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Neonatal Sepsis in a Tertiary Care NICU: A Prospective Observational Study of Clinical Profile, Risk Factors, Microbial Spectrum, and Short-Term Outcomes

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ABSTRACT

Background: Neonatal sepsis remains a leading cause of neonatal morbidity and mortality in India. Knowledge of the local clinical profile, risk factors, microbial spectrum, and antimicrobial susceptibility pattern is essential to guide rational empirical therapy and antimicrobial stewardship.

Objectives: To study the clinical profile, risk factors, bacteriological and fungal spectrum, antimicrobial susceptibility pattern, and short-term outcomes of neonates with suspected and culture-proven sepsis in a tertiary-care Sick Newborn Care Unit (SNCU).

Methods: This prospective observational study was conducted in the SNCU, Department of Paediatrics, Lady Dufferin Victoria Hospital, Kolkata, from February 2025 to January 2026. All neonates (≤28 days) with clinical features of sepsis and a positive sepsis screen were enrolled. Maternal, perinatal, and neonatal data were recorded prospectively. Blood culture was obtained before antibiotics, with antimicrobial susceptibility tested as per CLSI guidelines. Data were analysed using SPSS v.25 with chi-square test, multivariable logistic regression, and odds ratios; $p<0.05$ was considered significant.

Results: Of 1,452 SNCU admissions, 412 (28.4%) met the criteria for clinical sepsis. Early-onset sepsis (EOS) accounted for 62.6% (n=258) and late-onset sepsis (LOS) for 37.4% (n=154). The male-to-female ratio was 1.51:1; 63.6% were preterm and 68.9% were of low birth weight. Blood culture was positive in 121 neonates (29.4%). The most common clinical features were lethargy (75.7%), refusal of feeds (72.3%), and respiratory distress (59.7%). Gram-negative organisms predominated (69.4% of isolates), with Klebsiella pneumoniae (26.4%), Escherichia coli (18.2%), and Acinetobacter baumannii (14.9%) being the leading isolates. Multidrug resistance was high among Gram-negative isolates; meropenem (71.9–90.9%) and colistin (94.4–100%) retained the greatest activity. All S. aureus were susceptible to vancomycin and linezolid. The overall case-fatality rate was 18.9%; mortality was significantly higher in preterm (51.3% in <32 weeks vs 6.7% in term, $p<0.001$), VLBW (52.3% vs 7.0%, $p<0.001$), and culture-positive neonates (34.7% vs 12.4%, $p<0.001$).

Conclusions: Neonatal sepsis is a major contributor to morbidity and mortality in our setting, with a Gram-negative–predominant, multidrug-resistant flora. Aggressive control of perinatal risk factors, strict infection-prevention practices, periodic review of unit-specific microbial and resistance profiles, and antimicrobial stewardship are essential to improve outcomes.

Keywords*: neonatal sepsis; early-onset sepsis; late-onset sepsis; risk factors; blood culture; antimicrobial resistance; NICU; India.*

INTRODUCTION

Neonatal sepsis is defined as a clinical syndrome of bacteraemia or systemic infection presenting within the first 28 days of life, characterized by signs and symptoms of infection with or without accompanying bacteraemia. It remains one of the most important causes of neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries (LMICs). According to the World Health Organization (WHO) and global burden estimates, sepsis contributes to approximately 15–25% of all neonatal deaths globally, and the burden is disproportionately higher in South Asia.[1,2]

In India, the National Neonatal-Perinatal Database (NNPD) and the Delhi Neonatal Infection Study (DeNIS) have repeatedly demonstrated that sepsis is responsible for nearly one-third of all neonatal deaths in tertiary-care neonatal intensive care units (NICUs).[3,4] The DeNIS collaboration further highlighted the alarming rise of multidrug-resistant Gram-negative organisms in Indian neonatal units, severely limiting empirical antibiotic options and contributing to higher mortality.[4]

Neonatal sepsis is broadly classified, on the basis of age at onset, into early-onset sepsis (EOS; ≤72 h of life), which is usually acquired vertically from the maternal genital tract, and late-onset sepsis (LOS; >72 h), which is largely nosocomial or community-acquired.[5] The two entities differ substantially in their risk factors, causative organisms, and antimicrobial susceptibility, and therefore in the optimal empirical regimen. Local epidemiological data are critical, as the spectrum of pathogens and their resistance patterns vary not only between countries but also between individual neonatal units.[6,7]

Lady Dufferin Victoria Hospital is a tertiary-care teaching hospital in Kolkata catering to a large urban and peri-urban antenatal and neonatal population, with a busy Sick Newborn Care Unit (SNCU) handling both inborn and outborn neonates. Despite the high case load, contemporary unit-specific data on the clinical profile, risk-factor distribution, microbial spectrum, antibiotic susceptibility, and short-term outcomes of neonatal sepsis from this institution are limited. The present prospective observational study was undertaken to address this gap and to inform local empirical antibiotic policy and infection-control practices.

Aim

To study the clinical profile, risk factors, microbial spectrum, and short-term outcomes of neonatal sepsis in a tertiary care SNCU.

Objectives

1. To determine the proportion of clinical and culture-proven sepsis among neonates admitted during the study period.
2. To describe the demographic and clinical profile of neonates with sepsis.
3. To identify the maternal, perinatal, and neonatal risk factors associated with neonatal sepsis.
4. To characterize the bacteriological and fungal spectrum and to determine the antimicrobial susceptibility pattern of the isolates.
5. To assess the short-term outcomes (recovery, complications, and in-hospital mortality) of neonates with sepsis.

MATERIALS AND METHODS

Study design and setting

This was a single-centre, hospital-based, prospective observational study conducted in the Sick Newborn Care Unit (SNCU), Department of Paediatrics, Lady Dufferin Victoria Hospital, Kolkata, West Bengal, India — a tertiary-care teaching institution providing comprehensive obstetric and neonatal care to a large urban and peri-urban catchment population.

Study period

The study was carried out over a period of one year, from 1 February 2025 to 31 January 2026.

Study population

All neonates (age 0–28 days), both inborn and outborn, admitted to the SNCU during the study period with clinical features suggestive of sepsis were screened for inclusion.

Inclusion criteria

- Neonates aged ≤28 days.
- Presence of any two or more clinical features suggestive of sepsis, including lethargy, refusal of feeds, temperature instability, respiratory distress, apnoea, poor perfusion, abdominal distension, vomiting, seizures, or sclerema.

- Positive sepsis screen, defined as the presence of two or more of the following: total leucocyte count <5,000 or >20,000/mm³; absolute neutrophil count outside age-specific reference range (Manroe / Mouzinho charts); immature-to-total neutrophil (I:T) ratio >0.2; micro-ESR >15 mm in 1 h; and C-reactive protein (CRP) >10 mg/L.
- Written informed consent obtained from a parent or legal guardian.

Exclusion criteria

- Neonates with major congenital malformations or chromosomal anomalies incompatible with survival.
- Neonates with suspected inborn errors of metabolism mimicking sepsis.
- Neonates whose parents declined consent.
- Neonates who died or were transferred out within 6 hours of admission, before sepsis evaluation could be completed.

Operational definitions

Clinical sepsis: neonate with ≥2 clinical features of sepsis and a positive sepsis screen, irrespective of culture status.
Culture-proven (definite) sepsis: isolation of a pathogenic organism from blood and/or cerebrospinal fluid (CSF).
Early-onset sepsis (EOS): onset of clinical features within the first 72 hours of life.
Late-onset sepsis (LOS): onset of clinical features after 72 hours of life.
Meningitis: isolation of an organism from CSF and/or CSF cytochemical findings consistent with bacterial meningitis.

Sample size

Based on an estimated incidence of clinical sepsis among SNCU admissions of approximately 30% from previous Indian studies, with an absolute precision of 5% and 95% confidence, a minimum sample size of approximately 323 neonates was calculated. All eligible consecutive admissions during the study period were included; the final cohort comprised 412 neonates.

Data collection

A predesigned, pre-tested case-record form was used to collect data on maternal demographics and antenatal history (booking status, parity, antenatal infections, maternal fever, premature rupture of membranes, foul-smelling liquor, multiple per-vaginal examinations, intrapartum antibiotic prophylaxis, mode of delivery), and on neonatal variables (gestational age, birth weight, sex, place of birth, Apgar score, need for resuscitation, age at onset of symptoms, presenting features, and supportive interventions). Gestational age was determined using the date of last menstrual period and confirmed by the New Ballard Score. Birth weight was classified as low birth weight (LBW, <2500 g), very low birth weight (VLBW, <1500 g), and extremely low birth weight (ELBW, <1000 g).

Laboratory investigations

After clinical assessment and prior to administration of antibiotics, 1–2 mL of venous blood was collected under strict aseptic precautions for blood culture, complete blood count with peripheral smear, micro-ESR, and CRP. Blood was inoculated into paediatric culture bottles and processed by the BACTEC™ automated system in the Department of Microbiology. Identification of isolates and antimicrobial susceptibility testing were performed using standard microbiological techniques and the Kirby–Bauer disc diffusion method, with susceptibility interpreted in accordance with current Clinical and Laboratory Standards Institute (CLSI) guidelines.[8] Lumbar puncture was performed in clinically stable neonates with culture-proven sepsis or with features suggestive of meningitis.

Treatment

Empirical antibiotic therapy was initiated as per the unit protocol — typically a combination of ampicillin and gentamicin for suspected EOS, and an upgraded regimen (piperacillin–tazobactam ± amikacin, or a carbapenem) for LOS or for clinically deteriorating neonates — and was subsequently modified on the basis of culture and susceptibility results. Supportive management, including thermoregulation, fluid and electrolyte balance, respiratory support (oxygen, CPAP, or mechanical ventilation), inotropes, blood-product transfusion, and nutritional support, was provided as clinically indicated.

Outcomes

Neonates were followed up until discharge, in-hospital death, or transfer out. The primary outcome was in-hospital mortality. Secondary outcomes included need for mechanical ventilation, inotropic support, development of shock, disseminated intravascular coagulation, meningitis, necrotizing enterocolitis, acute kidney injury, and length of NICU stay.

Statistical analysis

Data were entered into Microsoft Excel and analysed using IBM SPSS Statistics version 25. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test, as appropriate. Continuous variables were expressed as mean ± standard deviation or median (interquartile range) and compared using Student's t-test or the Mann–Whitney U test. Univariate analysis was performed to identify risk factors associated with culture-positive sepsis and with mortality, and odds ratios (OR) with 95% confidence intervals (CI) were calculated.

Variables with p<0.10 on univariate analysis were entered into a multivariable logistic regression model. A two-tailed p-value <0.05 was considered statistically significant.

RESULTS

Incidence and demographic profile

During the one-year study period, a total of 1,452 neonates were admitted to the SNCU. Of these, 412 neonates fulfilled the inclusion criteria and were enrolled in the study, giving an incidence of clinical sepsis of 28.4% among SNCU admissions. The mean gestational age was 35.2 ± 3.4 weeks and the mean birth weight was 2,210 ± 720 g. Males predominated, with a male-to-female ratio of 1.51:1 (248 males vs 164 females). Preterm neonates (<37 weeks) constituted 63.6% of the cohort and low-birth-weight (<2500 g) neonates 68.9%. Inborn neonates accounted for 71.4% (n=294) and outborn for 28.6% (n=118). Early-onset sepsis was observed in 258 neonates (62.6%) and late-onset sepsis in 154 neonates (37.4%). Most early-onset cases (162/258, 62.8%) presented within the first 24 hours of life. The detailed demographic profile is presented in Table 1.

Table 1. Demographic and baseline characteristics of neonates with sepsis (N = 412).

Characteristic	Frequency (n)	Percentage (%)
Sex		
Male	248	60.2
Female	164	39.8
Gestational age		
<32 weeks (extreme/very preterm)	78	18.9
32–<37 weeks (moderate/late preterm)	184	44.7
≥37 weeks (term)	150	36.4
Birth weight		
<1500 g (VLBW)	86	20.9
1500–<2500 g (LBW)	198	48.1
≥2500 g (Normal)	128	31.0
Mode of delivery		
Vaginal delivery	256	62.1
Caesarean section	156	37.9
Place of birth		
Inborn	294	71.4
Outborn	118	28.6
Type of sepsis		
Early-onset sepsis (≤72 h)	258	62.6
Late-onset sepsis (>72 h)	154	37.4
Age at presentation		
0–24 hours	162	39.3
24–72 hours	96	23.3
4–7 days	74	18.0
8–28 days	80	19.4

Clinical profile at presentation

The clinical presentation of neonatal sepsis in our cohort was non-specific and varied. The most common clinical manifestations were lethargy / poor activity (75.7%), refusal of feeds (72.3%), and respiratory distress (59.7%), followed by temperature instability (44.7%), tachycardia / poor perfusion (37.9%), and jaundice (33.5%). Less frequent but clinically important presentations included abdominal distension (22.3%), apnoea (18.9%), vomiting (15.5%), seizures (12.6%), bleeding manifestations (6.8%), and sclerema (5.3%). Sclerema and bleeding manifestations were strongly associated with severe disease and high case-fatality. Most neonates presented with a combination of features rather than a single sign (Table 2).

Table 2. Clinical features at presentation among neonates with sepsis (N = 412).

Clinical Feature	Frequency (n)	Percentage (%)
Lethargy / poor activity	312	75.7
Refusal of feeds / poor feeding	298	72.3
Respiratory distress	246	59.7
Temperature instability (hypo/hyperthermia)	184	44.7
Tachycardia / poor perfusion	156	37.9

Jaundice	138	33.5
Abdominal distension	92	22.3
Apnoea	78	18.9
Vomiting	64	15.5
Seizures	52	12.6
Bleeding manifestations	28	6.8
Sclerema	22	5.3

Risk factor analysis

Multiple maternal, perinatal, and neonatal risk factors were identified. Among maternal and perinatal factors, the most prevalent were premature rupture of membranes >18 hours (32.0%), multiple per-vaginal examinations (23.3%), unbooked or inadequate antenatal care (21.4%), foul-smelling or meconium-stained liquor (18.4%), and prolonged or obstructed labour (16.5%). Maternal fever ≥38°C (14.1%), maternal urinary tract infection (10.2%), and clinical chorioamnionitis (5.8%) were also documented.

Among neonatal factors, low birth weight (68.9%) and prematurity (63.6%) were the most frequent, followed by prolonged NICU stay >7 days (32.0%), need for resuscitation at birth (28.2%), birth asphyxia (22.8%), and prior antibiotic exposure (20.9%). Invasive interventions such as mechanical ventilation (18.9%), umbilical or central venous catheterization (16.5%), and total parenteral nutrition (10.2%) were also significant contributors, particularly in late-onset sepsis (Table 3).

Table 3. Maternal, perinatal, and neonatal risk factors among neonates with sepsis (N = 412).

Risk Factor	Frequency (n)	Percentage (%)
Maternal / perinatal risk factors		
Premature rupture of membranes (>18 h)	132	32.0
Multiple per-vaginal examinations (>3)	96	23.3
Unbooked / inadequate antenatal care	88	21.4
Foul-smelling / meconium-stained liquor	76	18.4
Prolonged / obstructed labour	68	16.5
Maternal fever (≥38°C) within 2 weeks of delivery	58	14.1
Maternal urinary tract infection	42	10.2
Chorioamnionitis (clinical)	24	5.8
Neonatal risk factors		
Low birth weight (<2500 g)	284	68.9
Prematurity (<37 weeks)	262	63.6
Prolonged NICU stay (>7 days)	132	32.0
Need for resuscitation at birth	116	28.2
Birth asphyxia (Apgar <7 at 5 min)	94	22.8
Prior antibiotic exposure (>5 days)	86	20.9
Mechanical ventilation	78	18.9
Umbilical / central venous catheter	68	16.5
Total parenteral nutrition	42	10.2

On multivariable logistic regression analysis, prematurity (aOR 3.42; 95% CI 2.18–5.36; p<0.001), very low birth weight (aOR 2.86; 95% CI 1.74–4.71; p<0.001), prolonged rupture of membranes (aOR 2.94; 95% CI 1.86–4.65; p<0.001), and mechanical ventilation (aOR 4.18; 95% CI 2.42–7.22; p<0.001) emerged as independent predictors of culture-proven sepsis. Maternal fever, umbilical / central venous catheterization, and birth asphyxia were also independently associated with sepsis (Table 3b).

Table 3b. Independent predictors of culture-proven sepsis on multivariable logistic regression.

Variable	Adjusted OR	95% CI	p-value
Prematurity (<37 weeks)	3.42	2.18 – 5.36	<0.001
Very low birth weight (<1500 g)	2.86	1.74 – 4.71	<0.001
PROM >18 hours	2.94	1.86 – 4.65	<0.001
Mechanical ventilation	4.18	2.42 – 7.22	<0.001
Umbilical / central venous catheter	2.31	1.36 – 3.92	0.002
Maternal fever ≥38°C	2.07	1.18 – 3.63	0.011
Birth asphyxia (Apgar <7 at 5 min)	1.74	1.05 – 2.88	0.031

Microbial spectrum

Blood culture was positive in 121 of the 412 neonates, giving an overall culture-positivity rate of 29.4%. Culture positivity was higher in late-onset sepsis (72/154, 46.8%) than in early-onset sepsis (49/258, 19.0%) ($p<0.001$). Gram-negative organisms accounted for the majority of isolates (84/121, 69.4%), followed by Gram-positive organisms (32/121, 26.4%) and fungal isolates (5/121, 4.1%).

Among the Gram-negative isolates, Klebsiella pneumoniae was the single most common pathogen (32/121, 26.4%), followed by Escherichia coli (22/121, 18.2%), Acinetobacter baumannii (18/121, 14.9%), Pseudomonas aeruginosa (6/121, 5.0%), Enterobacter spp. (4/121, 3.3%), and Burkholderia cepacia (2/121, 1.7%). E. coli was the leading cause of EOS, while Klebsiella and Acinetobacter predominated in LOS, in keeping with their nosocomial profile.

Coagulase-negative staphylococci (CoNS) were the most common Gram-positive isolates (14/121, 11.6%), followed by Staphylococcus aureus (12/121, 9.9%), Enterococcus spp. (4/121, 3.3%), and Group B Streptococcus (2/121, 1.7%). Five fungal isolates (4.1%) were recovered, predominantly from late-onset cases in extremely-low-birth-weight neonates with prolonged antibiotic exposure: Candida albicans (n=3) and non-albicans Candida spp. (n=2) (Table 4).

Table 4. Microbial spectrum of culture-proven neonatal sepsis (n = 121 isolates).

Organism	Total (n=121), n (%)	EOS (n=49), n (%)	LOS (n=72), n (%)
Gram-negative organisms (n = 84)			
Klebsiella pneumoniae	32 (26.4)	13 (26.5)	19 (26.4)
Escherichia coli	22 (18.2)	16 (32.7)	6 (8.3)
Acinetobacter baumannii	18 (14.9)	4 (8.2)	14 (19.4)
Pseudomonas aeruginosa	6 (5.0)	1 (2.0)	5 (6.9)
Enterobacter spp.	4 (3.3)	2 (4.1)	2 (2.8)
Burkholderia cepacia	2 (1.7)	0 (0.0)	2 (2.8)
Gram-positive organisms (n = 32)			
Coagulase-negative staphylococci (CoNS)	14 (11.6)	4 (8.2)	10 (13.9)
Staphylococcus aureus	12 (9.9)	5 (10.2)	7 (9.7)
Enterococcus spp.	4 (3.3)	1 (2.0)	3 (4.2)
Group B Streptococcus	2 (1.7)	2 (4.1)	0 (0.0)
Fungal isolates (n = 5)			
Candida albicans	3 (2.5)	1 (2.0)	2 (2.8)
Non-albicans Candida spp.	2 (1.7)	0 (0.0)	2 (2.8)
Total	121 (100.0)	49 (100.0)	72 (100.0)

Antimicrobial susceptibility pattern

Gram-negative isolates demonstrated alarmingly high rates of resistance to the conventional first-line empirical agents. Susceptibility to ampicillin was virtually absent (Klebsiella 0%, E. coli 9.1%); susceptibility to third-generation cephalosporins was poor (cefotaxime/ceftriaxone: Klebsiella 15.6%, E. coli 22.7%, Acinetobacter 11.1%), and aminoglycoside susceptibility was modest (gentamicin 21.9–40.9%, amikacin 27.8–63.6%). Piperacillin–tazobactam retained moderate activity (33.3–72.7%). Carbapenem (meropenem) susceptibility was higher but variable across organisms — best preserved in E. coli (90.9%) and Klebsiella (71.9%) but markedly reduced in Acinetobacter (44.4%). Colistin retained the highest activity, with susceptibility rates of 96.9%, 100.0%, and 94.4% for Klebsiella, E. coli, and Acinetobacter respectively.

Among Gram-positive isolates, methicillin resistance (MRSA pattern) was identified in approximately half of the S. aureus isolates (cloxacillin/oxacillin susceptibility 50.0%); however, all Gram-positive isolates remained uniformly susceptible to vancomycin (100%) and linezolid (100%) (Table 5).

Table 5. Antimicrobial susceptibility pattern of major bacterial isolates (% susceptible).

Antibiotic	Klebsiella spp. (n=32)	E. coli (n=22)	Acinetobacter (n=18)	S. aureus (n=12)
Ampicillin	0	9.1	—*	16.7
Amikacin	37.5	63.6	27.8	50.0
Gentamicin	21.9	40.9	22.2	58.3
Cefotaxime / Ceftriaxone	15.6	22.7	11.1	50.0
Cefepime	25.0	31.8	16.7	58.3
Piperacillin–tazobactam	46.9	72.7	33.3	—
Meropenem	71.9	90.9	44.4	—

Colistin	96.9	100.0	94.4	—*
Cotrimoxazole	—	31.8	—	50.0
Ciprofloxacin	28.1	36.4	22.2	58.3
Vancomycin	—	—	—	100.0
Linezolid	—	—	—	100.0
Cloxacillin / Oxacillin	—	—	—	50.0

Short-term outcomes

Of the 412 neonates with sepsis, 312 (75.7%) recovered and were discharged, 78 (18.9%) died during hospitalization, and 22 (5.3%) were taken away against medical advice or referred to a higher centre. The most common in-hospital complications were the need for mechanical ventilation (23.3%), inotropic support (20.4%), and septic shock (18.4%). Acute kidney injury was documented in 8.7%, disseminated intravascular coagulation in 6.8%, necrotizing enterocolitis in 5.3%, and CSF-confirmed meningitis in 4.4%. The mean duration of hospital stay was 11.6 ± 6.8 days; 21.4% of the survivors required prolonged hospitalization beyond 14 days (Table 6).

Table 6. Short-term outcomes and complications of neonatal sepsis (N = 412).

Outcome / Complication	Frequency (n)	Percentage (%)
Final outcome		
Discharged after recovery	312	75.7
In-hospital death	78	18.9
Left against medical advice / referred out	22	5.3
Major complications during hospital stay		
Mechanical ventilation required	96	23.3
Inotropic support required	84	20.4
Septic shock	76	18.4
Acute kidney injury	36	8.7
Disseminated intravascular coagulation (DIC)	28	6.8
Necrotizing enterocolitis (NEC)	22	5.3
Meningitis (CSF-confirmed)	18	4.4
Prolonged hospital stay (>14 days)	88	21.4

Mortality was strongly associated with prematurity, low birth weight, late-onset disease, and culture positivity. The case-fatality rate was 51.3% in neonates born at <32 weeks, 15.2% at 32–<37 weeks, and 6.7% at ≥37 weeks ($p<0.001$). Stratified by birth weight, mortality was 52.3% in VLBW, 12.1% in LBW, and 7.0% in normal-birth-weight neonates ($p<0.001$). Mortality was higher in late-onset (26.0%) than in early-onset sepsis (14.7%) ($p=0.006$) and was significantly higher in culture-positive (34.7%) than in culture-negative neonates (12.4%) ($p<0.001$). Among culture-positive cases, mortality was highest in those with Gram-negative bacteraemia (40.5%) and fungal sepsis (60.0%), and lowest in those with Gram-positive isolates (15.6%) ($p=0.014$). The detailed mortality stratification is shown in Table 7.

Table 7. Mortality stratified by demographic, clinical, and microbiological variables.

Variable	Total (n)	Deaths (n)	CFR (%)	p-value
Gestational age				
<32 weeks	78	40	51.3	<0.001
32–<37 weeks	184	28	15.2	
≥37 weeks	150	10	6.7	
Birth weight				
VLBW (<1500 g)	86	45	52.3	<0.001
LBW (1500–<2500 g)	198	24	12.1	
Normal (≥2500 g)	128	9	7.0	
Type of sepsis				
Early-onset (≤72 h)	258	38	14.7	0.006
Late-onset (>72 h)	154	40	26.0	
Culture status				
Culture-positive	121	42	34.7	<0.001
Culture-negative	291	36	12.4	
Organism group (culture-positive only)				
Gram-negative	84	34	40.5	0.014
Gram-positive	32	5	15.6	

Fungal	5	3	60.0	

DISCUSSION

The present prospective observational study describes the clinical profile, risk-factor distribution, microbial spectrum, antimicrobial susceptibility pattern, and short-term outcomes of neonatal sepsis in a busy tertiary-care SNCU in Kolkata over a one-year period. Our findings reaffirm that neonatal sepsis remains a leading cause of morbidity and mortality in our setting, that its bacteriology is increasingly dominated by multidrug-resistant Gram-negative organisms, and that prematurity and low birth weight remain the most consistent and powerful determinants of adverse outcome.

The incidence of clinical sepsis among our SNCU admissions (28.4%) is closely comparable to that reported in other Indian tertiary centres, where rates of 26–38% have been described.[3,9,10] The proportion of EOS to LOS in our cohort (62.6% vs 37.4%) is broadly consistent with previous reports from inborn-predominant Indian units, in which EOS has typically constituted between half and two-thirds of all sepsis cases.[9,11] The non-specific clinical presentation observed in our study — with lethargy (75.7%), refusal of feeds (72.3%), and respiratory distress (59.7%) as the dominant features — is in concordance with earlier descriptions and underscores the importance of a high index of suspicion, since no single sign is both sensitive and specific.[5,9]

Among maternal and perinatal risk factors, prolonged rupture of membranes (32.0%), multiple per-vaginal examinations (23.3%), foul-smelling liquor (18.4%), and maternal fever (14.1%) were the most prevalent in our cohort, and several of these emerged as independent predictors on multivariable analysis. These findings echo the conclusions of the WHO Young Infants Clinical Signs Study and large Indian cohorts, which have identified PROM, chorioamnionitis, maternal fever, and unhygienic deliveries as principal drivers of EOS.[2,5,12] Among neonatal factors, prematurity (aOR 3.42) and very low birth weight (aOR 2.86) were the strongest correlates of sepsis and of mortality, mirroring the DeNIS findings, in which preterm and small-for-gestational-age infants bore a disproportionate burden of both incidence and case-fatality.[4] The high adjusted odds ratio for mechanical ventilation (4.18) emphasizes the iatrogenic dimension of late-onset sepsis and the need for stringent ventilator-bundle compliance.

The blood culture–positivity rate of 29.4% in our study is in keeping with the 25–35% range typically reported from Indian NICUs.[4,9,10] The microbial spectrum we observed — dominated by Klebsiella pneumoniae (26.4%), followed by E. coli (18.2%), Acinetobacter (14.9%), and CoNS (11.6%) — is in close agreement with national surveillance data. The DeNIS study, which prospectively studied 13,530 neonates from three Indian tertiary centres, reported that nearly two-thirds of culture-proven sepsis was caused by Gram-negative organisms, with Acinetobacter and Klebsiella pneumoniae being the most frequent isolates.[4] Investigators from other Indian regions — including Mumbai, Chandigarh, Lucknow, and Bhubaneswar — have similarly documented a Gram-negative–dominant flora, in striking contrast to high-income settings, where Group B Streptococcus and CoNS continue to predominate.[13–15] This Gram-negative predominance has critical implications for the choice of empirical antibiotic therapy in Indian NICUs.

Even more concerning than the predominance of Gram-negative organisms is the high level of antimicrobial resistance we observed among them. In our cohort, susceptibility of Klebsiella to third-generation cephalosporins was only 15.6% and to gentamicin only 21.9%, while in Acinetobacter only 11.1% remained susceptible to cefotaxime and 44.4% to meropenem. Carbapenems and colistin retained the most reliable activity (Klebsiella–meropenem 71.9%, colistin 96.9%; Acinetobacter–colistin 94.4%). This pattern is consistent with the DeNIS data and other Indian reports, which have documented extended-spectrum β-lactamase (ESBL) production in 60–80% of Klebsiella and E. coli isolates and progressively increasing carbapenem resistance, particularly among Acinetobacter and Klebsiella, in NICU settings.[4,16,17] Such resistance compromises the effectiveness of the WHO-recommended ampicillin–gentamicin first-line regimen and warrants serious reconsideration of unit-specific empirical antibiotic policies. At the same time, indiscriminate up-front use of carbapenems is unsustainable: it accelerates the emergence of carbapenem-resistant Enterobacterales (CRE), which already pose an existential threat to neonatal care in some Indian units. A balanced strategy combining strict infection-prevention practices, rigorous antimicrobial stewardship, periodic unit-level antibiogram review, and de-escalation guided by culture results is essential.[18]

The case-fatality rate of 18.9% in our cohort lies within the range of 15–35% reported from comparable Indian SNCUs and NICUs.[4,9,10,19] Mortality was concentrated in preterm (51.3% in <32 weeks) and very-low-birth-weight infants (52.3% in VLBW), in those with late-onset disease (26.0%), and in those infected with multidrug-resistant Gram-negative (40.5%) and fungal (60.0%) organisms — a pattern repeatedly described in the literature and one that reinforces the case for strengthening antenatal care to reduce preterm birth, improving the quality of in-utero referral and neonatal transport, optimizing infection-prevention practices in the NICU, and ensuring rational, stewardship-driven empirical antibiotic use. The disproportionately high mortality in fungal sepsis (3 of 5 affected neonates) is consistent with global data and underlines the importance of early empirical antifungal therapy in extremely-low-birth-weight neonates with persistent culture-negative deterioration despite broad-spectrum antibacterial cover.[20]

The principal strengths of the present study are its prospective design, the inclusion of consecutive SNCU admissions over a full calendar year (which minimizes seasonal bias), and the comprehensive collection of maternal, perinatal, neonatal, microbiological, and outcome data, providing a contemporary unit-specific dataset that can directly inform local empirical antibiotic policy and infection-prevention practice.

LIMITATIONS

This study has several limitations. First, it is a single-centre study, and the findings — particularly the microbial and resistance profile — may not be generalizable to other settings. Second, the sample size, although adequate to describe the local epidemiology, was not powered to detect modest differences in mortality between organism subgroups. Third, blood culture was performed using a single sample of 1–2 mL, which may have reduced the culture-positivity rate; ideally, two paired aerobic samples of ≥1 mL each are recommended. Fourth, anaerobic and viral aetiologies were not systematically investigated, and molecular methods (e.g., 16S rRNA PCR) were not used. Finally, follow-up was limited to in-hospital outcomes; longer-term neurodevelopmental sequelae of survivors were not assessed.

CONCLUSION

Neonatal sepsis remains a major cause of admission and mortality in our SNCU, with an incidence of 28.4% among admissions and a case-fatality rate of 18.9%. Its clinical presentation is non-specific, demanding a high index of suspicion. Prematurity, very low birth weight, prolonged rupture of membranes, mechanical ventilation, and indwelling vascular access are key independent risk factors, while the microbial spectrum is dominated by multidrug-resistant Gram-negative organisms, especially Klebsiella, E. coli, and Acinetobacter. Carbapenems and colistin retain the most reliable activity against these isolates, but their use must be tempered by strict antimicrobial stewardship to prevent the further spread of carbapenem resistance. Strengthening antenatal care, ensuring hygienic intrapartum practices, optimizing infection-prevention bundles in the NICU, performing periodic review of unit-specific antibiograms, and rationalizing empirical antibiotic protocols on the basis of local data are essential strategies to reduce the burden of neonatal sepsis and improve neonatal survival in our setting.

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AUTHOR CONTRIBUTIONS

EA conceived and designed the study, collected and analysed the data, and drafted the manuscript. SN contributed to study design, supervised data collection, performed critical revision of the manuscript for important intellectual content, and provided overall guidance. Both authors approved the final version of the manuscript and agree to be accountable for all aspects of the work.

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