

Research Article

Clinical Profile, Risk Factors, and Short-Term Outcomes of Neonatal Sepsis among Neonates Admitted to a Tertiary Care Hospital

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Abstract

Background: Neonatal sepsis is one of the leading causes of neonatal morbidity and mortality especially among the low birth weight and preterm neonates who need tertiary care.

Objective: To evaluate the clinical profile, maternal and neonatal risk factors, and short-term outcomes of neonatal sepsis among neonates admitted to a tertiary-care hospital.

Methodology: This was a prospective observational study carried out at Pakistan Institute of Medical Sciences (PIMS) Islamabad and Khalifa Gulnawaz Teaching Hospital Bannu, from March 2024 to February 2025. 300 neonates (≤ 28 days) who were suspected or confirmed to have neonatal sepsis were consecutively enrolled. All maternal, perinatal, neonatal, clinical, laboratory, microbiological and treatment-related data were obtained in a prospective manner. Assessment of outcomes was performed at hospital discharge, death, referral, or at 28 days of life. The Chi-square test, independent-samples t-test, Mann-Whitney U test, and multivariable logistic regression were used for statistical analysis.

Results: Among 300 neonates, 155 (51.67%) were premature and 159 (53.00%) had low birth weight. Late-onset sepsis (LOS) occurred in 172 (57.33%) neonates, while early-onset sepsis (EOS) occurred in 128 (42.67%). Poor feeding was the most common clinical manifestation, affecting 201 (67.00%) neonates, followed by respiratory distress in 184 (61.33%). Elevated CRP was observed in 191 (63.67%), thrombocytopenia in 127 (42.33%), and positive blood cultures in 83 of 276 (30.07%) cultured neonates. Mortality was significantly higher in late-onset than EOS (35, 20.35% vs. 12, 9.38%; $p=0.013$). Among all neonates, 47 (15.67%) died. Multivariable logistic regression identified prematurity ($aOR=2.14$, 95% CI: 1.08–4.25, $p=0.029$), LOS ($aOR=2.37$, 95% CI: 1.12–5.02, $p=0.024$), respiratory distress ($aOR=2.81$, 95% CI: 1.20–6.57, $p=0.017$), apnea ($aOR=2.94$, 95% CI: 1.35–6.41, $p=0.007$), seizures ($aOR=2.52$, 95% CI: 1.11–5.73, $p=0.027$), mechanical ventilation ($aOR=3.76$, 95% CI: 1.82–7.77, $p<0.001$), and septic shock ($aOR=5.21$, 95% CI: 2.37–11.45, $p<0.001$) as independent predictors of in-hospital mortality.

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Conclusion: LOS and severe clinical deterioration were associated with substantially poorer outcomes, highlighting the need for early recognition and timely management of high-risk neonates.

Introduction

Neonatal sepsis is a potentially life-threatening systemic inflammatory reaction to infection in the first 28 days of life [1]. Neonatal sepsis is still a significant cause of neonatal morbidity and mortality, despite significant advances in neonatal intensive care, antimicrobial therapy and infection prevention practices, worldwide [2]. The clinical signs are often mild and vague, and may include respiratory distress, temperature instability, decreased appetite, lethargy, abnormal heart rate, jaundice, apnea, or circulatory failure in affected neonates. This variability can complicate early detection, especially in resource-limited environments where diagnostic tools and neonatal care are scarce [3,4].

Sepsis in infants is divided into early-onset sepsis (EOS), usually occurring within the first 72 hours of life, and late-onset sepsis (LOS), occurring after 72 hours of life [5]. Maternal and perinatal risk factors such as prolonged rupture of membranes, maternal fever, chorioamnionitis, prematurity, low birth weight, and inadequate intrapartum infection prevention are commonly associated with early onset disease [6,7]. LOS is linked to longer hospital stays, invasive procedures, mechanical ventilation, intravenous catheterization, and exposure to healthcare-associated infections (HAIs). Neonates are especially susceptible due to immaturity of immune responses and physiological barriers, leading to more severe disease and outcomes, particularly in premature and low birth weight neonates [8].

Neonatal sepsis is a difficult diagnosis to make, and blood culture is generally regarded as the gold standard for establishing the diagnosis of bloodstream infection, but can be time consuming and may be negative despite clinical sepsis, especially after having received previous antibiotic treatment [9,10]. Therefore, the clinical features, maternal and neonatal risk factors, laboratory data and treatment

response are often used in the evaluation of suspected cases [11]. Failure to recognize or to treat early can result in complications including septic shock, disseminated intravascular coagulation, neurological injury, respiratory failure, prolonged hospital stays, and death [12].

To enhance recognition and management, it is therefore crucial to understand the clinical features, risk factors and short-term outcomes of neonatal sepsis in individual health care settings. Local assessment may also assist in identifying vulnerable groups of newborns and risk factors for poor outcomes, especially in tertiary-care hospitals that have high-risk pregnancies and very ill newborns.

Research Objective

To evaluate the clinical profile, associated maternal and neonatal risk factors, and short-term outcomes of neonatal sepsis among neonates admitted to a tertiary care hospital.

Methodology

Study Design and Setting

The study was a prospective observational study conducted at the Pakistan Institute of Medical Sciences (PIMS) Islamabad and Khalifa Gulnawaz Teaching Hospital MTI Bannu, tertiary-care hospitals providing specialized neonatal and intensive care. The hospital accepts neonates with a wide range of infectious and non-infectious conditions and offers diagnostic, therapeutic and supportive care for the neonates. The study was conducted to assess the clinical profile, maternal and neonatal risk factors, and short-term outcomes of neonatal sepsis among neonates admitted to the hospital. As an observational study, it did not involve any experimental intervention or alteration of routine clinical management for research purposes.

Study Duration and Population

The study was carried out from March 2024 till February 2025 for 12 months. The study population consisted of neonates admitted to the neonatal unit or neonatal intensive care unit during the study period and who met the predetermined criteria for suspected or confirmed neonatal sepsis, with an age of 28 completed days or less. Eligible neonates were enrolled prospectively at admission when sepsis was suspected or at the time they developed clinical features suggestive of sepsis during hospitalization. Each enrolled neonate was followed prospectively from the time of enrollment until hospital discharge, in-hospital death, or referral/transfer. Outcome assessment was limited to the first 28 days of life, where applicable.

Sample Size and Sampling Technique

The total number of neonates studied was 300. A sample size of 300 was predetermined, taking into account the number of eligible neonatal sepsis cases that would be available for the 12-month period of the study and the number of observations needed to describe the clinical profile, to evaluate the maternal and neonatal risk factors, and to assess the short-term outcomes – in-hospital mortality and major complications. The number of outcome events was used as a basis for determining the selected sample size, and was deemed adequate for planned comparative and multivariable analyses within the framework of the single center prospective study. Consecutive sampling was used, and all neonates that fulfilled the inclusion criteria were consecutively included until the desired sample size was reached. To avoid selective recruitment, and to ensure systematic inclusion of eligible cases presenting during the study period, consecutive recruitment was utilized.

Eligibility Criteria

Neonates aged 28 days or less who were admitted to the neonatal unit or neonatal intensive care unit and had clinical signs and symptoms of suspected neonatal sepsis and/or microbiological evidence of infection were included. Neonates were included when they underwent clinical evaluation for sepsis and

the treating neonatal team initiated a sepsis evaluation and/or antimicrobial therapy because of clinical suspicion of infection. All clinically suspected and culture-confirmed cases were eligible for enrollment, but had to meet the predetermined operational criteria for neonatal sepsis. Neonates older than 28 days, those with inadequate essential information about clinical presentation, risk factors, laboratory evaluation, or short-term clinical outcome were excluded, as well as those referred after prolonged antimicrobial therapy or intensive care at another healthcare facility, where it was not possible to obtain reliable information about their initial clinical status. Major congenital anomalies or severe pre-existing medical conditions which were likely to independently influence the clinical outcome and make assessment of the sepsis-related outcomes difficult were also excluded from the analysis of neonates.

Operational Definitions

Sepsis was considered neonatal if systemic infection (suspected or confirmed) was present for the first 28 completed days of life, and was diagnosed from the presence of compatible clinical signs, supportive laboratory features, and/or microbiological findings. Clinically suspected neonatal sepsis was confirmed by the presence of matching clinical features with laboratory evidence of infection and clinical judgment of the treating pediatric neonatal unit to start treatment with antimicrobial agents. Clinical illness with isolation of a pathogenic organism from a blood sample that had been properly collected was considered culture-confirmed neonatal sepsis. Sepsis occurring within 72 hours of birth was considered EOS and after 72 hours, LOS. Prematurity was classified as birth before 37 complete weeks of gestation and low birth weight was defined as less than 2,500 g. Healthcare-associated exposures were reported separately from baseline maternal and neonatal risk factors, since exposures could occur after admission; these exposures also were particularly associated with late onset or HAIs.

Data Collection Procedure

A structured and predesigned data collection form was used to collect the data prospectively. Data on the mothers and newborns were collected from maternal and neonatal medical records, clinical examination on admission, clinical laboratory reports, treatment notes, and clinical observation. Maternal and perinatal data was included which comprised of maternal age, antenatal care, parity, maternal fever/suspected infection, prolonged rupture of membranes, duration of rupture of membranes, mode of delivery, documented chorioamnionitis, and other perinatal complications. Demographic information for the neonates collected included age at presentation, sex, gestational age, birth weight, place of delivery, Apgar score (available), feeding status, history of resuscitation and previous neonatal hospitalization. The clinical characteristics were recorded at the time of enrolment prior to or at the onset of treatment directed to sepsis (capture of the clinical profile as a baseline). Clinical data consisted of temperature instability, respiratory distress, apnea, cyanosis, poor feeding, lethargy, abnormal activity, jaundice, abdominal distension, seizures, cardiovascular instability and other signs of systemic infection.

Clinical and Laboratory Assessment

The clinical assessment was performed in all enrolled neonates as per the routine neonatal care practice. Temperature, heart rate, respiratory rate, oxygen saturation (when clinically appropriate) and blood pressure (when clinically indicated) were recorded. Laboratory investigations were performed according to the clinical condition of each neonate and included complete blood count, total leukocyte count, differential leukocyte count, platelet count, blood glucose, C-reactive protein (CRP), and blood culture, where available. Other serum biochemical, radiological, and microbiological investigations were documented when clinically indicated. Blood cultures were collected with proper aseptic techniques before starting antibiotic treatment, if possible. Culture positive cases were noted for culture results, organisms identified, and

antimicrobial susceptibility patterns. Laboratory results were analyzed with the clinical presentation and not in isolation to make a diagnosis of neonatal sepsis.

Assessment of Risk Factors

Systematic assessment of potential risk factors associated with the mother, perinatal, baseline neonatal and healthcare was carried out. Maternal and perinatal factors considered were: prolonged rupture of membranes, maternal fever, suspected maternal infection, inadequate antenatal care, documented chorioamnionitis and mode of delivery. Neonatal factors that were considered as baseline were prematurity, low birth weight, sex, low Apgar score, resuscitation and other neonatal factors present prior to the evaluation of sepsis. Mechanical ventilation, intravenous lines, invasive procedures, and long-term hospitalizations were separately diagnosed and analyzed with special focus on LOS and adverse outcomes. These factors were quantified and compared by clinical presentation, early versus LOS, culture findings and short-term outcome.

Treatment and Clinical Management

Treatment was given as per clinical condition and as per the routine treatment practices followed by the treating team at the time of admission of all neonates. Antimicrobial therapy was commenced as appropriate and adjusted based on clinical response, laboratory results, culture and antimicrobial susceptibility data – where available. Oxygen supplementation, respiratory support, intravenous fluid, nutritional support, management of hypoglycemia, control of seizures, blood products and other intensive neonatal care was supplied as needed. As for the clinical course, the type and duration of antimicrobial therapy, need for respiratory support, mechanical ventilation and other major supportive interventions were documented. This was an observational study and treatment decisions were independent of the researchers and were not changed just for research.

Assessment of Short-Term Outcomes

Each enrolled neonate was followed

prospectively until hospital discharge, in-hospital death, or referral/transfer to another healthcare institution, with outcome assessment performed up to 28 days of life. The short-term outcomes assessed included survival to hospital discharge, in-hospital mortality, referral/transfer, major complications, duration of hospital stay, need for respiratory support or mechanical ventilation, need for intensive care, and clinical recovery after treatment. Major complications evaluated were sepsis, septic shock, respiratory failure, disseminated intravascular coagulation, seizures, or neurological complications, and other clinically recorded complications due to severe infection. Clinical recovery was outlined as documentation of clinical improvement or resolution of the major clinical manifestation(s) of sepsis with stabilization of the neonate with no continued need for escalation of sepsis-directed management at the time of the outcome assessment. Clinical condition at 28 days after the end-point was noted for neonates who were still in hospital at the end of the predefined outcome-assessment period and hospital status was recorded separately if known after this. In-hospital mortality was considered the primary outcome when analyzing the multivariable data, while the other short-term outcomes were considered secondary outcomes for which sufficient events could be reliably analyzed.

Statistical Analysis

Data was inputted, verified and processed with SPSS statistical software. Values were presented as mean and standard deviation for normally distributed data and as median and interquartile range for non-normally distributed data, and as frequencies and percentages for categorical data. Correlations between categorical variables were tested by Chi-square test. Independent-samples t-test was performed to compare continuous variables between outcome groups for normally distributed variables and Mann-Whitney U test for non-normally distributed variables. Where appropriate, subgroup analyses were carried out in order to compare

the early onset and late onset of sepsis and favourable versus unfavourable short-term outcomes. All the in-hospital deaths were analyzed using binary logistic regression to determine which factors were independently associated with death. In cases where there were enough events for a reliable estimation of the model, additional predefined adverse outcomes were added for multivariable analysis. Candidate variables were chosen based on clinical relevance and/or association with the outcome in the univariable analyses. Adjusted odds ratios (with 95% CIs) were calculated using the final multivariable model. A p-value of less than 0.05 was judged to be statistically significant (two-sided p-value).

Ethical Considerations

Before starting the study, ethical approval was sought from the relevant institutional ethics committee. The study was carried out in an ethical manner as per the accepted ethical principles involving human subjects. Eligible neonates and their parents/legal guardians were provided with information on the study and asked to sign informed consent forms when required by the institutional ethics committee. Participation in the study was voluntary, and refusal to participate did not affect the medical care provided to the neonate. All individuals involved in the study were kept confidential and privacy was maintained and study information was coded and only used for research. Identifiable clinical data was only available for authorized study personnel. No extra diagnostic or treatment procedures were done solely for research.

Results

Among 300 neonates, most mothers were aged 20–29 years (161, 53.67%), shown in [table 1](#). Adequate antenatal care was reported in 216 (72.00%), while maternal fever occurred in 73 (24.33%), prolonged rupture of membranes in 89 (29.67%), and chorioamnionitis in 35 (11.67%). Vaginal delivery occurred in 173 (57.67%) cases, and 82 (27.33%) neonates required resuscitation at birth.

Table 1: Maternal and Perinatal Characteristics of Neonates with Sepsis

Variable	Category	Numbe	%
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		Number of Patients (n)	%
Maternal age	<20 years	27	9.00
	20–29 years	161	53.67
	30–39 years	101	33.67
	≥40 years	11	3.67
Antenatal care	Adequate	216	72.00
	Inadequate	84	28.00
Maternal fever	Yes	73	24.33
	No	227	75.67
Prolonged rupture of membranes	Yes	89	29.67
	No	211	70.33
Chorioamnionitis	Yes	35	11.67
	No	265	88.33
Vaginal delivery	Yes	173	57.67
	No	127	42.33
Resuscitation at birth	Yes	82	27.33
	No	218	72.67

Male neonates constituted 174 (58.00%) of the study population (table 2). Prematurity was present in 155 (51.67%) neonates and low birth weight in 159 (53.00%). An Apgar score below 7 at 1 minute was recorded in 87 (29.00%), while 52 (17.33%) neonates had a history of previous hospitalization.

Table 2: Baseline Neonatal Characteristics

Variable	Category	Number of Patients (n)	%
Sex	Male	174	58.00
	Female	126	42.00
Prematurity	Yes	155	51.67

	No	145	48.33
Low birth weight	Yes	159	53.00
	No	141	47.00
Apgar <7 at 1 minute	Yes	87	29.00
	No	213	71.00
Previous hospitalization	Yes	52	17.33
	No	248	82.67

Among the 300 neonates with sepsis, LOS was more common than EOS (figure 1). LOS accounted for 172 (57.33%) cases, whereas EOS was identified in 128 (42.67%) neonates. Thus, more than half of the enrolled neonates developed sepsis after the first 72 hours of life, indicating a predominance of late-onset disease in this tertiary-care neonatal population.

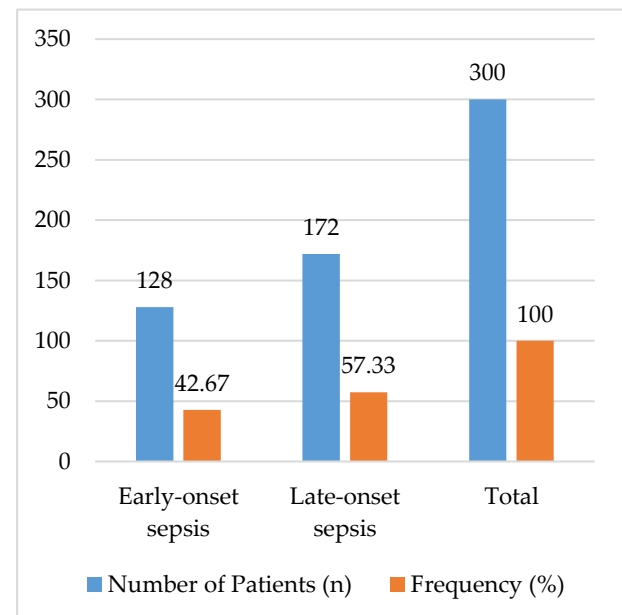


Figure 1: Distribution According to Onset of Sepsis

The clinical presentation of neonatal sepsis was characterized predominantly by poor feeding, respiratory manifestations, and altered general condition. Poor feeding was the most common finding, occurring in 201 (67.00%) neonates, followed by respiratory distress in 184 (61.33%), tachypnea in 169 (56.33%), and lethargy in 156 (52.00%). Temperature instability was observed in 112 (37.33%), while abnormal activity and jaundice occurred in 93 (31.00%) and 84 (28.00%), respectively. Cardiovascular instability was present in 63 (21.00%), abdominal distension

in 58 (19.33%), apnea in 47 (15.67%), hypotension in 48 (16.00%), seizures in 42 (14.00%), and cyanosis in 39 (13.00%). These findings demonstrate the broad and nonspecific clinical profile of neonatal sepsis, with feeding difficulty and respiratory abnormalities being the predominant presentations (figure 2).

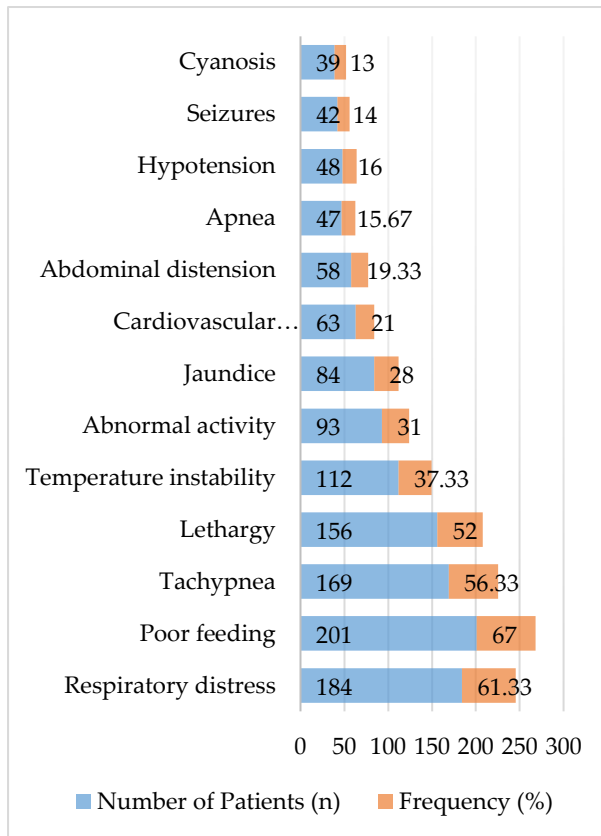


Figure 2: Clinical Profile of Neonates with Sepsis

Laboratory findings showed that 156 (52.00%) neonates had normal leukocyte counts, while leukocytosis was present in 95 (31.67%) and leukopenia in 49 (16.33%), shown in table 3. Thrombocytopenia was identified in 127 (42.33%) neonates, whereas 173 (57.67%) had normal platelet counts. CRP was elevated in 191 (63.67%) neonates. Among the 276 neonates who underwent blood culture, 83 (30.07%) had positive cultures and 193 (69.93%) had negative results, indicating that elevated CRP and thrombocytopenia were relatively common laboratory abnormalities.

Table 3: Laboratory and Microbiological Findings

Variable	Category	Numbe	%
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		r of Patient s (n)	
Leukocyte count	Leukopenia	49	16.33
	Normal	156	52.00
	Leukocytosis	95	31.67
Platelet count	Thrombocytopenia	127	42.33
	Normal	173	57.67
CRP	Elevated	191	63.67
	Normal	109	36.33
Blood culture	Positive	83	30.07 *
	Negative	193	69.93 *

Note: *Calculated among 276 neonates in whom blood culture was obtained.

Significant differences were observed in several maternal and neonatal factors between EOS and LOS (table 4). Prematurity was more frequent in LOS than EOS (62.21% vs. 37.50%; $\chi^2=17.21$, $p<0.001$), as was low birth weight (60.47% vs. 42.97%; $\chi^2=9.21$, $p=0.002$). In contrast, maternal fever (33.59% vs. 17.44%), prolonged rupture of membranes (39.84% vs. 22.09%), and chorioamnionitis (20.31% vs. 5.23%) were significantly more frequent in EOS (all $p<0.001$). Low Apgar score and need for resuscitation were also significantly associated with EOS, while previous hospitalization was markedly more common in LOS (27.91% vs. 3.13%; $\chi^2=31.10$, $p<0.001$).

Table 4: Comparison of Maternal and Neonatal Factors Between EOS and LOS (Pearson's Chi-square test)

Variable	EOS (n=128)	LOS (n=172)	χ^2	p-value
Prematurity	48 (37.50%)	107 (62.21%)	17.21	<0.001
Low birth weight	55 (42.97%)	104 (60.47%)	9.21	0.002
Maternal fever	43 (33.59%)	30 (17.44%)	11.51	<0.001
Prolonged rupture of	51 (39.84%)	38 (22.09%)	12.13	<0.001

membranes	%)	%)		
Chorioamnionitis	26 (20.31%)	9 (5.23%)	17.0 6	<0.0 01
Inadequate antenatal care	44 (34.38%)	40 (23.26%)	4.72	0.03 0
Low Apgar score	51 (39.84%)	36 (20.93%)	13.2 2	<0.0 01
Resuscitation required	49 (38.28%)	33 (19.19%)	13.5 2	<0.0 01
Previous hospitalization	4 (3.13%)	48 (27.91%)	31.1 0	<0.0 01

Short-term outcomes differed significantly between EOS and LOS (table 5). Clinical recovery was significantly higher among neonates with EOS than LOS (90.63% vs. 72.67%; $\chi^2=15.96$, $p<0.001$), whereas in-hospital mortality was higher in LOS (20.35% vs. 9.38%; $\chi^2=6.11$, $p=0.013$). Respiratory failure occurred in 26.74% of LOS compared with 14.06% of EOS ($\chi^2=7.04$, $p=0.008$), while septic shock occurred in 18.60% and 7.81%, respectively ($\chi^2=7.23$, $p=0.007$). Mechanical ventilation and major complications were also significantly more frequent in LOS (30.81% vs. 14.06%, $p<0.001$; and 38.37% vs. 23.44%, $p=0.007$, respectively)

Table 5: Comparison of Short-Term Outcomes Between EOS and LOS

Outcome	EOS (n=128)	LOS (n=172)	χ^2	p-value
Clinical	116	125	15.9	<0.00

recovery	(90.63%)	(72.67%)	6	1
In-hospital mortality	12 (9.38%)	35 (20.35%)	6.11	0.013
Respiratory failure	18 (14.06%)	46 (26.74%)	7.04	0.008
Septic shock	10 (7.81%)	32 (18.60%)	7.23	0.007
Mechanical ventilation	18 (14.06%)	53 (30.81%)	12.0 8	<0.00 1
Major complications	30 (23.44%)	66 (38.37%)	7.33	0.007

Comparison between survivors and non-survivors demonstrated several significant differences (table 6). Survivors had higher mean gestational age (35.2±3.1 vs. 32.7±3.8 weeks; $t=4.71$, $p<0.001$) and birth weight (2,310±684 vs. 1,925±612 g; $t=3.61$, $p<0.001$). Age at presentation and hospital stay also differed significantly. Prematurity was more frequent among non-survivors (72.34% vs. 47.83%; $\chi^2=8.97$, $p=0.003$), while respiratory distress, apnea, seizures, thrombocytopenia, positive blood culture, mechanical ventilation, and septic shock were significantly more common among non-survivors ($p\leq 0.015$). Low birth weight did not reach statistical significance ($p=0.061$).

Table 6: Comparison of Survivors and Non-Survivors

Variable	Survivors (n=253)	Non-survivors (n=47)	Test	p-value
Gestational age, weeks	35.2 ± 3.1	32.7 ± 3.8	$t = 4.71$	<0.001
Birth weight, g	2,310 ± 684	1,925 ± 612	$t = 3.61$	<0.001
Age at presentation, days	4.0 (2.0–9.0)	7.0 (3.0–14.0)	$U = 4,721$	0.002
Hospital stay, days	9.0 (6.0–14.0)	7.0 (3.0–12.0)	$U = 4,918$	0.011
Prematurity	121 (47.83%)	34 (72.34%)	$\chi^2 = 8.97$	0.003
Low birth weight	128 (50.59%)	31 (65.96%)	$\chi^2 = 3.52$	0.061
Respiratory distress	144 (56.92%)	40 (85.11%)	$\chi^2 = 12.87$	<0.001
Apnea	29 (11.46%)	18 (38.30%)	$\chi^2 = 20.61$	<0.001
Seizures	26 (10.28%)	16 (34.04%)	$\chi^2 = 17.07$	<0.001
Thrombocytopenia	99 (39.13%)	28 (59.57%)	$\chi^2 = 6.17$	0.013

Positive blood culture	63 (24.90%)	20 (42.55%)	$\chi^2 = 5.88$	0.015
Mechanical ventilation	43 (16.99%)	28 (59.57%)	$\chi^2 = 35.89$	<0.001
Septic shock	18 (7.11%)	24 (51.06%)	$\chi^2 = 50.12$	<0.001

Note: independent-samples *t*-test/Mann–Whitney *U* test and Chi-square analysis.

Multivariable logistic regression identified several independent predictors of in-hospital mortality (table 7). Prematurity (adjusted OR [aOR]=2.14, 95% CI: 1.08–4.25, $p=0.029$), LOS (aOR=2.37, 95% CI: 1.12–5.02, $p=0.024$), respiratory distress (aOR=2.81, 95% CI: 1.20–6.57, $p=0.017$), apnea (aOR=2.94, 95% CI: 1.35–6.41, $p=0.007$),

mechanical ventilation (aOR=3.76, 95% CI: 1.82–7.77, $p<0.001$), and septic shock (aOR=5.21, 95% CI: 2.37–11.45, $p<0.001$) were independently associated with increased mortality. Low birth weight, thrombocytopenia, and elevated CRP were not independently significant after adjustment ($p>0.05$).

Table 7: Multivariable Logistic Regression for In-Hospital Mortality

Predictor	Crude OR	95% CI	p-value	Adjusted OR	95% CI	p-value
Prematurity	2.84	1.39–5.81	0.004	2.14	1.08–4.25	0.029
Low birth weight	1.89	0.96–3.71	0.066	1.68	0.84–3.37	0.142
Late-onset sepsis	2.47	1.17–5.20	0.018	2.37	1.12–5.02	0.024
Respiratory distress	4.31	1.78–10.44	0.001	2.81	1.20–6.57	0.017
Apnea	4.79	2.14–10.72	<0.001	2.94	1.35–6.41	0.007
Seizures	4.51	2.02–10.08	<0.001	2.52	1.11–5.73	0.027
Thrombocytopenia	2.29	1.16–4.51	0.017	1.91	0.96–3.79	0.066
Elevated CRP	3.20	1.42–7.21	0.005	1.73	0.82–3.66	0.149
Mechanical ventilation	7.22	3.44–15.16	<0.001	3.76	1.82–7.77	<0.001
Septic shock	13.67	6.15–30.39	<0.001	5.21	2.37–11.45	<0.001

Note: OR = odds ratio; CI = confidence interval.

Discussion

In this prospective study of 300 neonates with sepsis, prematurity was present in 155 (51.67%) and low birth weight in 159 (53.00%), while 174 (58.00%) were male. The majority of cases were LOS with 172 (57.33%) cases, while there were 128 (42.67%) cases of EOS. This prevalence of LOS is in keeping with evidence that exposure to intensive care units, invasive procedures, vascular access, and prolonged hospital stays is associated with a higher risk of HAI. The specific susceptibility of premature and low birth weight neonates to LOS has also been highlighted recently [13]. The relatively high proportion of prematurity and low birth weight in the current cohort may have helped to account for the high burden of LOS that was observed.

Maternal and perinatal findings clearly showed EOS from LOS. Maternal fever was significantly more frequent in EOS than LOS (33.59% vs. 17.44%), as were prolonged rupture of membranes (39.84% vs. 22.09%) and chorioamnionitis (20.31% vs. 5.23%; all $p<0.001$). Other factors associated with EOS were low

Apgar score and resuscitation, while previous hospitalization was significantly more common in LOS (27.91% compared to 3.13%, $p<0.001$). These results are similar to those of a 2023 meta-analysis, which showed that chorioamnionitis, premature rupture of membranes, maternal/perinatal fever, lower gestational age, very low birth weight, and perinatal asphyxia were important risk factors for EOS [14]. On the other hand, the correlation found between previous hospitalization and LOS in this study is consistent with the known impact of healthcare exposure on late-onset infection.

The clinical profile also illustrated the lack of specificity of neonatal sepsis. Poor feeding occurred in 201 (67.00%) neonates, respiratory distress in 184 (61.33%), tachypnea in 169 (56.33%), and lethargy in 156 (52.00%), while apnea and seizures occurred in 47 (15.67%) and 42 (14.00%), respectively. These findings have clinical significance as they have been described in septic neonates, with respiratory distress, lethargy, poor feeding, and neurological changes being associated with severe disease. Respiratory

distress, poor feeding and convulsions were all independent risk factors for mortality in a prospective study in Ethiopia, with odds ratios of 2.72, 4.15, and 3.13, respectively [15]. Therefore, the respiratory and feeding abnormalities were frequent in the present cohort, highlighting the importance of early clinical recognition, rather than relying on a single diagnostic feature.

The laboratory results revealed that the CRP level was elevated in 191 (63.67%) neonates, while only 83 of 276 cultured neonates (30.07%) had positive blood cultures, and thrombocytopenia was observed in 127 (42.33%) neonates. This is a relatively low culture positivity rate despite frequent inflammatory abnormalities, which is in keeping with the known limitations of blood culture in neonatal sepsis, especially in clinically suspected cases. In a 2024 study, blood culture was positive in 27.7% of suspected neonatal sepsis cases and elevated CRP and thrombocytopenia were seen in about two thirds of the culture-positive cases [16]. Hence, the current results suggest complementing CRP, platelet count and clinical evaluation and not using negative culture as a definite exclusion of sepsis.

ST outcomes were significantly worse in LOS. Clinical recovery was 72.67% in LOS versus 90.63% in EOS ($p < 0.001$), while mortality was 20.35% versus 9.38% ($p = 0.013$). LOS was also associated with respiratory failure (26.74% vs. 14.06%), septic shock (18.60% vs. 7.81%), mechanical ventilation (30.81% vs. 14.06%), and major complications (38.37% vs. 23.44%). The results are similar to those of other studies which have shown that LOS is still a major contributor to neonatal morbidity and mortality in intensive care units [17]. The mortality seen in this cohort is also within the high mortality rates reported in neonatal sepsis studies in LMICs, but comparisons should take into account variations in case definition and severity of illness.

Lastly, prematurity (aOR 2.14), LOS (aOR 2.37), respiratory distress (aOR 2.81), apnea (aOR 2.94), seizures (aOR 2.52), mechanical ventilation (aOR 3.76), and septic shock (aOR 5.21) were each independently associated with mortality. Survivors also had greater mean gestational age (35.2 ± 3.1 vs. 32.7 ± 3.8 weeks) and birth weight ($2,310 \pm 684$ vs. $1,925 \pm 612$ g), while prematurity occurred in 72.34% of non-survivors. These findings are in close agreement with previous work that has shown that prematurity, respiratory

distress, convulsions, ventilation and shock are all significant factors in neonatal mortality [18]. The particularly high adjusted association with septic shock in the present study (aOR 5.21) highlights the importance of rapid recognition and aggressive supportive management of hemodynamic deterioration in septic neonates.

Strengths and Limitations

This study has several important strengths: its prospective observational design, the consecutive enrollment of 300 neonates, and the systematic assessment of maternal, perinatal, neonatal, clinical, laboratory, microbiological, and healthcare-associated factors. The study also compared early- and LOS and assessed clinically relevant short-term outcomes (mortality, respiratory failure, septic shock, mechanical ventilation, and major complications). Moreover, the results were adjusted for possible confounding factors by multivariable logistic regression, enhancing the interpretation of the results. There are, however, some drawbacks to be taken into account. The results of this study may not be applicable to other hospitals or community settings because of the single-center design at a tertiary-care hospital. Blood culture was collected from 276 (92.00%) neonates, and only 83 (30.07%) were positive, possibly due to prior antibiotic use or other limitations in blood culture. Diagnostic heterogeneity may also be introduced by the inclusion of clinically suspected as well as culture confirmed sepsis. Some exposures associated with health care may also be a consequence of severe illness, rather than a predisposing cause of sepsis, such as mechanical ventilation and invasive procedures, making causal interpretation difficult. Lastly, the relatively short follow-up period was limited to in-hospital outcomes, and long-term neurological, developmental, and functional outcomes were not evaluated.

Conclusion

Neonatal sepsis in this tertiary-care population was associated with high rates of prematurity, low birth weight and LOS, and poor feeding, respiratory distress, tachypnea, and lethargy were the most common clinical features. EOS was significantly associated with maternal fever, prolonged rupture of membranes and chorioamnionitis, while low birth weight, previous hospitalization and prematurity were

more common among neonates with LOS. LOS was linked with significantly poorer clinical recovery and increased mortality, respiratory failure, septic shock, mechanical ventilation and major complications. Importantly, multivariable analysis revealed that prematurity, LOS, respiratory distress, apnea, seizures, mechanical ventilation and septic shock were independent risk factors for in-hospital mortality, with septic

shock being the strongest association. These findings emphasize the importance of early identification of high-risk neonates, prompt recognition of clinical deterioration, appropriate infection-control practices, and timely supportive and antimicrobial management to reduce mortality and complications associated with neonatal sepsis.

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