Epidemiological Profile of Neonatal Sepsis in a tertiary care centre of western Uttar Pradesh - Prospective Study

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Abstract

Objectives: The study was designed with the objectives of evaluating the epidemiology of neonatal sepsis and factors associated with neonatal sepsis among neonates admitted to neonatal intensive care unit (NICU) in a tertiary care hospital in Meerut, Uttar Pradesh, India.

Design: Prospective cross-sectional study

Setting: The study was conducted in neonatal intensive care unit (NICU) at the Department of Paediatrics, LLRM Medical College, Meerut, Uttar Pradesh, India from April 2021 to March 2022.

Participants: Neonates.

Outcome measures: Presence of neonatal sepsis.

Results: Among 421 study participants, 199(47.3%) were males and 222(52.7%) were females. About 167(39.7%) were out born and 254(60.3%) were inborn, 216(51.3%) belonged to 32- 37 weeks period of gestation, 240(57%) were having birth weight between the 1500-2499 grams and 97(23%) had premature rupture of membranes. About 327(77.7%) and 94(22.3%) had early and late onset sepsis respectively. 252 had positive blood culture in which 17.8% were having E. Coli, 9.3% had Klebsiella, and 6.2% had Acinetobacter. Early onset sepsis was associated with the incidence of septic shock ($P = 0.020$) and DIC ($P = 0.047$). We also found a significant association between children born <37 weeks and incidence of septic shock ($P = 0.001$), and also between children born <32 weeks and DIC ($P = 0.001$).

Conclusion: This study reveals that early onset sepsis is more associated with septic shock and DIC. Association between proven and probable sepsis with morbidity indicators like DIC, septic shock and ventilatory support are well established.

Key words: Blood culture, DIC, Neonatal sepsis, Respiratory support, Septic shock

Introduction:

Sepsis is the commonest cause of neonatal mortality and is probably responsible for 30 to 50% of the total neonatal deaths each year in developing countries [1, 2]. In India, it contributes to around 23% of all neonatal deaths. The case fatality rates of neonatal sepsis may reach 52% contributing for almost one million deaths [3, 4]. It is estimated that 20% of all neonates develop sepsis and approximately 1% die of sepsis related causes. Sepsis related mortality is largely preventable with rational antimicrobial therapy with aggressive supportive care [5].

According to recent data, the incidence of neonatal sepsis has been reported to be 38 per 1000 intramural live births in tertiary care institutions. Septicaemia was the commonest clinical category with an incidence of 24 per 1000 live births. Klebsiella pneumoniae was the most frequently isolated pathogen (31.2%), followed by Staphylococcus aureus (17.5%) among the intramural live births. Among extramural babies admitted for neonatal problems, Klebsiella pneumoniae was the commonest organism (36.4%), followed by Staphylococcus aureus (14.3%) and Pseudomonas (13.2%).

Neonatal sepsis is defined as a clinical syndrome in an infant of 28 days of life or younger. It is manifested by systemic signs of infection and isolation of a bacterial pathogen from the bloodstream. The rates of blood stream infection (BSI) in neonates are 3-20 times higher in developing countries, and in some countries, approximately half of the patients in neonatal intensive care units (NICUs) acquire infection [6].

Even though sepsis related mortality is largely preventable with prevention of sepsis itself, timely recognition, rational antimicrobial therapy, and aggressive supportive care. Although high burden of neonatal sepsis related mortality and mortality are being reported from developing countries, most scientific evidence are derived from developed countries. The survivors of neonatal sepsis remain vulnerable to short and long-term neuro- developmental morbidity impacting the overall productivity of the child as adult [7].

Neonatal sepsis is primarily caused by diverse species of bacteria, viral and Candida [8]. This diverse nature of the organisms implicated in causing neonatal sepsis varies from region to region, and changes over time even in the same place which could be attributed to the changing pattern of antibiotic use and changes in lifestyle. Therefore, this study was designed with the objectives of evaluating the epidemiology of neonatal sepsis and factors associated with neonatal sepsis among neonates admitted to neonatal intensive care unit (NICU) in a tertiary care hospital in Meerut, Uttar Pradesh, India.

Materials and Methods:

Study setting: A prospective cross-sectional study was conducted in neonatal intensive care unit (NICU) at the Department of Paediatrics, LLRM Medical College, Meerut, Uttar Pradesh, India from April 2021 to March 2022.

Study participants: The study participants were all neonates (less than 28 days of life) with features of sepsis. The clinical features included the presence of one or more of the following,

a.   Hyperthermia
b.   Hypothermia
c.   Refusal to feed
d.   Irritability
e.   Abdominal distension
f.   Respiratory distress
g.   Convulsion
h.   Icterus
       Presence of any two or more laboratory criteria,
a.   Absolute neutrophil count <500,>1500 cells/mm3
b.   CRP >6gm/ litre
c.   micro ESR>15 mm for 1 hr

Exclusion criteria:

a.   Presence of congenital anomaly
b.   Presence of surgical problem
c.   Suspected metabolic disorder
d.   Birth asphyxia
e.   Taken antibiotics before admission
f.   Those where consent could not be obtained

Study methodology: The name, age, sex, address, date and time of birth, mode of delivery, place of birth, date of admission, inpatient number and a detailed clinical history was collected. A thorough head to toe examination including general examination and systemic examination was carried out.

For collection of blood sample for culture, the skin at the venopuncture site was meticulously prepared by thoroughly cleaning with 70% ethyl alcohol and by povidone iodine. These bactericidal agents were applied in concentric circles moving outwards from the centre. To avoid the possible irritation of iodine it was wiped off with alcohol. The skin was then allowed to dry for 1 minute before the blood could be withdrawn. Two ml of blood was withdrawn with aseptic precautions and inoculated into 5-10 ml of BACTEC™ culture media. The BACTEC™ culture was incubated aerobically at 37°c and observed for bacterial growth at 24 hrs, 48 hrs and 72 hrs to check the presence of any bacterial growth.

Sample size: Sample size was calculated based on the formula,

Sample size= 1.96 x 1.96 x p x (1-p)/l^2

In a study done by Shehab El-Din et al [9], the prevalence rate of suspected neonatal sepsis among the NICU admitted babies reported was found to be 45.9%. We took confidence interval at 95% and absolute error as 5% for calculating sample size, and it came to be 382. After adding 10% loss to follow up, the final sample size was 421.

Ethical issues: The study was conducted after getting permission from institutional ethical committee (IEC). Complete methodology was explained to the parents or attendants in their local language (Hindi) and a proper informed verbal and written consent was obtained.

Statistical analysis: Qualitative variables were expressed as means of frequencies and percentages. Continuous variables were expressed in terms of mean and standard deviation. A comparison of these parameters between the two groups was done using the independent samples two-tailed t-test and Mann Whitney U test in case of continuous variables and Chi-square test in case of qualitative variables. IBM SPSS software version 25 was used for the analysis and P value of less than 0.05 was considered to be statistically significant.

Results: Among 421 study participants, 199 (47.3%) were males and 222 (52.7%) were females. It was found that 167 (39.7%) were out born and 254 (60.3%) were inborn babies. More than half of the study population, 216 (51.3%) belonged to 32- 37 weeks period of gestation, 96 (22.8%) were having a period of gestation more than 37 weeks. About 92 (21.9%) were between 28 to 32 weeks of gestation, and 17 (4%) were less than 28 weeks of gestation.

In this study, 240 (57%) of the study population were having the birth weight between the 1500-2499 g and 86 (20.4%) were having a birth weight of more than 2500g. About 78 (18.6%) were very low birth weight, and 17 (4%) were extreme low birth weight. Antenatal risk factors for neonatal sepsis are illustrated in figure 1.

Figure 1: Bar chart representing Antenatal risk factors for neonatal sepsis
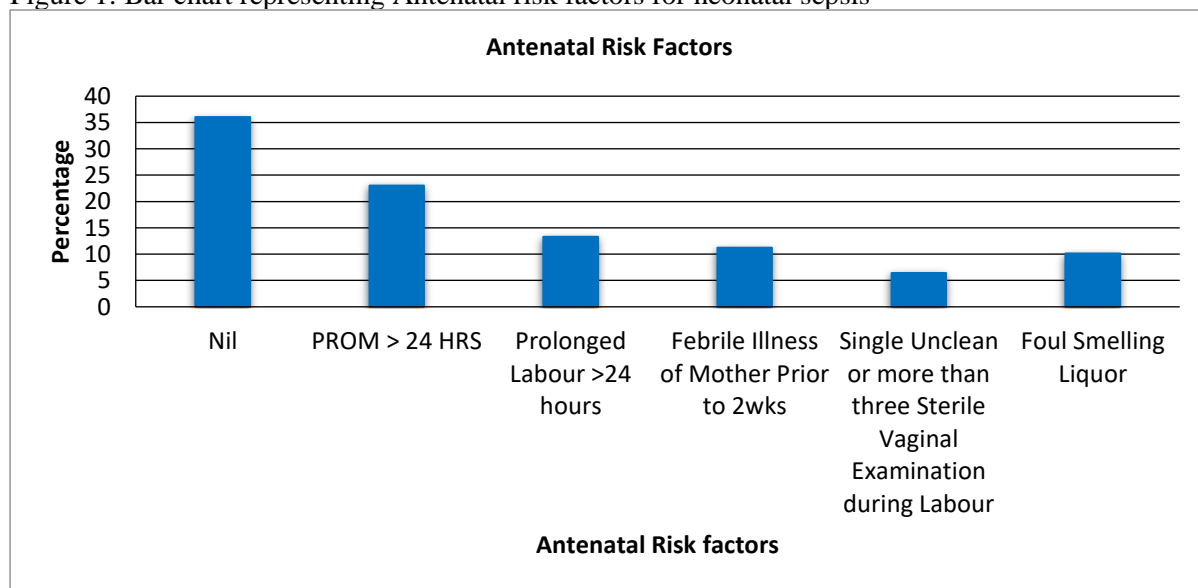
Out of 421 study population, 360 (85.6%) had no post-natal risk factors while 44 (10.5%) and 16 (3.9%) had faulty feeding and head shaving as post-natal risk factors respectively. Only 8 (1.9%) were born as home delivery.

About 327(77.7%) had early onset sepsis and 94 (22.3%) had late onset sepsis. 179 (42.5%) were having an absolute neutrophil count. Out of 421 study population, 209 (49.6%) blood culture was sterile, 252 were positive in which 17.8% were having E.coli, 9.3% had Klebsiella, 6.2% had Acinetobacter. The data is given in table 1.

Table 1: Bacterial Growth on Blood culture among study population

Culture	Frequency (N=421)	Percentage (%)
Sterile	209	49.6

Staph Aureus (CoNS)	22	5.2
E. Coli	75	17.8
Klebsiella	39	9.3
Pseudomonas	23	5.5
Acinetobacter	26	6.2
Enterococcus	23	5.5
Staph Aureus (MRSA)	4	1

Majority of the study population were hospitalized for a period of 3 to 7 days, 205 (48.7%) and 181 (43%) were in the hospital for more than 7 days. 20 (4.8%) were hospitalized between 24 to 72 hours and 15 (3.6%) were hospitalized for less than 24 hours. The clinical features observed in the study population is represented in table 2.

Table 2: Clinical features among study population

Clinical Features	Frequency (N)	Percentage (%)
Respiratory Distress	260	61.8
Refusal to feed	63	15
Abdominal Distension	25	5.9
Convulsions	24	5.7
Regurgitation of feed	17	4
Jaundice	16	3.8
Hypothermia	9	2.1
Hyperthermia	7	1.6

In this study, septic shock occurred in most of the cases 299 (71%) while 122 (29%) did not have septic shock. One third of cases required ventilatory support, 141 (33.5%) and DIC was reported in 166 (39.4%). Out of 421 cases, 285 (67.7%) got discharged, 95 (22.6%) expired, 39 (9.3%) left against medical advice and 2 (0.5%) got referred to higher center.

E. Coli was the major cause of sepsis in both inborn and out born babies. Also, E. Coli was the most common organism implicated in DIC, septic shock and requiring ventilatory support. The most dangerous bacteria in this study were Acinetobacter species followed by E. Coli as they were responsible for 9 (9.5%) and 8 (8.4%) deaths respectively. Bacterial growth in early and late onset sepsis is given in table 3.

Table 3: Type of Sepsis and Bacterial growth in Blood Culture

Type of Sepsis	Bacterial growth in Blood Culture	Frequency (N)	Percentage (%)
Early Onset Sepsis	Sterile	166	50.8
	Staph aureus (CoNS)	13	4
	E.coli	59	18
	Klebsiella	31	9.5
	Pseudomonas	19	5.8
	Acinetobacter	19	5.8
	Enterococcus	16	4.9
	Staph aureus (MRSA)	4	1.2
Late Onset Sepsis	Sterile	43	45.7
	Staph aureus (CoNS)	9	9.6
	E.coli	16	17
	Klebsiella	8	8.5
	Pseudomonas	4	4.3
	Acinetobacter	7	7.4
	Enterococcus	7	7.4

The association between demographic profile and morbidity and mortality data between early and late onset sepsis is given in table 4.

Table 4: Comparison of demographic profile & moratlity & morbidity in early onset & late onset sepsis

Variable	Sub variable	Early Onset Sepsis N (%)	Late Onset Sepsis N (%)	p value
Gender	Male	156 (47.7)	43 (45.7)	0.815
	Female	171 (52.3)	51 (54.3)	
Type of Admission	Inborn	242 (74)	12 (12.8)	**0.001**
	Out born	85 (26)	82 (87.2)	
Period of Gestation	>37 weeks	69 (21.1)	27 (28.7)	0.291
	<37 weeks	258 (78.9)	67 (71.3)	
Birth Weight	>2500 g	61 (18.7)	25 (26.6)	0.188
	< 2500g	266 (81.3)	69 (73.4)	
Culture	Positive	175 (53.5)	34 (36.2)	**0.002**
	Negative	152 (46.5)	60 (63.8)	
Incidence of DIC	Yes	121 (37)	45 (47.9)	**0.038**
	No	206 (63)	49 (52.1)	
Shock	Yes	223 (68.2)	76 (80.9)	**0.011**
	No	104 (31.8)	18 (19.1)	
Ventilatory Support	Yes	114 (34.9)	27 (28.7)	0.162
	No	213 (65.1)	67 (71.3)	
Outcome	Discharge	222 (67.9)	63 (67)	0.269
	Expiry	77 (23.5)	18 (19.1)	
	LAMA	26 (8)	13 (13.8)	
	Referral	2 (0.6)	13 (13.8)	

Based on the culture growth and type of sepsis, it was found that 46.5% had culture positivity in early onset sepsis and 53.5% had culture to be negative. Similarly in late onset sepsis, 63.8% had culture positivity and 36.2% had culture negative. There is significant association between inborn admission and early onset sepsis with a P value 0.001.

Early onset sepsis was significantly associated with the incidence of septic shock (P = 0.020) and DIC (P = 0.047), but not associated with mechanical ventilation (P = 0.321). We found significant statistical association between late onset sepsis and positive bacterial growth in blood culture with a P value of 0.003.

There was significant association between those with positive bacterial growth in blood culture with septic shock (P = 0.001), DIC (P = 0.001), mechanical ventilation (P = 0.001), and death (P = 0.001). We also found a statistically significant association between child born <37 weeks and incidence of septic shock (P = 0.001), and between child born <32 weeks and DIC (P = 0.001). Low and very low birth weight requiring ionotropic support was associated with septic shock (P = 0.001), DIC (P = 0.001), and mechanical ventilation (P = 0.001).

Discussion: This study revealed that the incidence of neonatal sepsis in preterm babies was four times higher compared to term babies. A study done by Graham et al also had similar results suggesting high prevalence of neonatal sepsis in preterm babies [10]. Preterm babies have reduced immunity and other associated maternal and fetal risk factors that put them at higher risk of developing neonatal sepsis. This study also exposed low birth weight babies were more prone for neonatal sepsis, like Ahmad et al [11]. Reduced host response to disease causing pathogens in low-birth-weight babies could be attributed to sepsis.

This study shows Antenatal risk factors are more attributed to early onset sepsis. Antenatal risk factors increase the colonization of birth tract with disease causing pathogens increasing the risk of sepsis to the newborns. In this study, EOS is the most common sepsis as compared to LOS. Mahich S et al in their study conducted in North India also reported the proportion of neonates with early and late onset sepsis to be 69% and 31% respectively [12].

Half of the neonatal sepsis patients' blood culture was sterile. Half of blood culture positive in which Gram-negative bacterial sepsis was most common. E. coli was the most common organism implicated in this study followed by Klebsiella and Staphylococcus aureus. In LOS more attributed to culture positive in this study. Pathak et al and their study showed similar results LOS patients had more culture positive cases compared to EOS [13].

In this study, the most common bacteria causing neonatal sepsis was E. Coli. Studies conducted by Mahich et al in North India , Pokhrel B et al in Nepal [14] and Bandyopadhyay T et al [15] revealed the most common organism causing neonatal sepsis as klebsiella species. The difference in bacterial species isolates in different places could be due to differences in infection control protocols being followed.

Ventilator support was needed in one third of neonates who required more than 7 days of hospital stay. Though EOS needed higher mechanical ventilation (80%) than LOS (20%), the difference was not significant. In the present study, one fifth neonates expired similar to studies conducted by Bandypopadhyay T et al and DeNIS [16] which revealed 26% mortality. The study can be repeated with larger sample size to increase the reliability and validity of the results.

Conclusion: This study reveals that early onset sepsis is more associated with septic shock and DIC. The study also showed the need of ventilator support depends on proven or probable sepsis and not on either EOS or LOS. Association between proven and probable sepsis with morbidity indicators like DIC, septic shock and ventilatory support are well established.

What is already known?
Neonatal sepsis is associated with mortality due to septic shock and DIC.

What the study adds?
E. Coli was the most common organism implicated in neonatal sepsis in the study participants.

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