DOI: https://doi.org/10.54393/pjhs.v5i10.2424

PAKISTAN JOURNAL OF HEALTH SCIENCES
(LAHORE)
https://thejas.com.pk/index.php/pjhs
ISSN (P): 2790-9352, (E): 2790-9344
Volume 5, Issue 10 (October 2024)

Original Article

OPEN ACCESS

Early Blood Pressure Changes in Neonatal Sepsis and the Risk of Mortality

Kamran Ali[1*], Tayyaba Haque[1], Ubedullah Bahalkani[1], Bakhtiar Ahmed Bhanbhro[2], Mumtaz Ali Bharo[3] and Faiza Kamran Ali[4]

[1]Department of Pediatrics, Khairpur Medical College, Hospital Khairpur Mir's, Khairpur, Pakistan
[2]Department of Pediatrics, Pir Abdul Qadir Shah Jillani Institute of Medical Science, Gambat, Pakistan
[3]Department of Pediatrics, Ghulam Muhammad Mahar Medical College, Sukkur, Pakistan
[4]Department of Gynecology, Rural Health Centre Atta Muhammad Hami, Khairpur, Pakistan

ARTICLE INFO

Keywords:
Blood Pressure, Neonatal Septic, Mortality Rate, Newborns

How to Cite:
Ali, K., Haque, T., Bahalkani, U., Bhanbhro, B. A., Bharo, M. A., & Ali, F. K. (2024). Early Blood Pressure Changes in Neonatal Sepsis and the Risk of Mortality: Early Blood Pressure Changes in Neonatal Sepsis and Mortality. Pakistan Journal of Health Sciences, 5(10). https://doi.org/10.54393/pjhs.v5i10.2424

***Corresponding Author:**
Kamran Ali
Department of Pediatrics, Khairpur Medical College, Hospital Khairpur Mir's, Khairpur, Pakistan
ga.shahani@gmail.com

Received Date: 7th September, 2024
Acceptance Date: 24th October, 2024
Published Date: 31st October, 2024

ABSTRACT

Neonatal sepsis is an increasingly common cause of mortality and morbidity in newborns, with hemodynamic abnormalities impacting prognosis. **Objectives:** To evaluate the relationship between blood pressure levels and in-hospital mortality rate in newborns with sepsis. **Methods:** The comparative cross-sectional study was conducted for six months from August 2023 to January 2024 at the Department in the Neonatal Intensive Care Unit of Khairpur Medical College to Khairpur Mir's Medical College Teaching Hospital. The total number of participants was n=300 (n=150 participants per group). Blood pressure was monitored at three different periods: 0-24 hours, 24-48 hours, and 48-72 hours. Data were analyzed using t-test independent, chi-square and multivariable logistic regression to assess the association between blood pressure parameters and in-hospital mortality. **Results:** Our findings indicated that lower systolic, diastolic, and mean blood pressures at all measured time points were closely linked to higher mortality rates in newborns. At 72 hours, culture-positive infants had a median systolic blood pressure of 64 mmHg, while those with clinical signs had a median of 70 mmHg (p=0.008). Each unit's reduction in blood pressure corresponded to a significant increase in the risk of death. **Conclusions:** It was concluded that neonates with sepsis had lower mean, diastolic, and systolic blood pressures have a higher mortality rate in hospitals which shows that sepsis with positive culture has a higher risk of severe hemodynamic instability when compared to sepsis with clinical signs.

INTRODUCTION

Neonatal sepsis poses a significant clinical challenge, contributing to neonatal morbidity and mortality globally. Timely detection and intervention are vital for improving outcomes in affected infants. Traditionally, clinical signs such as temperature instability, feeding difficulties, and respiratory distress have been relied upon for sepsis detection [1, 2]. However, these signs can be non-specific and may not manifest until the disease is advanced. Although less emphasised, blood pressure (BP) changes could serve as an early and sensitive indicator of disease progression in neonatal sepsis. Delayed identification of sepsis is a primary contributor to neonatal mortality [3, 4]. While BP is monitored continuously in the early days post-delivery and during critical illness, vital signs such as heart rate (HR), respiratory rate (RR), and pulse oximetry (SpO2) are also tracked throughout the hospital stay [5, 6]. Temperature is another important variable, though its measurement can be challenging due to external heat sources. Variations in vital signs often indicate normal physiological patterns but can also signify pathological decompensation [7, 8]. Clinical indicators and culture results are crucial for tracking sepsis progression in newborns. Abnormal temperature, delayed capillary refill time, and skin changes can suggest deterioration. Laboratory data, including white blood cell counts and C-reactive protein levels, provide insights into the inflammatory response and potential organ failure [9]. Positive blood cultures confirm the presence of microorganisms, essential for appropriate antibiotic therapy. The timely collection and analysis of these

DOI: https://doi.org/10.54393/pjhs.v5i10.2424

cultures, combined with ongoing clinical assessments, are critical for monitoring sepsis progression [10]. Focusing on BP changes, particularly hypotension, has been recognized as a critical marker of illness severity in neonates with sepsis. Early BP alterations may reflect underlying circulatory instability, making it a valuable early indicator of sepsis severity and mortality risk. By emphasizing BP changes, healthcare providers can implement quicker therapeutic interventions, potentially enhancing survival rates.

This study aimed to evaluate the relationship between blood pressure levels and the in-hospital mortality rate in newborns with sepsis.

METHODS

This comparative cross-sectional study was conducted in the Neonatal Intensive Care Unit (NICU) at Khairpur Mir's Medical College Teaching Hospital over six months, from August 2023 to January 2024. The inclusion criteria encompassed neonates diagnosed with sepsis through positive blood cultures and confirmed clinical signs, aged≤72 hours at diagnosis. Exclusion criteria included congenital heart defects, pre-existing hypertension, and other complications. The sample size was calculated to analyze the correlation between categorical variables, specifically survival and blood pressure fluctuations. Using the formula, n=(Zα/2+Zβ)2·[p1(1–p1) + p2(1–p2)] (p1–p2)2= where, for Zα/2=1.96 to get a 95% confidence level. Zβ=0.84 should be used for 80% power, a total of 300 participants were recruited, with 150 in each group (culture-positive sepsis and Clinical Sign Positive) [11]. Blood pressure was measured non-invasively every three hours for the first 72 hours. A positive sepsis screen required at least two indicators: elevated procalcitonin levels, increased total leukocyte or absolute neutrophil counts, and C-reactive protein levels >10 mg/L. Infant mortality was defined as the percentage of neonates who died during hospitalization. A stratified random sampling technique ensured representation across key demographic groups. Data were analyzed using SPSS version 23.0, employing multivariable logistic regression and Chi-square test to assess the association between early blood pressure changes and mortality risk, adjusting for birth weight and gestational age. The study received approval from the Institutional Review Board (KMC/RERC/82), with informed consent obtained from parents or guardians before enrollment.

RESULTS

A comparison of clinical and demographic features revealed similar profiles for newborns with clinical sign-positive and culture-positive neonatal sepsis, with mean ages of 10.5 days and 11.0 days, respectively (p>0.005). However, significant differences were found in the mode of delivery (60.0% vaginal births in culture-positive vs. 46.7% in clinical sign-positive; p<0.02) and sepsis onset (60.0% early onset in culture-positive vs. 40.0% in clinical sign-positive; p=0.04). Apgar scores did not differ significantly at 1 minute (7.0 vs. 6.8) or 5 minutes (8.5 vs. 8.3)(p=0.25 and p=0.35). Overall, demographic parameters were consistent, with notable variations in delivery method and sepsis onset in table 1.

Table 1: Demographic Characteristics of study participants

Demographic Characteristics	Culture-Positive Neonatal Sepsis (n=150)	Clinical Sign Positive Neonatal Sepsis (n=150)	p-Value
Age (Days)	10.5 ± 5.2	11.0 ± 6.1	0.45
Gestational Age (Weeks)	34.2 ± 2.5	34.0 ± 2.8	0.30
Birth Weight (Grams)	2100 ± 400	2050 ± 450	0.15
Sex			
- Male: n (%)	85 (56.7%)	78 (52.0%)	0.60
- Female: n (%)	65 (43.3%)	72 (48.0%)	
Maternal Age (Years)	28.0 ± 5.1	27.5 ± 4.8	0.55
Delivery Method			
- Vaginal: n (%)	90 (60.0%)	70 (46.7%)	0.02
- Cesarean: n (%)	60 (40.0%)	80 (53.3%)	
Apgar Score (1 min)	7.0 ± 1.5	6.8± 1.4	0.25
Apgar Score (5 min)	8.5 ± 1.0	8.3± 1.1	0.35
Sepsis Onset			
- Early Onset: n (%)	90 (60.0%)	60 (40.0%)	0.04
- Late Onset: n (%)	60 (40.0%)	90 (60.0%)	
Sepsis Onset			
- Fever: n (%)	70 (46.7%)	60 (40.0%)	0.45
- Poor Feeding: n (%)	80 (53.3%)	70 (46.7%)	0.15
- Respiratory Distress: n (%)	60 (40.0%)	65 (43.3%)	0.65
- Jaundice: n (%)	50 (33.3%)	55 (36.7%)	0.75
- Other: n (%)	30 (20.0%)	40 (26.7%)	0.35

In the first 24 hours, neonates with culture-positive sepsis had a median systolic blood pressure of 64 mmHg (IQR: 58, 72), compared to 69 mmHg (IQR: 63, 75) for those with clinical sign-positive sepsis (p=0.031). Non-survivors showed a significantly lower median of 60 mmHg (IQR: 55, 65) versus 70 mmHg (IQR: 65, 75) for survivors (p=0.001), with an unadjusted odd ratio (OR) for mortality of 0.45 (95% CI: 0.30, 0.68, p=0.001). By 48–72 hours, the median systolic blood pressure for non-survivors dropped to 64 mmHg (IQR: 59, 69), while survivors had 74 mmHg (IQR: 70, 78), and the unadjusted OR for mortality was 0.35 (95% CI: 0.22, 0.57, p=0.001) in table 2.

DOI: https://doi.org/10.54393/pjhs.v5i10.2424

Table 2: Assess the Relationship Between Neonatal Patients' SBP and In-Hospital Mortality by Comparing the Sepsis of Neonates with Both Clinical Sign Positive and Culture Positive Sepsis

Time Epochs	Culture-Positive Neonatal Sepsis	Clinical Sign Positive Neonatal Sepsis	p-value	Non-Survivors (n=90)	Survivors (n=210)	p-value	Unadjusted OR	95% CI (Lower, Upper)	p-value	Adjusted OR	95% CI (Lower, Upper)	p-value
0-24 hours	64 (58, 72)	69 (63, 75)	0.031	60 (55, 65)	70 (65, 75)	0.001	0.45	0.30, 0.68	0.001	0.50	0.30, 0.85	0.008
24-48 hours	69 (63, 75)	74 (68, 80)	0.025	62 (57, 67)	72 (68, 76)	0.002	0.40	0.25, 0.63	0.001	0.45	0.25, 0.80	0.007
48-72 hours	74 (68, 80)	79 (73, 85)	0.020	64 (59, 69)	74 (70, 78)	0.003	0.35	0.22, 0.57	0.001	0.40	0.22, 0.75	0.006

In newborns with culture-positive sepsis, the median diastolic blood pressure (DBP) during the first 24 hours was 36 mmHg, compared to 38 mmHg for those with clinical sign-positive sepsis (p=0.045). Non-survivors had a median DBP of 34 mmHg, significantly lower than the 40 mmHg in survivors (p=0.002). The unadjusted odds ratio (OR) for mortality was 0.45, indicating that decreased DBP significantly increases the risk of death. By 24-48 hours, median DBP rose to 38 mmHg for culture-positive cases and 40 mmHg for clinical sign-positive cases (p=0.038). In the 48–72-hour period, non-survivors continued to have lower DBP (38 mmHg) compared to survivors (44 mmHg), highlighting the correlation between higher DBP and better survival outcomes in table 3.

Table 3: Compare the Sepsis of Neonates with Both Clinically and Culture-Positive Sepsis, and Link DBP to Neonatal Patient Death in the Hospital

Time Epochs	Culture-Positive (n=150)	Clinical Sign Positive (n=150)	p-value (DBP)	Non-Survivors (n=90)	Survivors (n=210)	p-value (Survivors vs. Non-Survivors)	Unad justed OR	95% CI (Lower, Upper)	p-value (Unadjusted)	Adjusted OR	95% CI (Lower, Upper)	p-value (Adjusted)
0-24 hours	36 (32, 40)	38 (34, 42)	0.045	34 (30, 38)	40 (36, 44)	0.002	0.45	0.30, 0.70	0.001	0.50	0.30, 0.85	0.008
24-48 hours	38 (34, 42)	40 (36, 44)	0.038	36 (32, 40)	42 (38, 46)	0.001	0.40	0.25, 0.63	0.001	0.45	0.25, 0.80	0.007
48-72 hours	40 (36, 44)	42 (38, 46)	0.030	38 (34, 42)	44 (40, 48)	0.001	0.35	0.22, 0.57	0.001	0.40	0.22, 0.75	0.006

The bar graph provides a cleaner visual comparison of mean blood pressure in different neonatal sepsis groups and mortality outcomes across the time epochs in figure 1.

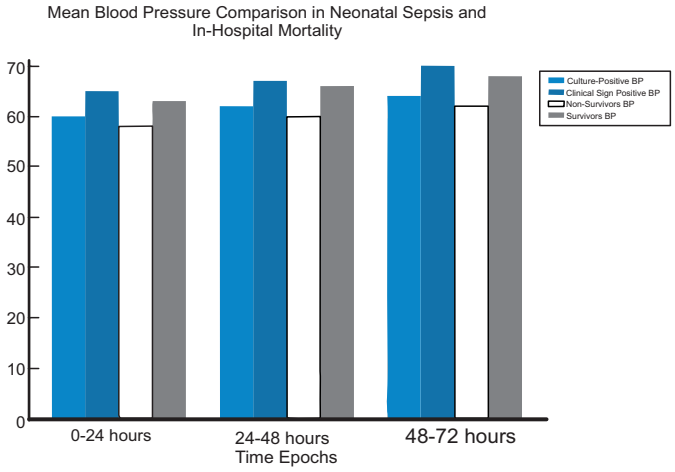

Figure 1: Visual Comparison of Mean Blood Pressure in Different Neonatal Sepsis Groups and Mortality Outcomes across the Time Epochs

The Culture-positive group has a higher mortality rate (30%) compared to the Clinical Sign group (20%), indicating a greater risk of severe hemodynamic instability associated with culture-positive sepsis see in table 4

Table 4: Risk of Mortality among Study Participants

Characteristic	Culture-Positive Neonatal Sepsis (n=150)	Clinical Sign Positive Neonatal Sepsis (n=150)	Total (n=300)
Number of Deaths (D)	45	30	75
Mortality Rate (%)	30%	20%	25%

DISCUSSION

To gain a better understanding of the relationship between blood pressure (BP) and newborn sepsis, this study looks at blood pressure values at the 72-hour mark, including the mean, diastolic, and systolic parameters. Additionally, in newborns with culture-positive and clinical sign-positive sepsis, we looked into the relationship between blood pressure trends and in-hospital mortality [11]. Our results, which show substantial differences in blood pressure levels throughout the two groups' lives, suggest that blood pressure is a crucial marker of mortality risk in sepsis-affected newborns. Clinical sign-positive sepsis is less likely to have this because the immune system may be able to control the infection better or because the infection may not have fully entered the bloodstream [12]. In the current study, to evaluate blood pressure patterns between newborns with clinical indications of sepsis and those with culture-positive sepsis, we computed BP Z-scores during 72 hours. During the initial 24-hour period, infants with positive cultures exhibited notably reduced systolic, diastolic, and mean blood pressure readings in contrast to those with clinical signs. For 48 and 72 hours, this pattern continued [13]. Even though it was small, this difference was statistically significant, indicating that sepsis in instances with positive cultures is more severe [14]. This

DOI: https://doi.org/10.54393/pjhs.v5i10.2424

finding corresponds to Celik *et al.*, which showed that sepsis with a positive culture typically indicates a higher bacterial load or a more invasive infection, leading to a more serious systemic inflammatory response and an increased risk of sepsis [15]. In this study, the results are consistent with the higher in-hospital mortality observed in other studies that show a correlation between lower systolic blood pressure (SBP) in the early stages of newborn sepsis [16]. Anti-inflammatory cytokines are elevated in the early stages of sepsis, causing widespread vasodilation and capillary leakage. We agreed with the previous study by Zhu *et al.*, which showed that despite cases in which damage to organs had not become readily apparent, the occurrence of hypotension during the first 24 hours of sepsis in pediatric patients significantly raised the risk of mortality [17]. The current study found that lower diastolic blood pressure (DBP) is related to an increased risk of in-hospital death in infant sepsis patients. Maintaining diastolic blood pressure is crucial for maintaining overall organ perfusion as well as coronary perfusion during cardiac relaxation [18]. Sepsis is caused by a higher level of inflammation which ends up in extensive vasodilation, mainly caused by cytokines, which cause a significant decrease in diastolic blood pressure. We were supported by Lee *et al.*, 2024, study showed the relationship between prolonged hypotension, particularly low DBP, and higher mortality in septic newborns [19]. Lower mean blood pressure (MBP) in the early stages of sepsis is a strong predictor of in-hospital mortality [20]. While the study contributes valuable insights into the association between early blood pressure changes and mortality risk in neonatal sepsis, these limitations and potential biases must be acknowledged and addressed in future research to strengthen the findings and improve clinical practice. Implementing a protocol for continuous or frequent non-invasive blood pressure monitoring in neonates, particularly those at high risk for sepsis, can facilitate early detection of hemodynamic instability. This could enable timely interventions and improve outcomes.

CONCLUSIONS

It was concluded that neonates with sepsis had a lower mean, diastolic, and systolic blood pressure have a higher mortality rate in hospitals. The significance of promptly identifying and treating septic neonates is highlighted by our findings, which show that sepsis with positive culture has a higher risk of severe hemodynamic instability when compared to sepsis with visible clinical signs.

Authors Contribution

Conceptualization: KA
Methodology: KA, TH, UB, BAB
Formal analysis: TH, FKA
Writing review and editing: MAB, FKA
All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

All the authors declare no conflict of interest.

Source of Funding

The author received no financial support for the research, authorship and/or publication of this article.

REFERENCES

[1] Yadav P and Yadav SK. Progress in Diagnosis and Treatment of Neonatal Sepsis: A Review Article. Journal of the Nepal Medical Association. 2022 Mar; 60(247): 318. doi: 10.31729/jnma.7324.

[2] Odabasi IO and Bulbul A. Neonatal sepsis. The Medical Bulletin of Sisli Etfal Hospital.2020; 54(2): 142-58. doi : 10.14744/SEMB.2020.00236.

[3] Eichberger J, Resch E, Resch B. Diagnosis of Neonatal Sepsis: The Role of Inflammatory Markers. Frontiers in Pediatrics.2022Mar;10:840288.doi: 10.3389/fped.2022.840288.

[4] Shoukry LR, Mohamed AN, Sharaf AE, Osman OB. Diagnostic Markers for Early Detection of Neonatal Sepsis. Journal of Scientific Research in Medical and Biological Sciences. 2021 Aug; 2(3): 13-26. doi: 10.47631/jsrmbs.v2i3.319.

[5] Russell N, Barday M, Okomo U, Dramowski A, Sharland M, Bekker A. Early-versus Late-Onset Sepsis in Neonates–Time to Shift the Paradigm? Clinical Microbiology and Infection.2024 Jan; 30(1): 38-43. doi: 10.1016/j.cmi.2023.07.023.

[6] Strunk T, Molloy EJ, Mishra A, Bhutta ZA. Neonatal Bacterial Sepsis. The Lancet. 2024 Jul; 404(10449): 277-93. doi: 10.1016/S0140-6736(24)00495-1.

[7] Al Maamari S, Al Shammakhi S, Alghamari I, Jabbour J, Al-Jawaldeh A. Young Children Feeding Practices: An Update from the Sultanate of Oman. Children. 2021 Sep; 8(9): 818. doi: 10.3390/children8090818.

[8] Plata-Menchaca EP, Ruiz-Rodríguez JC, Ferrer R. Early diagnosis of Sepsis: the role of biomarkers and Rapid Microbiological tests. InSeminars in Respiratory and Critical Care Medicine 2024 Jul 1. Thieme Medical Publishers, Inc. doi: 10.1055/s-0044-1787270.

[9] Kurul Ş, Simons SH, Ramakers CR, De Rijke YB, Kornelisse RF, Reiss IK *et al*. Association of Inflammatory Biomarkers with Subsequent Clinical Course in Suspected Late-Onset Sepsis in Preterm Neonates. Critical Care. 2021 Dec; 25: 1-0. doi: 10.1186/s13054-020-03423-2.

[10] Chen X, He H, Wei H, Chen F, Hu Y. Risk Factors for Death Caused by Early Onset Sepsis in Neonates: A Retrospective Cohort Study. BioMed Central Infectious Diseases.2023 Nov; 23(1): 844. doi: 10.1186/s12879-023-08851-3.

DOI: https://doi.org/10.54393/pjhs.v5i10.2424

[11] Dong Y, Basmaci R, Titomanlio L, Sun B, Mercier JC.Neonatal Sepsis: Within and Beyond China. Chinese Medical Journal. 2020 Sep; 133(18): 2219-28. doi: 10.1097/CM9.0000000000000935.

[12] Bazaid AS, Aldarhami A, Gattan H, Barnawi H, Qanash H, Alsaif G *et al*. Antibiogram of Urinary Tract Infections and Sepsis among Infants in Neonatal Intensive Care Unit. Children.2022 Apr; 9(5): 629. doi: 10.3390/children9050629.

[13] Wentowski C, Ingles DP, Nielsen ND. Sepsis 2021: A Review. Anaesthesia & Intensive Care Medicine. 2021 Nov; 22(11): 676-84. doi: 10.1016/j.mpaic.2021.10.001.

[14] Saini SS, Shrivastav AK, Sundaram V, Dutta S, Kumar P. Early Blood Pressure Changes in Neonatal Sepsis and the Risk of Mortality. Indian Journal of Pediatrics. 2023 Nov; 90(11): 1096-102. doi: 10.1007/s12098-023-04597-7.

[15] Celik IH, Hanna M, Canpolat FE, Pammi M. Diagnosis of Neonatal Sepsis: The Past, Present and Future. Pediatric Research.2022 Jan; 91(2): 337-50. doi: 10.1038/s41390-021-01696-z.

[16] Rhee C, Chiotos K, Cosgrove SE, Heil EL, Kadri SS, Kalil AC *et al*. Infectious Diseases Society of America Position Paper: Recommended Revisions to the National Severe Sepsis and Septic Shock Early Management Bundle (SEP-1) Sepsis Quality Measure. Clinical Infectious Diseases.2021 Feb; 72(4): 541-52. doi: 10.1093/cid/ciaa059.

[17] Zhu F, Baczynski M, Kharrat A, Ye XY, Weisz D, Jain A. Blood Pressure, Organ Dysfunction, and Mortality in Preterm Neonates with Late-Onset Sepsis. Pediatric Research.2022 Aug; 92(2): 498-504. doi: 10.1038/s41390-021-01768-0.

[18] Gorantiwar S and de Waal K. Progression from Sepsis to Septic Shock and Time to Treatments in Preterm Infants with Late-Onset Sepsis. Journal of Pediatrics and Child Health. 2021 Dec; 57(12): 1905-11. doi: 10.1111/jpc.15606.

[19] Lee EP, Yen CW, Hsieh MS, Lin JJ, Chan OW, Su YT *et al*. Diastolic Blood Pressure Impact on Pediatric Refractory Septic Shock Outcomes. Pediatrics & Neonatology.2024 May; 65(3): 222-8. doi: 10.1016/j.pedneo.2023.02.010.

[20] Niederman MS, Baron RM, Bouadma L, Calandra T, Daneman N, DeWaele J, Kollef MH, Lipman J, Nair GB. Initial antimicrobial management of sepsis. Critical care. 2021 Dec;25:1-1. doi: 10.1186/s13054-021-03736-w.