RESEARCH

Epidemiology and Outcome Determinants of Neonatal Sepsis in a Tertiary Care Neonatal Intensive Care Unit

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Abstract: Background: Neonatal sepsis remains a major cause of neonatal morbidity and mortality in developing countries. Early identification of risk factors and outcome determinants is essential for improving survival. The objective is to study the clinical profile, microbiological spectrum, and outcome of neonates diagnosed with sepsis in a tertiary care NICU. **Materials and Methods:** A prospective observational study was conducted in the NICU of a tertiary care teaching hospital over 18 months. All neonates with clinical suspicion of sepsis and positive sepsis screen were included. Demographic details, maternal risk factors, clinical features, laboratory parameters, culture reports, and outcomes were recorded. Statistical analysis was performed using chi-square test and logistic regression. **Results:** Among 150 enrolled neonates, 58% had early-onset sepsis (EOS) and 42% had late-onset sepsis (LOS). Prematurity (46%) and low birth weight (52%) were common. Culture positivity was 38%. Klebsiella pneumoniae (28%) and Staphylococcus aureus (21%) were the most common isolates. Overall mortality was 18%. Mortality was significantly associated with prematurity (p=0.003), positive blood culture (p=0.01), and need for mechanical ventilation (p<0.001). **Conclusion:** Neonatal sepsis is more common among preterm and low birth weight neonates. Gram-negative organisms predominated. Prematurity, culture positivity, and respiratory support requirement were significant predictors of mortality.

INTRODUCTION

Neonatal sepsis is defined as a systemic inflammatory response syndrome secondary to suspected or proven infection occurring within the first 28 days of life. It remains one of the most significant causes of neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries where the burden of infectious diseases is high and access to timely intensive care may be limited.[1] Despite substantial improvements in perinatal and neonatal care, infection continues to account for a considerable proportion of preventable neonatal deaths. Global estimates suggest that sepsis contributes to nearly one-third of neonatal mortality, underscoring its persistent public health importance.[2]

The clinical presentation of neonatal sepsis is often subtle and nonspecific, making early diagnosis challenging. Neonates may present with respiratory distress, poor feeding, lethargy, temperature instability, apnea, or circulatory compromise. The immature immune system of the newborn, characterized by impaired neutrophil function, reduced complement activity, and decreased immunoglobulin levels, further predisposes this population to invasive infections. Preterm and low birth weight infants are particularly vulnerable due to underdeveloped host defenses and frequent exposure to invasive procedures in the neonatal intensive care unit (NICU).

Neonatal sepsis is broadly classified into early-onset sepsis (EOS), occurring within the first 72 hours of life, and late-onset sepsis (LOS), occurring after 72 hours.[3] EOS is typically associated with vertical transmission of organisms from the maternal genital tract and is commonly linked to obstetric risk factors such as prolonged rupture of membranes, maternal fever, chorioamnionitis, and prematurity. In contrast, LOS is often attributed to nosocomial or community-acquired pathogens and is associated with prolonged hospitalization, indwelling catheters, mechanical ventilation, and breaches in infection control practices.

Several maternal and neonatal risk factors have been consistently implicated in the development of sepsis. These include prematurity, low birth weight, birth asphyxia, invasive resuscitation, prolonged rupture of membranes, and maternal infections.[4] The interplay of these factors significantly influences both the incidence and severity of disease. Moreover, the microbial spectrum of neonatal sepsis varies across geographical regions and healthcare settings, with gram-negative organisms predominating in many developing countries, often exhibiting multidrug resistance patterns.

Although advances in antimicrobial therapy, neonatal ventilation strategies, and infection control measures have improved survival rates, mortality associated with neonatal sepsis remains unacceptably high. Delayed diagnosis due to nonspecific clinical signs, limited sensitivity of blood cultures, and the emergence of antimicrobial resistance continue to pose major challenges[5]. Early identification of high-risk neonates and prompt initiation of appropriate therapy are therefore critical in reducing adverse

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outcomes.

Given the dynamic changes in bacterial epidemiology and resistance patterns, periodic evaluation of the clinical profile and microbiological characteristics of neonatal sepsis in individual centers is essential. Understanding local pathogen distribution and associated mortality predictors can guide empirical antibiotic policies, improve resource allocation, and strengthen preventive strategies.

In this context, the present study was undertaken to evaluate the demographic and clinical profile, bacteriological spectrum, and outcomes of neonates diagnosed with sepsis in a tertiary care NICU, and to identify factors associated with mortality.

MATERIAL AND METHODS

This prospective observational study was conducted in the Level III Neonatal Intensive Care Unit (NICU) of a tertiary care teaching hospital in India over a period of 18 months. The NICU functions as a referral center for both inborn and outborn neonates and is equipped with facilities for invasive ventilation, central venous access, advanced monitoring, and comprehensive neonatal care.

A total of 150 neonates diagnosed with clinical neonatal sepsis during the study period were enrolled consecutively. The sample size was determined based on an anticipated mortality rate of approximately 20% from previously published tertiary care studies, with a 95% confidence level and allowable error of 7%. All eligible neonates fulfilling the inclusion criteria were recruited after obtaining written informed consent from parents or legal guardians.

Neonates aged 0–28 days presenting with clinical features suggestive of sepsis and a positive sepsis screen were included in the study. Clinical suspicion of sepsis was based on the presence of symptoms such as respiratory distress, poor feeding, lethargy, apnea, temperature instability, seizures, or signs of shock. A positive sepsis screen was defined as the presence of at least two abnormal laboratory parameters, including elevated C-reactive protein (>10 mg/L), abnormal total leukocyte count (<5,000/mm³ or >20,000/mm³), elevated micro-ESR (>15 mm in the first hour), abnormal absolute neutrophil count as per gestational age, or an immature-to-total neutrophil (I/T) ratio greater than 0.2. Neonates with major congenital malformations, chromosomal abnormalities, or incomplete medical records were excluded from the study.

For each enrolled neonate, detailed maternal and neonatal information was recorded using a structured predesigned proforma. Maternal variables included maternal age, prolonged rupture of membranes (PROM >18 hours), maternal fever within two weeks prior to delivery, foul-smelling amniotic fluid, and mode of delivery. Neonatal variables included sex, gestational age, birth weight, Apgar scores at 1 and 5 minutes, age at onset of symptoms, and inborn or outborn status. Gestational age was determined based on last menstrual period and corroborated by the New Ballard Score when required. Prematurity was defined as gestational age less than 37 completed weeks, and low birth weight (LBW) as birth weight less than 2500 grams. Early-onset sepsis (EOS) was defined as onset of symptoms within 72 hours of life, while late-onset sepsis (LOS) referred to onset after 72 hours.

All neonates underwent baseline laboratory investigations including complete blood count, C-reactive protein estimation, blood glucose, and serum electrolytes. Blood culture was obtained under strict aseptic precautions prior to initiation of antibiotic therapy. Approximately 1–2 mL of venous blood was collected and inoculated into pediatric blood culture bottles and processed using an automated culture system. Organism identification was performed using standard microbiological techniques, and antibiotic susceptibility testing was conducted using the Kirby–Bauer disk diffusion method in accordance with Clinical and Laboratory Standards Institute (CLSI) guidelines.

Empirical antibiotic therapy was initiated as per institutional protocol and subsequently modified based on culture and sensitivity reports. Supportive management, including oxygen therapy, continuous positive airway pressure (CPAP), mechanical ventilation, intravenous fluids, inotropic support, and blood transfusion, was provided as clinically indicated.

The primary outcome measure was survival status at discharge (discharged or death). Secondary outcomes included duration of NICU stay, requirement for mechanical ventilation, need for inotropic support, and development of complications such as septic shock.

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 25. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test where appropriate. Multivariate logistic regression analysis was performed to identify independent predictors of mortality, and adjusted odds ratios with 95% confidence intervals were calculated. A p-value of less than 0.05 was considered statistically significant.

The study protocol was approved by the Institutional Ethics Committee prior to initiation. Written informed consent was obtained from parents or legal guardians of all enrolled neonates, and strict confidentiality of patient information was maintained throughout the study period.

RESULTS

The demographic characteristics of the study population are presented in [Table 1]. Among the 150 neonates, males constituted 58.7% (n=88), while females accounted for 41.3% (n=62), showing a male preponderance. Preterm neonates comprised 46% (n=69) of the study population, whereas 54% (n=81) were term babies. Low birth weight (LBW) was observed in 52% (n=78) of neonates, indicating that more than half of the affected neonates were underweight at birth. Early-onset sepsis (EOS) was more common, accounting for 58% (n=87) of cases, compared to late-onset sepsis (LOS), which constituted 42% (n=63).

These findings suggest that neonatal sepsis in our setting predominantly affected male neonates and was more frequent in the early neonatal period, with a substantial burden among preterm and low birth weight infants.

Table 1: Demographic Profile (n=150)

Variable	Frequency	Percentage
Male	88	58.7%
Female	62	41.3%
Preterm	69	46%
Term	81	54%
LBW	78	52%
Normal weight	72	48%
EOS	87	58%
LOS	63	42%

Maternal risk factors associated with neonatal sepsis are summarized in [Table 2]. Prolonged rupture of membranes (PROM >18 hours) was the most common maternal risk factor, present in 30% (n=45) of cases. Maternal fever was documented in 18.7% (n=28), while foul-smelling amniotic fluid was noted in 12.7% (n=19) of deliveries.

PROM emerged as the predominant maternal risk factor, reinforcing the importance of intrapartum monitoring and timely obstetric intervention in preventing early neonatal infections.

Table 2: Maternal Risk Factors

Risk Factor	n	%
PROM >18 hrs	45	30%
Maternal fever	28	18.7%
Foul smelling liquor	19	12.7%

The clinical features observed at presentation are shown in [Table 3]. Respiratory distress was the most common presenting symptom, observed in 61% (n=92) of neonates. Poor feeding was noted in 53% (n=80), followed by lethargy in 44.7% (n=67) and temperature instability in 38.7% (n=58). Seizures were present in 12% (n=18) of cases.

The predominance of respiratory distress highlights the nonspecific and systemic nature of neonatal sepsis, often overlapping with primary pulmonary conditions. Neurological manifestations such as seizures were less common but indicated severe systemic involvement.

Table 3: Clinical Features

Feature	n	%
Respiratory distress	92	61%
Poor feeding	80	53%
Lethargy	67	44.7%
Temperature instability	58	38.7%
Seizures	18	12%

Blood culture was positive in 38% (57/150) of neonates. The distribution of organisms isolated is detailed in [Table 4]. Gram-negative organisms predominated, accounting for 61% of culture-positive cases. Klebsiella pneumoniae was the most frequently isolated organism (28%), followed by Staphylococcus aureus (21%) and Escherichia coli (17.5%). Acinetobacter species accounted for 15.8%, while coagulase-negative staphylococci (CoNS) were isolated in 10.5% of cases. Other organisms constituted 7%.

The predominance of gram-negative pathogens, particularly Klebsiella pneumoniae, indicates a significant burden of hospital-acquired or vertically transmitted resistant organisms in the NICU setting.

Table 4: Organisms Isolated (n=57)

Organism	n	%
Klebsiella pneumoniae	16	28%
Staphylococcus aureus	12	21%
E. coli	10	17.5%
Acinetobacter spp.	9	15.8%
CoNS	6	10.5%
Others	4	7%

Gram-negative organisms accounted for 61%.

Regarding supportive management, 28% (n=42) of neonates required mechanical ventilation, while 24% (n=36) were managed with continuous positive airway pressure (CPAP). Inotropic support was required in 20.7% (n=31) of neonates.

The relatively high proportion of neonates requiring respiratory and circulatory support reflects the severity of illness among admitted cases.

The overall mortality rate in the study was 18% (27/150), while 82% (n=123) of neonates were discharged after clinical improvement [Table 5].

Table 5: Outcome Distribution

Outcome	n	%
Discharged	123	82%
Death	27	18%

The association between various clinical variables and mortality is presented in [Table 6]. Mortality was significantly higher among preterm neonates (28%, p=0.003) and low birth weight infants (25%, p=0.01). Culture-positive sepsis was associated with higher mortality (30%, p=0.01). The strongest association was observed with mechanical ventilation, where mortality reached 45% (p<0.001). No statistically significant difference in mortality was observed between EOS and LOS groups (p=0.21).

These findings indicate that prematurity, low birth weight, microbiologically confirmed infection, and need for advanced respiratory support are important determinants of poor outcome.

Table 6: Factors Associated with Mortality

Variable	Mortality %	p-value
Preterm	28%	0.003
LBW	25%	0.01
Culture positive	30%	0.01
Mechanical ventilation	45%	<0.001
EOS vs LOS	NS	0.21

On multivariate logistic regression analysis [Table 7], prematurity (Adjusted OR 2.8; 95% CI: 1.3–6.1; p=0.007), culture positivity (Adjusted OR 2.4; 95% CI: 1.1–5.2; p=0.02), and requirement of mechanical ventilation (Adjusted OR 4.5; 95% CI: 2.0–9.8; p<0.001) emerged as independent predictors of mortality.

Mechanical ventilation was identified as the strongest independent predictor, increasing the odds of mortality by more than fourfold.

Table 7: Multivariate Analysis

Variable	Adjusted OR	95% CI	p-value
Prematurity	2.8	1.3–6.1	0.007
Culture positivity	2.4	1.1–5.2	0.02
Mechanical ventilation	4.5	2.0–9.8	<0.001

DISCUSSION

Neonatal sepsis continues to be a leading cause of neonatal morbidity and mortality, particularly in low- and middle-income countries. The present study evaluated the clinical characteristics, microbiological spectrum, and outcome determinants of neonatal sepsis in a tertiary care NICU and identified key predictors of mortality.

In our study, early-onset sepsis (EOS) accounted for 58% of cases, while late-onset sepsis (LOS) constituted 42%. This predominance of EOS is comparable to findings reported by the Investigators of the Delhi Neonatal Infection Study (DeNIS) Collaboration,[6] who documented a substantial burden of early-onset infections in Indian tertiary units. The higher proportion of EOS in our cohort may be attributed to maternal risk factors such as prolonged rupture of membranes and intrapartum infections, which facilitate vertical transmission. These findings reinforce the importance of timely obstetric management and adherence to aseptic delivery practices.

Prematurity (46%) and low birth weight (52%) were common among neonates with sepsis in the present study. Similar observations have been reported by Shah et al,[7] and Muley et al,[8] who demonstrated increased susceptibility to sepsis among preterm and low birth weight infants. The biological plausibility of this association lies in the immaturity of innate and adaptive immune responses, decreased complement activity, impaired neutrophil function, and reduced transplacental transfer of maternal immunoglobulins in preterm neonates. Additionally, such infants often require prolonged NICU stay and invasive interventions, further increasing infection risk.

The blood culture positivity rate of 38% observed in this study is comparable to previously reported rates ranging between 30% and 45% in Indian NICUs.[9] While blood culture remains the diagnostic gold standard, the moderate positivity rate may reflect prior empirical antibiotic exposure or low-level bacteremia. Gram-negative organisms predominated (61%) in our study, with Klebsiella pneumoniae being the most frequently isolated pathogen. This pattern is consistent with findings reported by Jyothi et al,[10] and the DeNIS Collaboration,[6] both of which highlighted the predominance of gram-negative bacilli in neonatal sepsis cases in India. The high prevalence of gram-negative pathogens is clinically significant due to their association with antimicrobial resistance, rapid clinical deterioration, and increased risk of septic shock.

The overall mortality rate of 18% in our cohort is within the range of 15–25% reported in tertiary care NICUs.[7,11] Although advances in neonatal intensive care and antimicrobial therapy have improved survival rates over the years, neonatal sepsis continues to carry substantial mortality, particularly among vulnerable populations such as preterm and low birth weight infants.

On univariate analysis, prematurity, low birth weight, culture positivity, and requirement of mechanical ventilation were significantly associated with mortality. Multivariate logistic regression demonstrated that prematurity, culture-positive sepsis, and need for mechanical ventilation were independent predictors of mortality. Similar associations have been described by Hornik et al,[12] who reported increased mortality among preterm infants with culture-confirmed sepsis, and by Sankar et al,[13] who identified low birth weight and need for intensive respiratory support as strong predictors of adverse outcome.

The strong association between mechanical ventilation and mortality likely reflects severity of illness rather than the intervention itself. Neonates requiring ventilatory support often have multi-organ dysfunction, severe respiratory compromise, or septic shock. Additionally, invasive respiratory support increases the risk of secondary infections, which may worsen prognosis. The independent association of culture positivity with mortality suggests that microbiologically confirmed infections may represent higher bacterial load, virulent organisms, or delayed initiation of effective antibiotic therapy.

No statistically significant difference in mortality was observed between EOS and LOS in the present study, suggesting that host factors and severity at presentation may be more important determinants of outcome than timing of onset alone.

Overall, the findings of this study reaffirm the continued burden of gram-negative neonatal sepsis in tertiary care settings and highlight prematurity and need for advanced respiratory support as critical determinants of mortality. Strengthening antenatal surveillance, improving infection control practices, and implementing rational antibiotic policies remain essential strategies to reduce neonatal sepsis -related deaths.

CONCLUSION

Neonatal sepsis remains a major contributor to NICU admissions and mortality. Early-onset sepsis predominates. Gram-negative organisms are the leading pathogens. Prematurity, culture positivity, and need for mechanical ventilation are significant predictors of mortality. Strengthening infection control practices and early risk stratification may improve neonatal outcomes.

REFERENCES

1. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. Lancet. 2017 Oct 14;390(10104):1770-1780.
2. World Health Organization: WHO. Newborn mortality. 2021. https://www.who.int/news-room/fact-sheets/detail/newborn-mortality
3. Polin RA; Committee on Fetus and Newborn. Management of neonates with suspected or proven early-onset bacterial sepsis. Pediatrics. 2012 May;129(5):1006-15.
4. Puopolo KM, Draper D, Wi S, Newman TB, Zupancic J, Lieberman E, Smith M, Escobar GJ. Estimating the probability of neonatal early-onset infection on the basis of maternal risk factors. Pediatrics. 2011 Nov;128(5):e1155-63.
5. Laxminarayan R, Duse A, Wattal C, Zaidi AK, Wertheim HF, Sumpradit N, et al. Antibiotic resistance-the need for global solutions. Lancet Infect Dis. 2013 Dec;13(12):1057-98.
6. Investigators of the Delhi Neonatal Infection Study (DeNIS) collaboration. Characterisation and antimicrobial resistance of sepsis pathogens in neonates born in tertiary care centres in Delhi, India: a cohort study. Lancet Glob Health. 2016 Oct;4 (10):e752-60.
7. Shah BA, Padbury JF. Neonatal sepsis: an old problem with new insights. Virulence. 2014 Jan 1;5(1):170-8.
8. Muley VA, Ghadage DP, Bhore AV. Bacteriological Profile of Neonatal Septicemia in a Tertiary Care Hospital from Western India. J Glob Infect Dis. 2015 Apr-Jun;7(2):75-7.
9. West BA, Peterside O. Sensitivity pattern among bacterial isolates in neonatal septicaemia in port Harcourt. Ann Clin Microbiol Antimicrob. 2012 Mar 26;11:7.
10. Jyothi P, Basavaraj MC, Basavaraj PV. Bacteriological profile of neonatal septicemia and antibiotic susceptibility pattern of the isolates. J Nat Sci Biol Med. 2013;4(2):306-309.
11. Thaver D, Zaidi AK. Burden of neonatal infections in developing countries: a review of evidence from community-based studies. Pediatr Infect Dis J. 2009 Jan;28(1 Suppl):S3-9.
12. Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK Jr, Smith PB, Manzoni P, Jacqz-Aigrain E, Kaguelidou F, Cohen-Wolkowiez M. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. Early Hum Dev. 2012 May;88 Suppl 2(Suppl 2):S69-74.
13. Sankar MJ, Agarwal R, Deorari AK, Paul VK. Sepsis in the newborn. Indian J Pediatr. 2008 Mar;75(3):261-6. doi: 10.1007/ s12098-008-0056-z. PMID: 18376095.