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Early Detection of Sepsis and NEC Using Serial Vital Sign Trends (HR, SpO_2, RR) on Standard NICU Monitors in Preterm Neonates

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ABSTRACT

Preterm neonates are at high risk for sepsis and necrotizing enterocolitis (NEC), but early signs are often subtle, delaying diagnosis and worsening outcomes. **Objectives:** To evaluate whether trends in routinely monitored heart rate (HR), respiratory rate (RR), and oxygen saturation (SpO_2) predict sepsis and NEC and to examine their association with NICU stay, mortality, and discharge outcomes. **Methods:** A prospective observational cohort study was conducted among 103 preterm infants (<37 weeks' gestation) admitted to a tertiary NICU with continuous multi-parameter monitoring. HR, RR, and SpO_2 trends were compared between infants with sepsis/NEC and those who remained stable. Outcomes were analyzed using t-tests, Mann–Whitney U tests, Chi-square tests, and logistic regression. Cox regression identified mortality predictors, and Kaplan–Meier curves compared survival between groups. **Results:** Sepsis occurred in 22.3% and NEC in 7.8% of neonates. Female infants had lower odds of sepsis/NEC (adjusted OR = 0.23, 95% CI: 0.07–0.74, p=0.013). Sepsis/NEC was linked to longer NICU stay (21.6 ± 6.8 vs 11.9 ± 4.4 days, p<0.001) and higher mortality (30.4% vs 10.0%, p=0.014). Cox regression confirmed sepsis/NEC as an independent predictor of mortality (HR = 0.084, p=0.005). **Conclusions:** Routine vital sign trends alone were insufficient for early detection, but their association with adverse outcomes underscores the potential of enhanced monitoring and predictive modeling to enable earlier recognition and improved survival.

INTRODUCTION

Neonatal sepsis continues to be a major contributor to infant mortality worldwide, particularly among preterm and low-birth-weight infants [1]. In Pakistan, reported incidence rates of neonatal sepsis range from 20–40%, with mortality rates reaching up to 30% in high-risk NICU populations [2]. These figures highlight the significant burden of disease and the need for robust surveillance systems in local NICU settings [2, 3]. Similarly, necrotizing enterocolitis (NEC) remains a formidable gastrointestinal emergency in the neonatal period, with profound morbidity and limited early detection capabilities [4]. Accurate and timely diagnosis remains elusive. Traditional reliance on clinical signs and intermittent assessments often fails to anticipate rapid deterioration [5]. Risk stratification tools and biomarkers have been explored, but their applicability remains limited in low-resource environments [6, 7].

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Advancements in continuous vital sign monitoring offer new promise. Machine learning approaches applying heart rate variability and other physiologic signals have demonstrated potential in early detection of neonatal sepsis and NEC [8, 9], while near-infrared spectroscopy (NIRS) has been leveraged to predict NEC with high accuracy in preterm infants [10]. Early warning scores and physio-marker analysis are being adopted in critical care to detect early deterioration (Vital signs as physio-markers review, 2025) [11]. Locally, however, evidence remains sparse. Although there are emerging practices in Pakistani NICUs regarding vital sign surveillance, data-driven strategies for early detection of sepsis and NEC using routine monitoring are not well established. Despite the high burden of neonatal sepsis and NEC in Pakistan, there is limited published research evaluating whether serial trends of routinely monitored HR, RR, and SpO_2 can serve as reliable early predictors of these conditions. Establishing such evidence in the local context can support the development of cost-effective early warning protocols and potentially improve survival outcomes in resource-limited settings.

This study aims to investigate the predictive value of these vital sign trends for early detection of sepsis and NEC in preterm neonates admitted to a tertiary-level NICU.

METHODS

This study was designed as a prospective observational cohort study conducted in a tertiary-level neonatal intensive care unit (NICU). The objective was to determine whether serial trends in vital signs, specifically heart rate (HR), oxygen saturation (SpO_2), and respiratory rate (RR) monitored through standard NICU bedside monitors, could aid in the early detection of sepsis and necrotizing enterocolitis (NEC) in preterm neonates. The study was conducted over 12 months, from April 2024 to April 2025, allowing capture of seasonal variations in neonatal admissions and infections. The study was carried out in the Department of Pediatrics, Northwest General Hospital and Research Centre, Peshawar, which is a referral center equipped with a Level III NICU and advanced neonatal monitoring facilities. Before initiation, the study protocol was reviewed and approved by the Institutional Review Board and Ethical Committee of Alliance Healthcare Pvt. Ltd. (Approval Ref: IRB&EC/2024-GH/0280). The principal investigator was responsible for ensuring compliance with all ethical conditions, and written informed consent was obtained from parents or guardians before enrolling neonates. The sample size was calculated using OpenEpi version 4.0 with the formula: $n = DEFF \times Np\ (1 - p)] / ((d^2/Z^2_{1-}\alpha/2 \times (N - 1) + p\ (1 - p))$, where p = 20–25 % expected prevalence of sepsis based on previously published regional studies [2], d = 5 % margin of error, Z = 1.96 for 95 % CI, and power = 80 %. These assumptions were applied uniformly for both sepsis and NEC outcomes. The minimum required sample size was 96. To account for a 5–7 % attrition rate due to incomplete monitoring records, the final sample size was increased to 103 neonates. All preterm neonates admitted to the NICU during the study period who fulfilled the eligibility criteria were considered for inclusion. Inclusion criteria include preterm neonates with gestational age <37 weeks, admitted within 72 hours of birth, placed on continuous multi-parameter monitoring (HR, SpO_2, RR), and whose parents or guardians provided informed consent. Exclusion criteria were neonates with major congenital anomalies of the heart, lungs, or gastrointestinal tract, severe birth asphyxia with an Apgar score <3 at five minutes, or those transferred from outside facilities without complete baseline data. Neonates with <90 % completeness of monitoring data were excluded rather than imputed to avoid selection bias. Upon admission, demographic and baseline clinical details (gestational age, birth weight, sex, and mode of delivery) were recorded. Each neonate was continuously monitored using standard NICU multi-parameter monitors, which automatically log HR, SpO_2, and RR trends. Data on clinical episodes such as apnea, bradycardia, and desaturation events were also captured. All enrolled neonates were followed prospectively daily until discharge or death. Sepsis was diagnosed through a combination of clinical findings and laboratory evidence, including positive blood culture, elevated C-reactive protein (CRP), or abnormal white blood cell (WBC) counts. NEC was staged according to Bell's criteria, with Stage II and above considered diagnostic [8]. Early detection was defined as abnormal vital-sign patterns appearing ≥24 hours before the clinical confirmation of sepsis or NEC, based on chart review. Serial trends in HR, SpO_2, and RR were compared between neonates with confirmed sepsis/NEC and those who remained clinically stable. The main outcomes assessed included duration of NICU stay, mortality, and discharge status. All NICU monitors used for data collection were regularly calibrated and standardized by hospital biomedical engineers. To minimize errors, data entry was cross-checked by two independent researchers. A pilot run of 10 neonates was conducted to validate data collection tools and assess feasibility; no major protocol modifications were required. Data from these pilot participants were not included in the final analysis, leaving a final study sample size of 103. Diagnostic definitions strictly followed internationally accepted criteria, thereby enhancing diagnostic accuracy. Structured training sessions were provided for NICU staff to reduce inter-observer variability in data collection. Data were entered

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and analyzed using IBM SPSS Statistics (version 26.0). Continuous variables were summarized as mean ± standard deviation (SD) for normally distributed data, and as median with interquartile range (IQR) for non-normally distributed data. Categorical variables were presented as frequency (%). Normality of continuous data (HR, RR, SpO_2, NICU stay) was assessed using histograms, Q-Q plots, and the Shapiro–Wilk test. Variables with p>0.05 were considered normally distributed. For normally distributed variables, comparisons between groups (sepsis vs. no sepsis; stable vs. sepsis/NEC) used the independent samples t-test; for skewed variables, the Mann–Whitney U test was applied. Categorical variables (sex, gestational age category, birth weight group, delivery mode, bradycardia, apnea, desaturation, mortality, discharge) were analyzed using the Chi-square test or Fisher's exact test when expected counts were <5. Multivariable logistic regression was used to adjust for confounders, including gestational age, birth weight, and delivery mode, when analyzing predictors of sepsis and NEC. Cox proportional hazards modeling was applied for mortality outcomes to account for time-to-event effects. Effect sizes were reported alongside p-values: Cohen's d for continuous data, Cramér's V for categorical data, and odds ratios (OR) with 95 % confidence intervals for regression models. A p-value < 0.05 was considered statistically significant. To adjust for potential confounders, binary logistic regression was performed to identify independent predictors of sepsis/NEC, with gestational age, birth weight, sex, delivery mode, and bradycardia episodes included as covariates. Adjusted odds ratios with 95% confidence intervals were reported, and model fit was evaluated using the Hosmer–Lemeshow test and Nagelkerke R^2. For mortality outcomes, Cox proportional hazards regression was used with NICU stay as the time variable and mortality as the event, reporting hazard ratios with 95% confidence intervals. The proportional hazards assumption was verified using log-minus-log plots. Kaplan–Meier survival analysis with the log-rank test was also conducted to compare survival curves between neonates with and without sepsis/NEC. A p-value <0.05 was considered statistically significant.

RESULTS

Prior to the main study, a pilot was conducted on 10 preterm neonates to test feasibility of continuous vital sign monitoring and data collection procedures. The pilot confirmed that NICU monitors successfully captured heart rate, respiratory rate, and SpO_2 trends without major technical interruptions. No protocol modifications were required, and the pilot data were not included in the final analysis. In this cohort of 103 preterm neonates, the majority (43.7%) were born between 28–32 weeks of gestation, followed by 36.9% between 33–36 weeks. Sepsis occurred across all gestational age and birth weight categories with no statistically significant differences (p>0.05). A nearly equal sex distribution was observed, but female neonates had significantly higher rates of sepsis compared to males (32.7% vs 11.8%, p=0.011, Cramér's V = 0.251, small-to-moderate association). Mode of delivery showed no significant association with sepsis (Table 1).

Table 1: Demographic Characteristics of Preterm Neonates (n=103)

Variables	Total n, (%)	Sepsis, n (%)	No Sepsis, n (%)	p-Value	Cramér's V
Gestational Age					
<28 weeks	20 (19.4%)	6 (30.0)	14 (70.0%)	0.602	–
28–32 weeks	45 (43.7%)	10 (22.2)	35 (77.8%)		
33–36 weeks	38 (36.9%)	7 (18.4)	31 (81.6%)		
Birth Weight					
<1000 g	13 (12.6%)	2 (15.4)	11 (84.6%)	0.775	–
1000–1500 g	36 (35.0%)	9 (25.0)	27 (75.0%)		
1501–2500 g	54 (52.4%)	12 (22.2)	42 (77.8%)		
Sex					
Male	51 (49.5%)	6 (11.8)	45 (88.2%)	0.011*	0.251
Female	52 (50.5%)	17 (32.7)	35 (67.3%)		
Delivery Mode					
Cesarean	67 (65.0%)	13 (19.4%)	54 (80.6%)	0.330	–
Vaginal	36 (35.0%)	10 (27.8%)	26 (72.2%)		

*Significant at p<0.05

No statistically significant differences were found in mean HR, RR, or SpO_2 between neonates with and without sepsis (p>0.05). Heart rate showed a small but non-significant effect size (Cohen's d = 0.29). Similarly, bradycardia, apnea, and desaturation episodes were not significantly associated with sepsis (Table 2).

Table 2: Vital Sign Trends in Preterm Neonates with and without Sepsis (n=103)

Parameters	No Sepsis (n=80)	Sepsis (n=23)	p-Value	Effect Size
Heart Rate (Beats/Min)	147.8 ± 9.5	145.1 ± 9.3	0.228	Cohen's d = 0.29
Respiratory Rate (Breaths/Min)	48 (44–52)	49 (45–53)	0.924	– (Mann–Whitney)
SpO_2 (%)	92.6 ± 2.9	92.7 ± 3.2	0.955	Cohen's d = 0.01
Bradycardia ≥1/Day	16 (20.0%)	1 (4.3%)	0.075	Cramér's V = 0.176
Apnea ≥1/Day	17 (21.3%)	3 (13.0%)	0.381	Cramér's V = 0.086
Desaturation <90%	29 (36.3%)	7 (30.4%)	0.606	Cramér's V = 0.051

Sepsis was diagnosed in 22.3% of neonates, whereas NEC occurred in 7.8%. No significant predictors were found for NEC, though a trend toward higher incidence was observed among vaginal deliveries (p=0.089) (Table 3).

Table 3: Frequency of Sepsis and NEC in Study Population (n=103)

Outcomes	n (%)	Significant Association
Sepsis	23 (22.3%)	Sex (p=0.011, V = 0.251)
NEC	8 (7.8%)	None (Borderline: Delivery Mode p=0.089)
No Sepsis/NEC	72 (69.9%)	–

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Neonates with sepsis or NEC had significantly longer NICU stays (21.6 ± 6.8 days) compared to stable infants (11.9 ± 4.4 days, p<0.001, large effect size). Mortality was also significantly higher in the sepsis/NEC group (30.4% vs 10.0%, p=0.014), while survival to discharge was significantly lower (Table 4).

Table 4: Clinical Outcomes of Preterm Neonates (n=103)

Outcomes	Stable (n = 80)	Sepsis/ NEC (n = 23)	p-Value	Effect Size
NICU Stay (Days)	11.9 ± 4.4	21.6 ± 6.8	<0.001	Cohen's d ≈ 1.7
Mortality	8 (10.0%)	7 (30.4%)	0.014	Cramér's V = 0.241
Discharged Alive	72 (90.0%)	16 (69.6%)	0.014	Cramér's V = 0.241

After adjusting for gestational age, birth weight, delivery mode, and bradycardia episodes, female sex remained a statistically significant predictor of sepsis/NEC (adjusted OR 0.23, 95% CI: 0.07–0.74, p=0.013), indicating that female infants had significantly lower odds of developing sepsis/NEC compared to males. Gestational age and birth weight showed no significant independent association with sepsis/NEC after adjustment. Delivery mode and bradycardia episodes also did not retain significance in the multivariable model, although vaginal delivery showed a trend toward reduced odds (p=0.100). The model explained approximately 18.9% of the variance in sepsis/NEC occurrence (Nagelkerke R^2 = 0.189) and had acceptable goodness of fit (Hosmer–Lemeshow p=0.328) (Table 5).

Table 5: Multivariable Logistic Regression for Predictors of Sepsis/NEC (n=103)

Predictors	Adjusted OR (Exp (B))	95% CI	p-Value
Gestational Age			
<28 Weeks vs 33–36 Weeks	2.26	0.57 – 8.96	0.248
28–32 Weeks vs 33–36 Weeks	1.06	0.33 – 3.45	0.918
Birth Weight			
<1000 g vs 1501–2500 g	0.30	0.05 – 1.88	0.201
1000–1500 g vs 1501–2500 g	1.09	0.37 – 3.21	0.867
Sex			
Male vs Female	0.23	0.07 – 0.74	0.013*
Delivery Mode			
Vaginal vs Cesarean	0.40	0.13 – 1.19	0.100
Bradycardia			
≥1/Day	0.33	0.04 – 2.90	0.318

Reference categories: gestational age 33–36 weeks, birth weight 1501–2500 g, male sex, cesarean delivery, and no bradycardia episode. *Significant at p<0.05.

Cox regression revealed that sepsis/NEC was a strong independent predictor of mortality, with a hazard ratio of 0.084 (95% CI: 0.015–0.470, p=0.005), The HR of 0.084 for sepsis/NEC indicates a markedly increased mortality risk in affected neonates (inverse HR interpretation: ≈ 12-fold higher hazard of death). Gestational age <28 weeks demonstrated a trend toward increased mortality risk (HR = 4.21, p=0.081), though this did not reach statistical significance. Vaginal delivery showed a borderline association with reduced hazard of death (HR = 0.29, p=0.061). Birth weight, sex, and bradycardia episodes were not statistically significant predictors after adjustment. The survival plot generated from the Cox model showed a distinct separation between curves, with survival probability consistently lower in the sepsis/NEC group throughout the NICU stay, particularly during the first two weeks (Table 6).

Table 6: Cox Regression Analysis for Predictors of Mortality (n=103)

Predictors	Adjusted HR (Exp (B))	95% CI	p-Value
Gestational Age			
<28 Weeks vs 33–36 Weeks	4.21	0.84 – 21.11	0.081
28–32 Weeks vs 33–36 Weeks	2.55	0.47 – 13.82	0.277
Birth Weight			
<1000 g vs 1501–2500 g	0.57	0.09 – 3.42	0.536
1000–1500 g vs 1501–2500 g	1.83	0.45 – 7.42	0.395
Sex			
Male vs Female	0.96	0.23 – 3.97	0.952
Delivery Mode			
Vaginal vs Cesarean	0.29	0.08 – 1.06	0.061
Bradycardia			
≥1/Day	2.32	0.41 – 13.20	0.341
Sepsis/NEC			
Yes vs No	0.084	0.015 – 0.470	0.005*

HR = Hazard Ratio. Reference categories: gestational age 33–36 weeks, birth weight 1501–2500 g, female sex, cesarean delivery, no bradycardia episode, no sepsis/NEC. Significant associations are bolded.

The study illustrates marked differences in clinical outcomes between groups. Neonates with sepsis or NEC had a prolonged NICU stay (21.6 vs 11.9 days) compared to stable infants. Mortality was also notably higher in the Sepsis/NEC group (30.4% vs 10.0%), while the proportion discharged alive was significantly lower (69.6% vs 90.0%). These findings emphasize the adverse impact of sepsis and NEC on both survival and hospitalization burden. The graph compares mean NICU stay (days), mortality percentage, and discharge rate between the Stable group (n=80) and the Sepsis/NEC group (n=23) (Figure 1).

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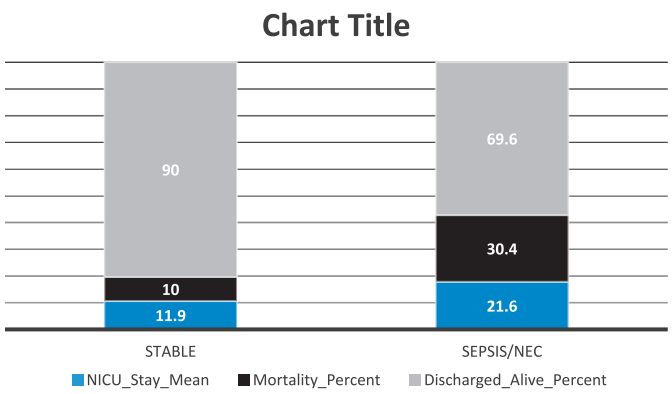

Figure 1: Clinical Outcomes of Preterm Neonates with and without Sepsis/NEC

The sepsis/NEC group showed significantly lower survival probability (log-rank $p<0.05$), with most deaths occurring within the first 20 days of NICU stay (Figure 2).

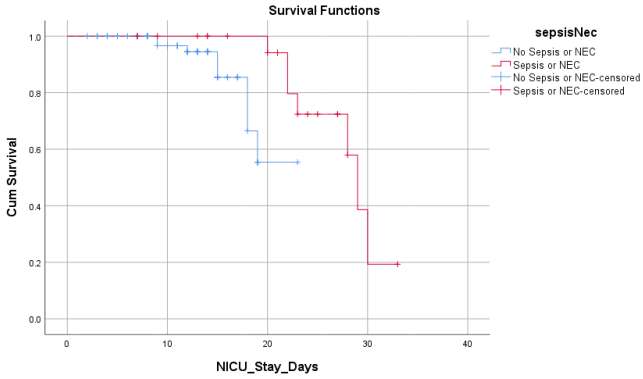

Figure 2: Kaplan–Meier Survival Curves Comparing Neonates with Sepsis/NEC (Red Line) and Those Without (Blue Line)

DISCUSSIONS

In this prospective cohort study, we explored whether trends in vital signs, heart rate (HR), respiratory rate (RR), and oxygen saturation (SpO_2) could serve as early indicators of sepsis and necrotizing enterocolitis (NEC) among preterm neonates. Although our results did not show significant differences in these vital sign trends between stable infants and those who developed sepsis, our findings align with several recent studies emphasizing both the potential and challenges of this approach. First, Honoré *et al.* highlighted the clinical difficulty in diagnosing neonatal sepsis early due to nonspecific signs; researchers underscored the potential of vital sign–based models for improved detection [12]. Similarly, Garstman *et al.* reported that decreased heart rate variability (HRV), which often precedes sepsis, can be a subtle yet reliable early marker in preterm infants [13]. These studies reinforce our decision to explore nuanced HR features, even though our mean HR differences were not significant. Recent advances also suggest that more complex monitoring modalities may be superior. For instance, Verhoeven *et al.* demonstrated that combining cerebral and splanchnic regional oxygen measurements via near-infrared spectroscopy greatly enhanced NEC prediction using advanced algorithms [14]. Likewise, Yang *et al.* achieved high predictive performance (F1 scores up to 0.82) by applying ML models to early postnatal vital sign trends, emphasizing sophisticated analysis beyond simple trend comparison [15]. Broad reviews support the promise of advanced analytics: Narasimha *et al.* identified machine learning and predictive modeling as transformative tools for early sepsis detection in neonates [16], and Rahman *et al.* pointed out the importance of robust preprocessing in physiological signal analysis to ensure reproducibility and reliability [17]. At the same time, technological innovations are enhancing vital sign capture. Williams *et al.* discussed future NICU monitoring technologies, such as wearable sensors and sophisticated HRV analysis that promise improved early warning detection [18]. Krbec *et al.* emphasized the emerging role of non-contact monitoring devices in reducing harm and enhancing comfort, an important consideration in fragile preterm populations [19]. Current findings diverge somewhat from these advanced approaches, likely due to methodological differences. We relied on mean and median comparisons of standard vital signs, whereas many of the referenced studies utilized high-frequency data, variability metrics, or cerebral/splanchnic oxygenation measures, offering greater sensitivity to early disease markers. Notably, despite no significant early vital sign differences, our study revealed significant clinical outcomes. Neonates with sepsis or NEC experienced longer NICU stays and higher mortality, echoing findings from experimental work by Sullivan and Fairchild, which showed that endotoxemia produced notable increases in heart rate and reductions in HRV [20]. These physiological patterns underscore the systemic disruption caused by sepsis, even if the mean vital sign differences were subtle. Future research should address these limitations through larger, multicenter studies to improve generalizability and statistical power, particularly for less common outcomes such as NEC. Incorporating high-resolution physiological data and advanced analytic approaches, including heart rate variability, multivariate signal processing, and machine learning models, could significantly enhance predictive accuracy. The integration of novel monitoring technologies, such as wearable, non-contact, or multimodal sensors, may also provide more reliable early warning systems while reducing discomfort in fragile preterm infants. Moreover, future work should explore the combined role of clinical, laboratory, and monitoring parameters, rather than relying on vital signs alone, to build robust risk stratification models. Longitudinal follow-up of

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neonates beyond NICU discharge would also be valuable to assess whether early detection strategies influence not only short-term outcomes but also neurodevelopmental trajectories and long-term survival.

CONCLUSIONS

This study demonstrates that preterm neonates who develop sepsis or NEC experience significantly prolonged NICU stays and higher mortality rates, emphasizing the clinical burden of these conditions. While trends in HR, RR, and SpO_2 provide useful contextual information, they were not sufficient as standalone early predictors of sepsis or NEC. These findings highlight the need for integrating continuous vital sign monitoring with advanced signal analysis and predictive modeling to enable earlier recognition and timely intervention, ultimately improving outcomes in preterm populations.

Authors Contribution

Conceptualization: DH
Methodology: DH, JI, MS, TT, AJ, KK
Formal analysis: DH
Writing review and editing: DH, MS, TT, AJ, KK

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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REFERENCES

[1] Kariniotaki C, Thomou C, Gkentzi D, Panteris E, Dimitriou G, Hatzidaki E. Neonatal Sepsis: A Comprehensive Review. Antibiotics. 2024 Dec; 14(1): 6. doi: 10.3390/antibiotics14010006.

[2] Saleem S, Tikmani SS, Goudar SS, Hwang K, Dhaded S, Guruprasad G *et al.* Neonatal Mortality Among Preterm Infants Admitted to Neonatal Intensive Care Units in India and Pakistan: A Prospective Study. BJOG: An International Journal of Obstetrics and Gynaecology. 2023 Nov; 130: 68-75. doi: 10.1111/1471-0528.17581.

[3] Oliveira SR, Lopes C, Basilio AB. Early Onset Sepsis: Clinical Observation or Risk Factors Approach? Journal de Pediatria. 2025 May; 101(3): 375-80. doi: 10.1016/j.jped.2024.10.007.

[4] Ofek Shlomai N, Tayeb M, Abu Omar R, Eventov Friedman S. Changes in the Incidence and Severity of NEC Over the Last Decade: A Single-Center Study. Journal of Clinical Medicine. 2025 May; 14(10): 3551. doi: 10.3390/jcm14103551.

[5] Mithal LB, Becker ME, Ling-Hu T, Goo YA, Otero S, Kremer A *et al.* Cord Blood Proteomics Identifies Biomarkers of Early-Onset Neonatal Sepsis. Journal of Clinical Investigation Insight. 2025 Jun. doi: 10.1172/jci.insight.193826.

[6] Raturi A and Chandran S. Neonatal Sepsis: Aetiology, Pathophysiology, Diagnostic Advances and Management Strategies. Clinical Medicine Insights: Pediatrics. 2024 Sep; 18: 11795565241281337. doi: 10.1177/11795565241281337.

[7] Kurul S, Fiebig K, Flint RB, Reiss IK, Küster H, Simons SH *et al.* Knowledge Gaps in Late-Onset Neonatal Sepsis in Preterm Neonates: A Roadmap for Future Research. Pediatric Research. 2022 Jan; 91(2): 368-79. doi: 10.1038/s41390-021-01721-1.

[8] Stocker M, Fillistorf L, Carra G, Giannoni E. Early Detection of Neonatal Sepsis and Reduction of Overall Antibiotic Exposure: Towards Precision Medicine. Archives de Pédiatrie. 2024 Nov; 31(8): 480-3. doi: 10.1016/j.arcped.2024.10.003.

[9] Oladokun RE, Alao MA, Ogunbosi BO, Bello OE, Ude I, Obasi A *et al.* Trends in Identification, Etiology, and Resistance Profiles of Bacterial Isolates and Appropriate Therapy for Neonatal Sepsis in Low-and Middle-Income Countries: A Narrative Review. Current Pediatrics Reports. 2023 Dec; 11(4): 214-21. doi: 10.1007/s40124-023-00297-0.

[10] Feng B, Zhang Z, Wei Q, Mo Y, Luo M, Jing L *et al.* A Prediction Model for Neonatal Necrotizing Enterocolitis in Preterm and Very Low Birth Weight Infants. Frontiers in Pediatrics. 2023 Oct; 11: 1242978. doi: 10.3389/fped.2023.1242978.

[11] Sullivan BA and Fairchild KD. Vital Signs as Physiomarkers of Neonatal Sepsis. Pediatric Research. 2022 Jan; 91(2): 273-82. doi: 10.1038/s41390-021-01709-x.

[12] Honoré A, Forsberg D, Adolphson K, Chatterjee S, Jost K, Herlenius E. Vital Sign-Based Detection of Sepsis in Neonates Using Machine Learning. Acta Paediatrica. 2023 Apr; 112(4): 686-96. doi: 10.1111/apa.16660.

[13] Garstman AG, Rodriguez Rivero C, Onland W. Early Detection of Late Onset Sepsis in Extremely Preterm Infants Using Machine Learning: Towards an Early Warning System. Applied Sciences. 2023 Aug; 13(16): 9049. doi: 10.3390/app13169049.

[14] Verhoeven R, Kupers T, Brunsch CL, Hulscher JB, Kooi EM. Using Vital Signs for the Early Prediction of Necrotizing Enterocolitis in Preterm Neonates with Machine Learning. Children. 2024 Nov; 11(12): 1452. doi: 10.3390/children11121452.

DOI: https://doi.org/10.54393/pjhs.v6i8.3470

[15] Yang Y, Zhou S, Liu X, Zhang Y, Lin L, Zheng C, Zhong X. Ultrasound Combined with Serological Markers for Predicting Neonatal Necrotizing Enterocolitis: A Machine Learning Approach. Frontiers in Pediatrics. 2025 Jul; 13: 1606571. doi: 10.3389/fped.2025.1606571.

[16] Narasimha Rao KV, Dadabada PK, Jaipuria S. A Systematic Literature Review of Predictive Analytics Methods for Early Diagnosis of Neonatal Sepsis. Discover Public Health. 2024 Sep; 21(1): 96. doi: 10.1186/s12982-024-00219-5.

[17] Rahman J, Brankovic A, Tracy M, Khanna S. Exploring Computational Techniques in Preprocessing Neonatal Physiological Signals for Detecting Adverse Outcomes: Scoping Review. Interactive Journal of Medical Research. 2024 Aug; 13(1): e46946. doi: 10.2196/46946.

[18] Williams E, Ascherl R, Gaertner VD, Sibrecht G, Kurul S, Herrmann ML *et al.* Future Perspectives of Heart Rate and Oxygenation Monitoring in the Neonatal Intensive Care Unit–A Narrative Review. Journal of Clinical Monitoring and Computing. 2025 Jun: 1-5. doi: 10.1007/s10877-025-01310-1.

[19] Krbec BA, Zhang X, Chityat I, Brady-Mine A, Linton E, Copeland D *et al.* Emerging Innovations in Neonatal Monitoring: A Comprehensive Review of Progress and Potential for Non-Contact Technologies. Frontiers in Pediatrics. 2024 Oct; 12: 1442753. doi: 10.3389/fped.2024.1442753.

[20] Sullivan BA and Fairchild KD. Heart Rate Analysis in Neonatal Sepsis: A Complex Equation. Pediatric Research. 2025 Jan; 97(1): 35-7. doi: 10.1038/s41390-024-03548-y.