglycemia and metabolic acidosis. Specific features related to various systems[5]:-

- Central nervous system (CNS): bulging anterior fontanel, vacant stare, excessive crying, stupor/coma, seizures, neck retardation.
- Cardiac: hypotension, poor perfusion, shock.
- Gastrointestinal: Feed intolerance, vomiting, diarrhea, abdominal distension, paralytic ileus, necrotizing enterocolitis.
- Hepatic: Hepatomegaly, direct hyperbilirubinemia.
- Renal: Acute renal failure.
- Skin changes: Multiple pustules, abscess, sclerema, mottling, umbilical redness and discharge.

The most common causes of EOS are Group b *Streptococci* (GBS), *Escherichia coli* (*E. coli*) and Listeria monocytogenes in developed countries and gram-negative organisms especially Escherichia coli (*E. coli*), *Klebsiella* and *Enterobacter species* and Coagulase-negative staphylococci (CONS) in developing countries.[6] Another important aspect is diagnosis of neonatal sepsis.

The warning signs and symptoms of neonatal sepsis are often subtle and non-specific and thus makes it difficult to establish an early clinical diagnosis indeed a high index of suspicion is needed for early diagnosis.

Blood culture is still considered to be the ‘’gold standard’’, however its accuracy has been questioned because of spurious positive results due to contamination and negative blood cultures in fatal generalized bacterial infections. The yield of a positive blood culture ranges from 8-13% as shown in serious studies.

Haematological markers (white blood cell counts , absolute neutrophil counts, ratio of immature to total cells) have been suggested and evaluated as diagnostic tests for neonatal sepsis. Wide variety of counts and acute phase reactants have been evaluated for diagnosis of systemic infections in neonates.

The pattern of organisms causing infections and their antibiotic sensitivity and resistance pattern also varies considerably from one hospital to other.

This study will also help in identifying the commonest organisms and their sensitivity pattern in our NICU among neonates with early onset sepsis. This will aid in appropriate usage of antibiotics, thereby avoiding irrational use.

METHODS

This was a prospective observational study conducted on one hundred term neonates admitted in neonatal ICU of Sri Guru Ram Das Institute of Medical Sciences and Research, from December 2015 till December 2017,after seeking approval from the ethical committee of the institute and taking informed consent from the parents of patients. The neonates with clinical and laboratory findings suggestive of early onset sepsis infection admitted to neonatal ICU within the first three postnatal days of life who were >37 weeks of gestation were enrolled. To corroborate the diagnosis of early onset neonatal sepsis (EONS)a septic screen including total leukocyte count, absolute neutrophil count, blood smear evaluation, blood cultures and C-reactive protein (CRP) were performed in all neonates with suspected sepsis. Epidemiological parameters including gender of the neonate, mode of delivery, rural/urban residence were recorded in addition to the clinical profile.

Inclusion criteria

The sepsis criteria used in the study defined by Gittoet al:[7]

- Highly probable sepsis: at least three sepsis related clinical signs, CRP>5mg/dl, at least two other altered parameters in addition to CRP, blood cultures; positive or negative.
- Probable sepsis: less than 3 sepsis –related clinical signs, CRP>5mg/dl, at least two other altered parameters in addition to CRP, blood cultures; negative.
- Possible sepsis: Less than 3 sepsis –related clinical signs, CRP<5mg/dl, less than 2 other altered parameters, blood culture; negative.
- No sepsis: CRP<5mg/dl, no altered parameters, blood cultures; negative.
- Sepsis related clinical signs: Temperature instability, apnea, need for supplemented oxygen, need for ventilation, tachycardia/bradycardia, hypotension, feeding intolerance, abdominal distension, necrotizing enterocolitis and seizures. Parameters: CRP, other than CRP: white blood cell count, absolute neutrophil count, platelet count, and blood cultures were also recorded.

Exclusion criteria

- Out born admitted after 72 hours of life
- Major congenital abnormality
- Maternal clinical chorioamnionitis
- Premature rupture of membranes.

Statistical analysis

The data were statistically analysed using the SPSS software, version 16.

Venous sample of neonates was collected for septic screen. Samples for blood cultures were taken with all aseptic and antiseptic precautions and then were cultured on blood agar and McConkey agar after overnight enrichment as per standard guidelines. The organisms were identified using Vi-tech 2and AST was then interpreted as per CLSI guidelines.

RESULTS

This prospective observational study was conducted in the NICU of Sri Guru Ram Das Institute of Medical Sciences and Research, Sri Amritsar. Higher number of cases were reported in males (62%) (Table 1).

Table 1: Gender wise distribution.

Gender	Cases	
	No.	%
Male	62	62.0
Female	38	38.0
Total	100	100.0

In total 31 neonates (31.0%) with EONS were born by NVD and 69 (69.0%) were delivered by LSCS (Table 2).

Table 2: Distribution according to mode of delivery.

Mode of delivery	Cases	
	No.	%
NVD	31	31.0
LSCS	69	69.0
Total	100	100.0

Thus, EONS was more in those delivered by LSCS. Out of total 100 cases with EONS, 78 (78.0%) cases belonged to rural and 22 (22.0%) to urban area (Table 3).

Table 3: Distribution according to rural/urban background.

Rural/urban	Cases	
	No.	%
Rural	78	78.0
Urban	22	22.0
Total	100	100.0

Out of total 100 cases with EOS, 65 (65.0%) neonates had highly probable sepsis, 24 (24.0%) had probable sepsis and 11 (11.0%) neonates had possible sepsis (Table 4).

Table 4: Distribution of cases according to sepsis.

Sepsis	No. of cases	%
Highly probable sepsis	65	65.0
Probable sepsis	24	24.0
Possible sepsis	11	11.0
Total	100	100.0

Respiratory distress was the most common presentation in the form of tachypnea which was seen in 63 (63.0%) neonates and chest retractions in 40 (40.0%) cases. 64 (64%) neonates needed supplemental oxygen and 23 (23%) neonates required ventilation (Table 5). Lethargy was seen in 35 (35.0%), and refusal to feed in 22(22.0%) cases. Poor perfusion and prolonged capillary refill time was seen in 20 (20.0%) neonates each followed by temperature instability seen in 14 (14.0%) cases.

Table 5: Distribution of neonates in relation to symptoms of sepsis.

Symptoms	No. of cases	%
Lethargy	35	35.0
Refusal to feed	22	22.0
Poor cry	9	9.0
High pitched cry	4	4.0
Sclerema	6	6.0
Hypothermia/fever	14	14.0
Cyanosis	4	4.0
Tachypnea	63	63.0
Chest retractions	40	40.0
Bleeding	17	17.0
Poor perfusion	20	20
Prolonged capillary refill time	20	20
Shock	11	11
Vomiting	19	19.0
Feeding intolerance	12	12.0
Abdominal distension	9	9.0
Necrotizing enterocolitis	1	1.0
Seizures	1	1.0
Bulging anterior fontanelle	5	5.0
Need for supplemental oxygen	64	64.0
Need for ventilation	23	23.0

Blood cultures were positive in 50 (50%) neonates (Table 6).

Table 6: Distribution of neonates in relation to blood culture positivity.

Blood culture	No. of cases	% Age
Negative	50	50.0
Positive	50	50.0
Total	100	100.0

Table 7: Organisms isolated.

Organism	No. of cases	% Age
Staphylococcus aureus	14	28.0
Staphylococcus epidermidis	8	16.0
Staphylococcus hominis	7	14.0
Coagulase negative staphylococcus	2	4.0
Staphylococcus haemolyticus	2	4.0
Enterococcus spp.	2	4.0
Granulicatella adiacens	1	2.0
Acinetobacter baumannii	5	10.0
Klebsiella pneumonae	5	10.0
Escherichia coli	3	6.0
Enterobacter spp.	1	2.0
Total	50	100.0

In present study, *Staphylococcus aureus* was the most common organism isolated in 14 neonates (28.0%) followed by *Staphylococcus epidermidis* seen in 8 neonates (16%) and *Staphylococcus hominis* in 7 cases (14%) (Table 7). Coagulase negative *staphylococcus*, *Staphylococcus haemolyticus* and *Enterococcus* were seen in 2 neonates each. *Acinetobacter baumannii* and *Klebsiella pneumonae* were the most common gram-negative organism isolated in 5 cases each followed by *Escherichia coli* seen in 3 cases. *Enterobacter* was seen only in 1 case. In present study, *Staphylococcus auereus* was highly sensitive to linezolid, vancomycin and daptomycin, whereas *Acinetobacter* and *Kleibsella*, were primarily sensitive to colistin and tigecycline (Table 8).

Table 8: Blood culture and sensitivity of organisms.

	Staphylococcus aureus n (14)	*Staph epidermidis* n (8)	*Acinetobacter* n (5)	*Klebsiella pneumonae* n (5)
Ampicillin			1	
Ciprofloxacin		1		
Gentamicin	3	5		
Tetracycline	2			
Piperacillin-tazobactam			1	
Cotrimoxazole	3	5 (62%)		
Tetracycline	4	6 (75%)		
Ciprofloxacin		2		
Linezolid	12 (85%)	7 (87%)		
Minocycline			3 (60%)	
Colistin			5(100%)	3 (60%)
Tigecycline	8 (57%)	3	5(100%)	5(100%)
Ticarcillin			2	
Polymyxin B				1
Daptomycin	12 (85%)	5		
Teicoplanin	10 (71%)	7 (87%)		
Vancomycin	12 (85%)	7 (87%)		
Nitrofurantoin	10 (71%)	6 (75%)		
Rifampicin	10 (71%)	8 (100%)		
Levofloxacin	2	2		
Clindamycin	4	2		

DISCUSSION

Neonatal sepsis is one of the major health problems throughout the world and one of the commonest causes of neonatal mortality and morbidity. It is estimated to cause almost 1 million deaths that accounts for more than 25% of neonatal deaths in worldwide.[8] Early onset sepsis is defined as bloodstream infection at less than or equal to 72 h of age.

It is generally associated with the acquisition of microorganisms from the mother and usually presents with respiratory distress and pneumonia.[1] The warning signs and symptoms are often subtle and non-specific and thus makes it difficult to establish an early clinical diagnosis.

The study was conducted healthy term neonates with early neonatal sepsis and various findings were recorded. It was observed that blood culture and sensitivity came out to be positive in 50 (50%) cases. Almost similar blood culture positivity rates were observed by Sharma et al and Sodani et al as 56% and 42.2% respectively.[9,10] On the other hand, comparative lower blood culture positivity rates were recorded bySanuja Sarasam E et al, Samaga MP and Mondal et al as 36.4%, 35.1 % and 32% respectively in cases with neonatal sepsis.[11-13] This difference in culture positivity rates might be because of the way samples were collected.

Furthermore, it was also found that early neonatal sepsis was more commonly seen in males (62%) as compared to their female (32%) counterparts. Similar pattern was observed by Sanuja Sarasam E et al, Samaga MP, Aletayeb S et al, Celicia C et al, Rabia S et al, Ahmad A et al, Karambin and Zarkesh, and Al-Shamahy et al which reported higher number of male neonatal septicaemia than female neonatal septicaemia, that correlates with present study.[11,12,14-19]

Probable reason for the male prepondrence might be because of males having only one x chromosome which is probably regulating the synthesis of gamma

globulins.[20] It was noticed that 31% babies in the study group were delivered vaginally while 69% were born by caeserian section. Similar to these findings, Sanuja Sarasam E et al revealed neonatal sepsis was more in babies delivered by caesarean section (54.45%) as compared to those delivered vaginally (47.6%). Early neonatal sepsis usually presents with respiratory distress and pneumonia. In present study respiratory distress in form of tachypnea (63%) and chest retractions (40%) was the most common clinical feature. Sanuja SE et al witnessed similar findings with respiratory distress (21.4%) as the most common presentation. Predominant organisms isolated from present study were staphylococcus aureus (28%), staphylococcus epidermidis (16%), staphylococcus hominis (14%), *Acineto bacterbaumannii* (10%) and *Klebsiella pneumonae* (10%). In contrast to this Sanuja Sarasam E et al and Samaga MP observed *Klebsiella pneumonae* as the most common isolate in early neonatal sepsis.

This difference might be because of the prevalence of different microorganism profile in our hospital as compared to the above study groups. In present study, *Staphylococcus auereus* was highly sensitive to linezolid, vancomycin and daptomycin.

Staph epidermidis also had similar sensitivity in addition to 100% for rifampicin. With respect to *Acinetobacter* and *Kleibsella*, sensitivity was maximum for colistin and tigecycline. Thus, the organisms were resistant to commonly used antibiotics similar to that observed by Samaga MP Guha et al and Monga et al.[12,21,22]

CONCLUSION

To conclude, respiratory distress was the most common presentation in the form of tachypnoea, seen in 63 (63.0%) neonates.

Staphylococcus aureus was the most common organism isolated followed by *Staphylococcus epidermidis*, *Staphylococcus hominis*, *Acinetobacter baumannii* and *Klebsiella pneumonae*.

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