IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 24, Issue 6 Ser.7 (June 2025), PP 34-41
www.iosrjournals.org

Comparative analysis of laboratory predictors of mortality in neonates with septic shock: a prospective study of survivors and non-survivors in a tertiary care setting, in Central India

Monali Datta, Junior Resident, Gandhi Medical College, Bhopal, Madhyapradesh
Syamali Mandal Datta, Assistant Professor, P.C.Sen Government Medical College, Arambagh, Hooghly, West Bengal

Abstract
Background
Neonatal septic shock is a major cause of morbidity and mortality, particularly in resource-limited settings. Early identification of high-risk neonates is crucial for improving survival. This study aims to evaluate and compare laboratory predictors of mortality between survivors and non-survivors of neonatal septic shock in a tertiary care center.
Methods
This prospective observational study included 360 term neonates (≥37 to ≤42 weeks of gestation) diagnosed with septic shock and admitted to the Special Newborn Care Unit (SNCU) at Gandhi Medical College, Bhopal, India, over 18 months. Clinical and laboratory parameters, including hematological, biochemical, and metabolic markers, were analyzed and compared between survivors and non-survivors. Multivariate logistic regression identified independent predictors of mortality.
Results
The overall mortality rate was 45.6%. Non-survivors had significantly lower admission weight (2.36 ± 0.38 kg vs. 2.51 ± 0.34 kg, p=0.01), platelet count (p<0.01), and total WBC count (p=0.04). Elevated CRP (p<0.01), urea (p<0.01), creatinine (p=0.01), and lactate levels (p<0.01) were significantly associated with mortality. Metabolic acidosis (p<0.01) and hypernatremia (p=0.01) were also strong predictors. In multivariate analysis, weight on admission (AOR: 0.48, p=0.04), platelet count (AOR: 0.94, p=0.002), CRP (AOR: 1.03, p=0.03), urea (AOR: 1.03, p<0.01), and bicarbonate levels (AOR: 0.96, p=0.01) remained independently associated with mortality.
Conclusion
Laboratory markers, particularly thrombocytopenia, elevated CRP, urea, metabolic acidosis, and hypernatremia, are strong predictors of mortality in neonatal septic shock. Early identification of these risk factors can improve clinical outcomes. Future research should focus on integrating these markers into predictive models for targeted interventions.
Keywords
Neonatal sepsis, septic shock, mortality, laboratory predictors, CRP, metabolic acidosis, thrombocytopenia

---

Date of Submission: 08-06-2025 Date of Acceptance: 20-06-2025

I. Introduction

Neonatal septic shock is a life-threatening condition characterized by systemic infection, hemodynamic instability, and multi-organ dysfunction, contributing significantly to neonatal morbidity and mortality worldwide. Despite advancements in neonatal care, it remains a major challenge, particularly in low- and middle-income countries, where the burden is disproportionately high. Early identification of high-risk neonates is crucial for timely intervention and improved survival outcomes.(1) The pathophysiology of neonatal septic shock involves a systemic inflammatory response, endothelial dysfunction, and impaired tissue perfusion, leading to progressive organ failure.(2) Neonates, especially preterm infants, have an immature immune system, making them highly susceptible to bacterial and fungal infections.(3) Clinical manifestations such as temperature instability, respiratory distress, hypotension, and metabolic acidosis often overlap with other neonatal conditions, making early diagnosis challenging.

Laboratory biomarkers play a pivotal role in assessing disease severity and predicting mortality. Hematological markers such as leukopenia (<4,000/mm³) and thrombocytopenia (<100,000/mm³) have been associated with worse outcomes, indicating bone marrow suppression and consumptive coagulopathy.(4) Biochemical markers such as elevated serum lactate levels and reduced lactate clearance reflect tissue hypoxia and metabolic stress, both of which are linked to higher mortality rates. Additionally, base excess <–20 mEq/L and hyperglycemia >180 mg/dL have been implicated in the pathophysiology and prognosis of neonatal septic shock.(5)

Emerging biomarkers, including procalcitonin (PCT), presepsin (sCD14-ST), soluble triggering receptor expressed on myeloid cells-1 (sTREM-1), and interleukin-6 (IL-6), have shown potential in risk stratification of neonatal sepsis and septic shock. However, while individual biomarkers provide valuable insights, there is limited data on their comparative prognostic value between survivors and non-survivors. Understanding these differences can guide clinical decision-making, enabling early and targeted interventions for neonates at higher risk of mortality.(6)

Despite these advancements, there remains a need for comprehensive analyses comparing the laboratory profiles of survivors and non-survivors of neonatal septic shock. Understanding these differences is crucial for developing risk stratification models and optimizing therapeutic strategies to improve neonatal outcomes. This study aims to conduct a comparative analysis of laboratory predictors of mortality in neonatal septic shock by evaluating and contrasting the laboratory profiles of survivors and non-survivors.

II. Materials And Methods

This prospective observational study was conducted to evaluate the predictive value of the laboratory parameters in assessing mortality risk in term neonates with septic shock. The study was conducted at the Special Newborn Care Unit (SNCU), Department of Paediatrics, Gandhi Medical College, Bhopal, India, a tertiary-level neonatal care center managing critically ill neonates from both urban and rural regions. The study spanned a duration of 18 months, from July 2022 to January 2024, covering patient recruitment, data collection, follow-up, and statistical analysis.

The study population consisted of term neonates (37 to 42 weeks of gestation) diagnosed with septic shock who were admitted to the SNCU during the study period. Neonates were included if they were born at term (≥37 to ≤42 weeks of gestation), diagnosed with septic shock based on clinical and laboratory criteria, and required vasoactive and inotropic support within 24 hours of admission. Neonates who expired within 48 hours of admission, those who had received inotropic drugs before SNCU admission, or those with congenital anomalies or major surgical conditions affecting cardiovascular stability were excluded from the study. The sample size was estimated by assuming an expected mortality rate of 40% based on the previous 2-year hospital data and using a 95% confidence interval with a 5% margin of error, the minimum required sample size was determined to be 360 neonates. A consecutive sampling technique was employed, enrolling all eligible neonates meeting the inclusion criteria during the study period until the required sample size was achieved.

Data collection was performed using a structured case record form (CRF), which included demographic and clinical details such as birth history, gestational age, APGAR scores, and perinatal risk factors. Clinical signs of septic shock, including perfusion status, temperature instability, respiratory distress, and metabolic acidosis, were recorded. Laboratory investigations included complete blood count (CBC), platelet count, C-reactive protein (CRP), serum lactate, arterial blood gas (ABG) analysis, and blood culture. The structured CRF was pre-tested on 10% of the sample before the main study to ensure clarity, consistency, and feasibility, and necessary modifications were made based on feedback. A team of trained pediatric residents and neonatal nurses collected data, following standardized protocols and clinical assessment. Training sessions were conducted to ensure inter-observer reliability and minimize errors in data collection.

The primary outcome measure of the study was mortality in neonates with septic shock, while secondary outcomes included laboratory parameters and their association with mortality. Statistical analysis was performed using STATA version14. Descriptive statistics, including mean, standard deviation, and frequency distributions, were used to summarize demographic and clinical data. Chi-square tests and independent t-tests were applied to compare differences between survivors and non-survivors. Multivariate logistic regression analysis was performed to identify independent predictors of mortality, with statistical significance set at $p < 0.05$.

Data management was ensured through password-protected electronic storage, with random double-entry verification performed on 10% of cases to maintain data integrity. Ethical approval was obtained from the

Institutional Ethics Committee (IEC) of Gandhi Medical College, Bhopal. Written informed consent was obtained from the parents or legal guardians of all enrolled neonates, and strict measures were taken to ensure confidentiality and anonymity of patient data throughout the study.

III. Results

We have included a total of 360 participants for the final analysis. The analysis of neonatal sepsis outcomes showed no significant difference in gender distribution (p=0.686). However, neonates younger than 10 days had a higher survival rate (59.1%, p=0.005). Non-survivors were older on average (11.62 ± 6.18 days vs. 10.07 ± 5.06 days, p=0.01). While birth weight was comparable (p=0.13), admission weight was significantly lower in non-survivors (2.36 ± 0.38 kg vs. 2.51 ± 0.34 kg, p=0.01) as shown in Table 1.

Table 1: Comparative Analysis of demographic details among Survivors and Non-Survivors in Neonatal Sepsis (N=360)

Variable	Non-Survivors (n=164)	Survivors (n=196)	Total (N=360)	p-value
Gender				
Male	101 (61.6%)	81 (38.4%)	182 (50.6%)	0.686
Female	95 (53.4%)	83 (46.6%)	178 (49.4%)	0.686
Age category in days				
Age < 10 days	67 (40.9%)	129 (59.1%)	196 (54.4%)	0.005
Age ≥ 10 days	80 (48.8%)	84 (51.2%)	164 (45.6%)	0.005
Mean Age (days) ± SD	11.62 ± 6.18	10.07 ± 5.06	10.8 ± 5.6	0.01
Mean Birthweight (kg) ± SD	2.48 ± 0.30	2.53 ± 0.33	2.50 ± 0.31	0.13
Mean Weight on Admission (kg) ± SD	2.36 ± 0.38	2.51 ± 0.34	2.42 ± 0.36	0.01

In neonatal sepsis, presenting symptoms varied significantly between survivors and non-survivors (p<0.01) as shown in Table 2. Refusal to feed was more common among non-survivors (40.9% vs. 15.8%), while respiratory distress was more frequent in survivors (33.7% vs. 26.2%). Fever was significantly higher in survivors (29.6% vs. 14.6%). Gestational age distribution showed no significant difference (p=0.110), with most neonates born at 37±2 weeks. Birth classification based on weight was also similar between groups (p=0.549), with the majority being appropriate for gestational age (AGA).

Table 2: Comparative Analysis of Presenting Symptoms, Gestational Age, and Birth Classification among Survivors and Non-Survivors in Neonatal Sepsis (N=360)

Variable	Non-Survivors (n=164)	Survivors (n=196)	Total (N=360)	p-value
Presenting symptoms				
Convulsions	22 (13.4%)	26 (13.3%)	48 (13.3%)	**<0.01**
Hypoglycaemia	6 (3.7%)	14 (7.1%)	20 (5.6%)	
Refusal to feed	67 (40.9%)	31 (15.8%)	98 (27.2%)	
Respiratory distress	43 (26.2%)	66 (33.7%)	109 (30.3%)	
Severe dehydration	2 (1.2%)	0 (0.0%)	2 (0.6%)	
Fever	24 (14.6%)	58 (29.6%)	82 (22.8%)	
Loose stool	0 (0.0%)	1 (0.5%)	1 (0.3%)	
Gestational age				
36±2 weeks	2 (1.2%)	0 (0.0%)	2 (0.6%)	0.110
37±2 weeks	126 (76.8%)	168 (85.7%)	284 (78.9%)	
38±2 weeks	35 (21.3%)	28 (14.3%)	58 (16.1%)	
40±2 weeks	1 (0.6%)	0 (0.0%)	1 (0.3%)	
Weight based on gestational age				
AGA	123 (75.0%)	148 (75.5%)	271 (75.3%)	0.549
LGA	1 (0.6%)	0 (0.0%)	1 (0.3%)	
SGA	40 (24.4%)	48 (24.5%)	88 (24.4%)	

The comparison of physiological parameters between survivors and non-survivors in neonatal sepsis revealed notable differences as shown in Figure 1. Non-survivors had a lower mean heart rate (139.58 bpm) compared to survivors (150.22 bpm, p-value <0.03). Respiratory rate was also lower in non-survivors (54.87 vs. 59.85 breaths per minute, p-value <0.02). Oxygen saturation (SpO_2) was slightly higher in non-survivors (94.15% vs. 93.70%, p-value <0.12). However, mean body temperature was marginally lower in non-survivors (36.96°C) compared to survivors (37.08°C, p-value <0.25, Figure 1).

*Hear rate and respiratory rate were statistically significant – p-value<0.05

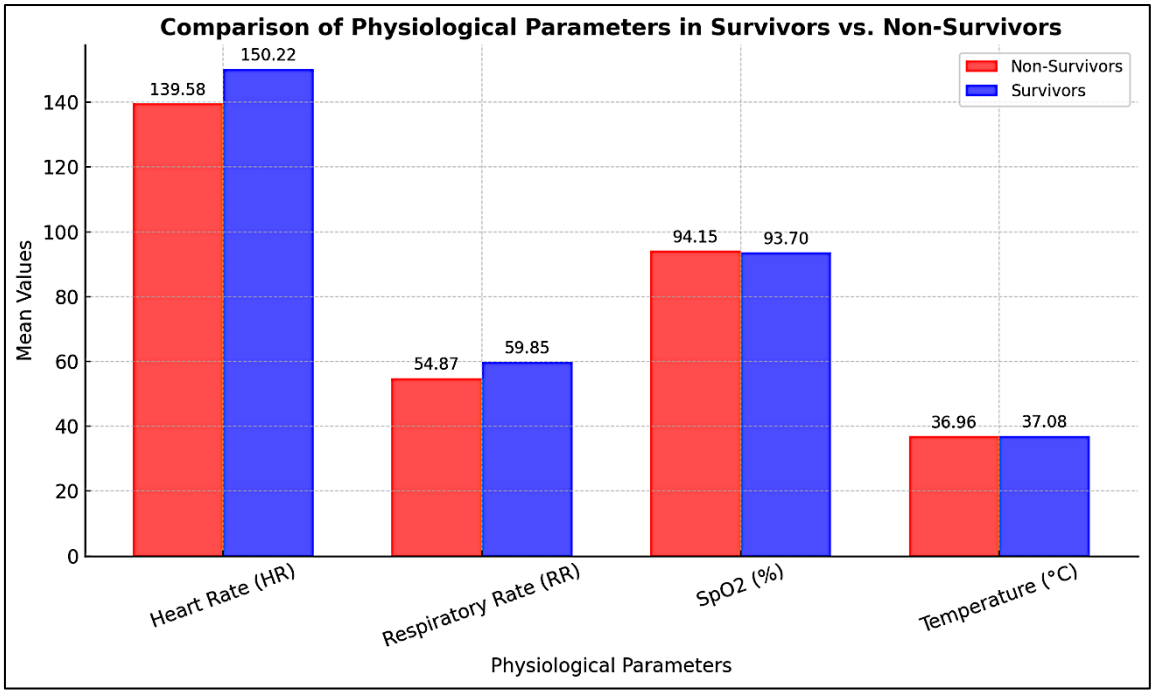

Figure 1: Comparison of physiological parameters among Survivors and Non-Survivors in Neonatal Sepsis

The comparison of laboratory parameters between survivors and non-survivors in neonatal sepsis revealed significant differences in key markers. Non-survivors had lower platelet counts (74,592.68 ± 44,683.63 vs. 101,192.2 ± 78,198.44/µL, p<0.01), higher CRP levels (46.54 ± 22.29 vs. 37.21 ± 13.08 mg/dL, p<0.01), higher urea (36.76 ± 23.20 vs. 26.55 ± 13.29 mg/dL, p<0.01), and higher creatinine (1.47 ± 0.83 vs. 1.22 ± 0.66 mg/dL, p=0.01), indicating greater systemic inflammation and renal dysfunction. Sodium levels were significantly higher in non-survivors (137.08 ± 9.08 vs. 134.13 ± 5.53 mEq/L, p=0.01), while pH was lower (7.21 ± 0.20 vs. 7.29 ± 0.12, p<0.01), suggesting metabolic acidosis. HCO3 was significantly lower in non-survivors (19.55 ± 10.14 vs. 24.99 ± 8.77 mEq/L, p<0.01), and lactate was markedly elevated (3.23 ± 2.99 vs. 1.97 ± 1.68 mmol/L, p<0.01), reflecting tissue hypoxia. Other parameters, including RBS, hemoglobin, AST, ALT, and pCO2, did not show significant differences as shown in Table 3.

Table 3: Comparison of Laboratory Parameters in Survivors and Non-Survivors of Neonatal Sepsis (N=360)

Laboratory Parameter	Non-Survivors (n=164) Mean ± SD	Survivors (n=196) Mean ± SD	p-value
RBS (mg/dL)	92.26 ± 37.86	93.95 ± 23.56	0.60
Hemoglobin (g/dL)	13.04 ± 3.23	13.58 ± 2.70	0.08
Total WBC Count (/cmm)	8100.30 ± 8003.76	10018.83 ± 9597.05	0.04
Platelet Count (/µL)	74592.68 ± 44683.63	101192.2 ± 78198.44	<0.01
CRP (mg/dL)	46.54 ± 22.29	37.21 ± 13.08	<0.01
Urea (mg/dL)	36.76 ± 23.20	26.55 ± 13.29	<0.01
Creatinine (mg/dL)	1.47 ± 0.83	1.22 ± 0.66	0.01
Sodium (mEq/L)	137.08 ± 9.08	134.13 ± 5.53	0.01
Potassium (mEq/L)	3.46 ± 1.01	3.39 ± 0.65	0.44
AST (U/L)	21.58 ± 10.59	20.08 ± 7.11	0.11
ALT (U/L)	55.20 ± 27.00	56.69 ± 26.48	0.59
S. Bilirubin (mg/dL)	11.24 ± 4.06	11.69 ± 4.01	0.29
pH	7.21 ± 0.20	7.29 ± 0.12	<0.01
pCO2 (mmHg)	30.32 ± 15.81	30.71 ± 9.71	0.77
pO2 (mmHg)	101.24 ± 42.12	101.29 ± 33.99	0.90
HCO3 (mEq/L)	19.55 ± 10.14	24.99 ± 8.77	<0.01
Lactate (mmol/L)	3.23 ± 2.99	1.97 ± 1.68	<0.01

The comparison of categorical laboratory parameters between survivors and non-survivors in neonatal sepsis revealed significant differences in key metabolic and renal markers. Low hemoglobin and low WBC count were more frequent in non-survivors (32.93% vs. 18.37%, p=0.02; 28.05% vs. 17.86%, p=0.02). Thrombocytopenia (low platelet count) was observed in 75.61% of non-survivors compared to 69.39% of survivors, but this difference was not statistically significant (p=0.19). Elevated urea levels were significantly associated with mortality (71.34% vs. 47.96%, p<0.01), as was high creatinine (64.02% vs. 49.49%, p=0.02), reflecting renal dysfunction in critically ill neonates. Sodium abnormalities were more common in non-survivors, with 14.63% exhibiting hyponatremia and 34.15% hypernatremia, compared to 2.04% and 29.59% in survivors (p<0.01). Acid-base imbalances were more prevalent in non-survivors, with metabolic acidosis in 59.76%, followed by respiratory acidosis in 16.46%, compared to 60.71% and 9.69% in survivors, respectively (p=0.01). Normal ABG findings were more frequent in survivors (19.39% vs. 11.59%) as shown in Table 3.

Table 3: Comparison of Laboratory Parameters in Survivors and Non-Survivors of Neonatal Sepsis (N=360)

Variable	Category	Non-Survivors (n=164) Frequency (%)	Survivors (n=196) Frequency (%)	p-value
Hemoglobin	Low	54 (32.93%)	36 (18.37%)	0.02
	Normal	110 (67.07%)	160 (81.63%)	
Total WBC	Low	46 (28.05%)	35 (17.86%)	0.02
	Normal	118 (71.95%)	161 (82.14%)	
Platelet Count	Low	124 (75.61%)	136 (69.39%)	0.19
	Normal	40 (24.39%)	60 (30.61%)	
Urea	High	117 (71.34%)	94 (47.96%)	<0.01
	Normal	47 (28.66%)	102 (52.04%)	
Creatinine	High	105 (64.02%)	97 (49.49%)	0.02
	Normal	59 (35.98%)	99 (50.51%)	
Sodium	Low	24 (14.63%)	4 (2.04%)	<0.01
	Normal	84 (51.22%)	132 (67.35%)	
	High	56 (34.15%)	58 (29.59%)	
ABG Analysis				
	Metabolic Acidosis	98 (59.76%)	119 (60.71%)	0.01
	Metabolic Alkalosis	6 (3.66%)	6 (3.06%)	
	Normal	19 (11.59%)	38 (19.39%)	
	Respiratory Acidosis	27 (16.46%)	19 (9.69%)	
	Respiratory Alkalosis	14 (8.54%)	14 (7.14%)	

The comparison of blood culture sensitivity results between survivors and non-survivors in neonatal sepsis revealed significant differences in bacterial isolates. Acinetobacter was significantly more prevalent in survivors (15.24% vs. 3.06%, p<0.01), suggesting a possible difference in response to treatment. CONS sepsis was the most frequent isolate in non-survivors (29.59% vs. 10.37%), while E. coli and Klebsiella showed similar distributions between the two groups (20.92% vs. 14.63% and 17.86% vs. 24.39%, respectively). MRSA was slightly higher in survivors (15.85% vs. 11.73%), while MSSA was more frequent in non-survivors (4.59% vs. 2.44%). Pseudomonas was also more commonly detected in survivors (13.41% vs. 9.69%). Enterococcus was identified only in survivors (0.61%), while Staph aureus sepsis was rare in both groups (1.02% vs. 1.22%).

The logistic regression analysis identified several laboratory parameters significantly associated with neonatal mortality as shown in Table 5. In the bivariate analysis, lower weight on admission (OR: 0.31, p<0.01), reduced total WBC count (OR: 0.96, p=0.033), lower platelet count (OR: 0.87, p<0.01), higher CRP (OR: 1.03, p<0.01), elevated urea (OR: 1.04, p<0.01), increased creatinine (OR: 1.58, p=0.002), higher sodium levels (OR: 1.06, p<0.01), and elevated lactate levels (OR: 1.26, p<0.01) were significantly associated with mortality. However, in the multivariate model, weight on admission (AOR: 0.48, p=0.04), total WBC count (AOR: 0.96, p=0.04), platelet count (AOR: 0.94, p=0.002), CRP (AOR: 1.03, p=0.03), urea (AOR: 1.03, p<0.01), and bicarbonate levels (AOR: 0.96, p=0.01) remained independently associated with neonatal mortality. Lower pH values were highly significant in bivariate analysis (OR: 0.05, p<0.01), but the adjusted model did not retain this association (AOR: 0.56, p=0.569). Parameters such as birth weight, creatinine, sodium, potassium, AST, ALT, bilirubin, and respiratory markers (pCO_2, pO_2) were not independently predictive of mortality as shown in Table 5.

Table 5: Bivariate and multivariate Logistic Regression analysis to find the laboratory parameters associated with neonatal mortality (N=360)

Variables	Crude Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)	p-value
Age in years	1.83 (1.20 - 2.81)	0.005	1.37 (0.84 - 2.26)	0.208
Male (Female as reference)	0.92 (0.61 - 1.39)	0.686	-	
Birth Weight (kg)	0.60 (0.31 - 1.18)	0.137		
Weight on Admission (kg)	0.31 (0.17 - 0.57)	<0.01	**0.48 (0.23 - 0.98)**	**0.04**
RBS (mg/dL)	0.99 (0.99 - 1.01)	0.606		
Hemoglobin (g/dL)	0.94 (0.87 - 1.01)	0.082		
Total WBC Count (/cubic mm)	0.96 (0.91 - 0.98)	0.033	**0.96 (0.93 – 0.98)**	**0.04**
Platelet Count (/microlitre)	0.87 (0.81 – 0.92)	<0.01	**0.94 (0.89 – 0.97)**	**0.002**
CRP (mg/dL)	1.03 (1.02 - 1.05)	<0.01	**1.03 (1.01 - 1.08)**	**0.03**
Urea (mg/dL)	1.04 (1.02 - 1.06)	<0.01	**1.03 (1.02 - 1.05)**	**<0.01**
Creatinine (mg/dL)	1.58 (1.18 - 2.10)	0.002	1.94 (0.65 - 1.36)	0.748
Sodium (mEq/L)	1.06 (1.03 - 1.09)	<0.01	1.00 (0.96 - 1.04)	0.855
Potassium (mEq/L)	1.10 (0.86 - 1.42)	0.446		
AST (U/L)	1.02 (0.99 - 1.05)	0.117		
ALT (U/L)	0.99 (0.99 - 1.01)	0.595		
S. Bilirubin (mg/dL)	0.97 (0.92 - 1.02)	0.292		
pH	0.05 (0.01 - 0.19)	<0.01	0.56 (0.08 - 4.08)	0.569
pCO2 (mmHg)	0.99 (0.98 - 1.01)	0.773	-	
pO2 (mmHg)	1.00 (0.99 - 1.01)	0.990	-	
HCO3 (mEq/L)	0.94 (0.92 - 0.96)	<0.01	**0.96 (0.93 - 0.99)**	**0.01**
Lactate (mmol/L)	1.26 (1.14 - 1.40)	<0.01	1.11 (0.97 - 1.26)	0.117

*p-value of <0.05 was included in the multivariate model.

IV. Discussion

The study aimed to identify laboratory predictors of mortality in neonatal septic shock by comparing survivors and non-survivors. The analysis revealed that lower weight on admission, reduced total WBC count, lower platelet count, elevated CRP, higher urea levels, and decreased bicarbonate levels were independently associated with neonatal mortality. Additionally, metabolic acidosis and elevated lactate levels were observed more frequently in non-survivors, highlighting the critical role of metabolic dysfunction in adverse outcomes.

This study emphasizes the importance of laboratory biomarkers in early identification and management of neonatal septic shock. Recognition of high-risk indicators—such as low platelets, elevated CRP, increased urea, metabolic acidosis, and high lactate levels—can guide clinicians toward timely interventions like targeted fluid therapy, appropriate antibiotics, and hemodynamic support. The prevalence of multidrug-resistant Acinetobacter and Klebsiella species highlights the necessity for robust antimicrobial stewardship and tailored antibiotic guidelines.(7) Integrating these laboratory predictors into clinical protocols can enhance early diagnosis, effective treatment escalation, and resource allocation, ultimately improving neonatal survival in intensive care settings.

Comparing with existing literature

The mortality rate in our study was 45.6%, which is relatively high compared to several previous studies on neonatal sepsis. Ogunlesi & Ogunfowora(8) (2010) reported a neonatal sepsis mortality rate of 28.3%, while Iqbal & Razzaq(9) (2022) found a lower rate of 33.1%. However, our findings align more closely with those of Saini et al.(10) (2021), who documented a mortality rate of 47.5% in cases of severe neonatal sepsis. The variation in mortality rates across studies may be attributed to differences in study populations, the severity of sepsis cases included, healthcare infrastructure, and early intervention strategies. Facilities with advanced neonatal intensive care units (NICUs), early sepsis screening, and aggressive antibiotic therapy tend to report lower mortality rates, whereas resource-limited settings with delayed referrals and inadequate supportive care often experience higher mortality. Additionally, the presence of multi-drug-resistant bacterial infections, variations in immune responses, and differences in the definitions used for sepsis severity may contribute to discrepancies in reported mortality rates across studies.

Our study found no significant difference in gender distribution between survivors and non-survivors (p=0.686), similar to the findings of Ogunlesi & Ogunfowora(8) (2010), who reported that gender was not a predictor of neonatal sepsis mortality. However, neonates younger than 10 days had a significantly higher survival rate (p=0.005), which aligns with the study by Vizcarra-Jiménez et al.(11) (2022), indicating that mortality risk increases with age, possibly due to the delayed immune response development in neonates older than 10 days. This is biologically plausible as younger neonates still benefit from maternal antibodies and have a relatively intact adaptive immune response, whereas older neonates exhibit waning passive immunity and increased susceptibility to severe infections.(12)

Admission weight was significantly lower in non-survivors (p=0.01), consistent with studies indicating that lower birth and admission weights are risk factors for sepsis-related mortality (Saini et al., 2021(10)). Low admission weight may indicate pre-existing malnutrition, impaired immune function, and an increased risk of complications during infection. Neonates with low weight often have underdeveloped organs, particularly the liver and kidneys, which play critical roles in immune defense and toxin clearance, making them more vulnerable to systemic infections and metabolic imbalances.

Significant differences were observed in presenting symptoms, with non-survivors exhibiting higher rates of feeding refusal (40.9% vs. 15.8%, p<0.01) and respiratory distress being more common among survivors (33.7% vs. 26.2%). This corresponds with Chen et al.(13) (2020), who found that feeding difficulty and respiratory distress are early markers of poor prognosis in neonatal sepsis. Feeding refusal may indicate severe systemic infection, with metabolic derangements affecting gastrointestinal function and energy utilization. Conversely, a higher incidence of respiratory distress in survivors suggests that early intervention and mechanical support may improve outcomes in neonates with respiratory involvement.(14)

The higher fever incidence among survivors (29.6% vs. 14.6%) suggests that febrile response may be a positive prognostic indicator, reflecting an intact immune response. Studies such as that by Mannan & Jahan(15) (2022) have shown that neonates with hypothermia rather than fever often have poorer outcomes, as hypothermia signifies an overwhelming systemic infection leading to immune suppression and metabolic failure.

Our study found that non-survivors exhibited significantly lower platelet counts (p<0.01) and total WBC counts (p=0.04). These findings align with Ahmed & Ahmad(16) (2015), who reported that thrombocytopenia and leukopenia indicate severe sepsis and a dysfunctional immune response. Platelet dysfunction in sepsis is associated with disseminated intravascular coagulation (DIC) and endothelial damage, contributing to multi-organ failure. Sepsis-induced thrombocytopenia results from excessive platelet consumption, bone marrow suppression, and increased destruction due to cytokine-mediated endothelial activation and coagulation abnormalities.(17)

Elevated CRP levels were significantly associated with mortality (p<0.01), supporting the work of Wang & Tian(18) (2021), who found that CRP is a robust predictor of sepsis severity. CRP, an acute-phase reactant, is upregulated in response to inflammatory cytokines and reflects systemic inflammation and tissue injury. The excessive inflammatory cascade in non-survivors suggests a dysregulated immune response, where excessive cytokine production leads to endothelial injury, capillary leakage, and shock.(19) Non-survivors had significantly elevated urea (p<0.01) and creatinine levels (p=0.01), indicating acute kidney injury (AKI), a common complication of sepsis. Similar findings were reported by Iqbal & Razzaq(9) (2022), highlighting that renal dysfunction due to hypoperfusion and inflammatory cytokine-mediated kidney injury worsens sepsis outcomes. Renal dysfunction in sepsis is primarily driven by decreased renal perfusion, oxidative stress, and inflammatory-mediated tubular injury, leading to fluid and electrolyte imbalances that further complicate metabolic homeostasis.

Sodium levels were significantly higher in non-survivors (p=0.01), with more cases of hypernatremia. Hypernatremia in sepsis often results from dehydration, impaired renal function, and dysregulated antidiuretic hormone secretion. The inability to regulate sodium homeostasis contributes to increased osmolarity, leading to cellular dehydration, neurological impairment, and worsening cardiovascular instability in critically ill neonates.(20) Non-survivors had significantly lower pH levels (p<0.01) and bicarbonate (p<0.01), indicative of metabolic acidosis, consistent with Hisamuddin & Azlan(21) (2012). Metabolic acidosis in sepsis arises from lactic acidosis due to impaired tissue perfusion and anaerobic metabolism, a key indicator of poor prognosis. Elevated lactate levels in non-survivors (3.23 ± 2.99 vs. 1.97 ± 1.68 mmol/L, p<0.01) emphasize tissue hypoxia as a central driver of sepsis mortality. This aligns with multiple studies (Mannan & Jahan, 2022(15)), where lactate clearance is proposed as a more reliable predictor of sepsis outcomes than initial lactate levels. Lactic acidosis reflects mitochondrial dysfunction and inadequate oxygen delivery, leading to cellular damage and irreversible organ failure.

Strengths and limitations

This study has several strengths, including its well-defined cohort of neonates with sepsis, a comprehensive analysis of both clinical and laboratory parameters, and the use of multivariate regression to identify independent predictors of mortality. The inclusion of key metabolic and hematological markers enhances the study's relevance for clinical practice, allowing for early risk stratification and targeted interventions. However, certain limitations must be acknowledged. The study was conducted at a single center, which may limit the generalizability of findings to broader neonatal populations. Additionally, the observational design precludes causal inference, and potential residual confounders, such as treatment variations and comorbid conditions, may have influenced outcomes. Future multicenter studies with larger sample sizes and prospective validation of identified predictors are needed to strengthen the applicability of these findings.

V. Conclusion

This study highlights critical predictors of neonatal mortality in sepsis, emphasizing the role of early identification and targeted management. Key findings indicate that lower admission weight, thrombocytopenia, elevated CRP, urea, and metabolic acidosis are significant independent predictors of mortality. The predominance of CONS sepsis in non-survivors and the higher prevalence of Acinetobacter in survivors suggest the need for tailored antibiotic stewardship. Based on these findings, we recommend routine screening of neonates with sepsis for early markers of systemic inflammation and metabolic dysfunction, such as CRP, platelet count, and lactate levels, to guide timely interventions. Additionally, weight-based risk stratification at admission and close monitoring of neonates with metabolic acidosis should be prioritized. Future research should focus on the development of predictive models integrating clinical and laboratory parameters to enhance neonatal sepsis management and improve survival outcomes.

References

[1]. Singh M, Alsaleem M, Gray CP. Neonatal Sepsis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 [cited 2024 Oct 5]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK531478/

[2]. Mahapatra S, Heffner AC. Septic Shock. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Mar 15]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK430939/

[3]. Sharma AA, Jen R, Butler A, Lavoie PM. The developing human preterm neonatal immune system: A case for more research in this area. Clin Immunol Orlando Fla. 2012 Oct;145(1):61–8.

[4]. Boscarino G, Migliorino R, Carbone G, Davino G, Dell'Orto VG, Perrone S, et al. Biomarkers of Neonatal Sepsis: Where We Are and Where We Are Going. Antibiotics. 2023 Jul 26;12(8):1233.

[5]. Gude SS, Peddi NC, Vuppalapati S, Venu Gopal S, Marasandra Ramesh H, Gude SS. Biomarkers of Neonatal Sepsis: From Being Mere Numbers to Becoming Guiding Diagnostics. Cureus. 14(3):e23215.

[6]. Li Z, Wang H, Liu J, Chen B, Li G. Serum Soluble Triggering Receptor Expressed on Myeloid Cells-1 and Procalcitonin Can Reflect Sepsis Severity and Predict Prognosis: A Prospective Cohort Study. Mediators Inflamm. 2014;2014:641039.

[7]. Wenzler E, Goff DA, Humphries R, Goldstein EJC. Anticipating the Unpredictable: A Review of Antimicrobial Stewardship and Acinetobacter Infections. Infect Dis Ther. 2017 Jun;6(2):149–72.

[8]. Ogunlesi TA, Ogunfowora OB. Predictors of Mortality in Neonatal Septicemia in an Underresourced Setting. J Natl Med Assoc. 2010 Oct;102(10):915–22.

[9]. Iqbal M, Razzaq A, Malik FA, Ali M, Imran M, Shehzadi M. Association of Lactate Clearance with Morbidity and Mortality in Neonates with Sepsis and Septic Shock at RECEP Tayyip Erdogan Hospital Muzaffargarh. Pak J Med Health Sci. 2022 Oct 30;16(10):471–3.

[10]. Saini SS, Shrivastav AK, Kumar J, Sundaram V, Mukhopadhyay K, Dutta S, et al. Predictors of Mortality in Neonatal Shock: A Retrospective Cohort Study. Shock. 2022 Feb;57(2):199–204.

[11]. Vizcarra-Jiménez D, Copaja-Corzo C, Hueda-Zavaleta M, Parihuana-Travezaño EG, Gutierrez-Flores M, Rivarola-Hidalgo M, et al. Predictors of Death in Patients with Neonatal Sepsis in a Peruvian Hospital. Trop Med Infect Dis. 2022 Oct 31;7(11):342.

[12]. Niewiesk S. Maternal Antibodies: Clinical Significance, Mechanism of Interference with Immune Responses, and Possible Vaccination Strategies. Front Immunol. 2014 Sep 16;5:446.

[13]. Chen J, Yu JL. Predictive factors for poor prognosis of neonates with early-onset sepsis. Zhongguo Dang Dai Er Ke Za Zhi. 2020 Feb;22(2):146-151. Chinese.

[14]. Yadav S, Lee B. Neonatal Respiratory Distress Syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2025 Mar 17]. Available from: http://www.ncbi.nlm.nih.gov/books/NBK560779/

[15]. Mannan MA, Jahan MA, Hossain MA, Shuma AI, Moni SC, Jahan I, et al. Septic Shock in Neonate: Clinical Profile and its Outcome. [cited 2025 Mar 17]; Available from: https://www.fortunejournals.com/articles/septic-shock-in-neonate-clinical-profile-and-its-outcome.html

[16]. Ahmed A, Ahmad I, Ahmad S, Iqbal J, Din WN, Bashir Y, et al.Hematological and biochemical predictors of mortality in neonatalsepsis. Natl J Med Res 2015;5:169-73.

[17]. Iba T, Watanabe E, Umemura Y, Wada T, Hayashida K, Kushimoto S, et al. Sepsis-associated disseminated intravascular coagulation and its differential diagnoses. J Intensive Care. 2019 May 20;7:32.

[18]. Wang Y, Tian JH, Yang XF, Li SX, Guo JY. Predictive value of lactate concentration combined with lactate clearance rate in the prognosis of neonatal septic shock. Zhonghua Er Ke Za Zhi. 2021 Jun 2;59(6):489-494. Chinese.

[19]. Jarczak D, Nierhaus A. Cytokine Storm—Definition, Causes, and Implications. Int J Mol Sci. 2022 Oct 3;23(19):11740.

[20]. Sonani B, Naganathan S, Al-Dhahir MA. Hypernatremia. In StatPearls Publishing; 2023 [cited 2025 Mar 17]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK441960/

[21]. Hisamuddin NA, Azlan K. The use of laboratory and physiological parameters in predicting mortality in sepsis induced hypotension and septic shock patients attending the emergency department. Med J Malaysia. 2012 Jun;67(3):259-64.