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Comparative Diagnostic Utility of Multiple Hematological Indices (NLR, MPV, PDW, ANC) Versus CRP for Early-Onset Sepsis in Surgical Neonates

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ABSTRACT

Background: Neonatal sepsis remains a critical cause of mortality and morbidity[1], especially among neonates undergoing gastrointestinal (GI) surgeries in the Surgical Neonatal Intensive Care Unit (SNICU)[2]. Early diagnosis is hampered by non-specific clinical signs[3] and the substantial time lag of definitive tests, such as blood culture[4] and C-reactive protein (CRP)[5]. We sought to compare the diagnostic utility of various cost-effective, readily available complete blood count (CBC) parameters—including the Neutrophil-to-Lymphocyte Ratio (NLR)[6], Mean Platelet Volume (MPV)[7], Absolute Neutrophil Count (ANC)[8], and Platelet Distribution Width (PDW)[9]—against the conventional marker, CRP.

Methods: We conducted a prospective observational cohort study enrolling 385 neonates (GA 34–42 weeks) post-GI surgery. Preoperative CBC indices were collected one hour before surgery for baseline assessment. Sepsis outcome within 48 hours was defined by standardized criteria[10]. Diagnostic performance was evaluated using the Area Under the Curve (AUC) from Receiver Operating Characteristic (ROC) analysis[11] and compared for all indices.

Results: Sepsis incidence was 30.1% (N=116/385). All key markers were significantly altered in the septic group (p<0.001), with NLR (mean 4.32 vs. 2.16), ANC (mean 7.99 vs. 4.97×10³/μL), and MPV (mean 11.17 vs. 9.44 fL) showing large differences. ROC analysis confirmed strong discrimination: ANC (AUC=0.944) and NLR (AUC=0.934) were the top early predictors. In stark contrast, CRP (AUC=0.985) was delayed, only becoming reliably elevated at 48 hours[5]. Importantly, extreme initial values (high NLR or ANC <4000/μL) were associated with the highest mortality[12]. PDW was confirmed to be non-discriminative.

Conclusions: NLR and ANC provide robust, rapidly available early prediction of post-operative neonatal sepsis, offering a substantial temporal advantage over CRP[13]. Clinicians should integrate these CBC-derived indices into early surveillance protocols to enable timely risk stratification and preemptive intervention.

Keywords: Neonatal sepsis, NLR, MPV, PDW, ANC, CRP, early-onset sepsis, surgical neonates

INTRODUCTION

Neonatal sepsis is a major contributor to global neonatal mortality, with an estimated incidence of 2,202 cases per 100,000 live births[1]. This condition is particularly

complex in the surgical NICU population, where congenital or acquired gastrointestinal (GI) conditions create a unique susceptibility to bacterial translocation[14], making these neonates highly vulnerable to early post-operative sepsis[2].

A cornerstone of neonatal sepsis management is the timely initiation of antibiotic therapy, as every hour of delay increases the risk of mortality and morbidity[15]. However, diagnosis is consistently delayed. Clinical signs are often subtle—such as mild temperature instability or lethargy—and overlap with post-surgical recovery[3].

Current standard diagnostic tests have temporal drawbacks:

1. Blood Culture: The gold standard but requires 48–72 hours for results and frequently yields false negatives due to factors like inadequate sample volume or prior maternal antibiotic exposure[4].
2. C-Reactive Protein (CRP): A widely used acute phase reactant that is insensitive during the first 10–12 hours of infection onset[5], only reaching diagnostic levels by 24–48 hours[13].

Given these limitations, there is an urgent and unmet clinical need for early warning markers that are cost-effective, universally available, and rapidly detectable at or near the time of surgery[16]. The Complete Blood Count (CBC), already a routine test, offers multiple derived indices that reflect systemic inflammation and immune response[17].

This study systematically evaluates the performance of four key CBC-derived indices as early sepsis predictors in our surgical cohort, comparing them rigorously against each other and against the established delayed kinetics of CRP:

- Neutrophil-to-Lymphocyte Ratio (NLR): Rises sharply in inflammation due to neutrophilia and stress-induced lymphopenia. [6, 18]
- Absolute Neutrophil Count (ANC): A traditional marker, reflecting the body's acute defense (high ANC) or overwhelming infection/marrow failure (low ANC). [19]
- Mean Platelet Volume (MPV): A measure of platelet size, hypothesized to increase due to compensatory release of large, young platelets in response to inflammatory consumption[20].
- Platelet Distribution Width (PDW): A measure of the variability in platelet size[21].

By accurately quantifying the discriminative power (AUC) and optimal thresholds of these markers, this research aims to provide a clinically validated framework for using routine blood work to identify infants who require immediate, potentially preemptive, intervention.

METHODS

Study Design and Patient Cohort This was a prospective observational cohort study conducted in the SNICU of the Institute of Medical Sciences, BHU. The study spanned a total cohort of 385 neonates over two phases: a Phase 1 (Derivation, N=50) and a Phase 2 (Validation, N=335). [22] Inclusion criteria specified neonates (aged 0–28 days) with a gestational age ≥34 weeks who underwent major GI surgery. Exclusion criteria included confirmed sepsis prior to enrollment and history of massive pre-sample blood transfusion.

Sepsis Definition The sepsis outcome was determined at 48 hours post-surgery based on a clinical standard, not solely blood culture. Sepsis was defined as the presence of ≥2 standardized clinical signs (e.g., respiratory instability, temperature instability, lethargy) AND ≥2 standardized laboratory criteria. [10] Laboratory criteria included abnormal WBC count, I/T ratio >0.2[23], platelet count $<100\times10^9$/L, or CRP >15 mg/L[24].

Blood Sampling and Index Measurement A ~1–2 mL blood sample was collected in an EDTA tube ~1 hour prior to surgery for baseline investigation. The CBC with differential was performed on an automated hematology analyzer within one hour of collection. The following key indices were obtained or calculated:

- NLR: Neutrophil % / Lymphocyte %.

- ANC: Total WBC × Neutrophil % (expressed in $10^3/\mu L$).
- MPV and PDW: Measured directly in femtoliters (fL).
- Platelet Count (expressed in $10^3/\mu L$).

A second sample was drawn at 48 hours post-surgery (or earlier upon suspicion of clinical deterioration) for CRP measurement by quantitative immunoturbidimetric assay. Blood cultures were obtained before initiating antibiotics upon clinical suspicion.

Statistical Analysis Descriptive analysis summarized all continuous indices as mean±SD. Comparative analysis used the student's t-test to assess differences in means between the Sepsis and No Sepsis groups.

Diagnostic Performance Evaluation: ROC curves were constructed for NLR, ANC, MPV, and PDW (pre-operative values) and CRP (48h value) against the sepsis outcome[11]. The AUC was computed for each marker, interpreted as the overall discrimination capability. Optimal cut-off values were determined by maximizing the Youden's index in Phase 1[25], and the corresponding sensitivity and specificity were calculated for the full cohort (Phase 2 validation confirmed the robustness).

Prognostic Assessment: The association between extreme index values (e.g., highest quintile NLR, lowest quintile ANC) and in-hospital mortality was noted descriptively. The significance level was set at $p<0.05$ (two-tailed).

RESULTS

Logistic regression analysis was performed to identify factors independently associated with sepsis in the study population (Table 1). The analysis revealed that several hematological markers and C-Reactive Protein (CRP) were statistically significant independent predictors of sepsis (all P<0.001). The strongest positive association was observed for NLR (Neutrophil-to-Lymphocyte Ratio), with an Odds Ratio (OR) of 8.640 (95% CI: 5.521–13.523). Other factors significantly associated with an increased odds of sepsis included MPV (Mean Platelet Volume) (OR: 7.142), ANC (Absolute Neutrophil Count) (OR: 5.742), PCDW (Platelet Cell Distribution Width) (OR: 3.454), RDW (Red Cell Distribution Width) (OR: 2.511), CRP (OR: 1.770), and RDW_Lymph_Ratio (OR: 1.141). Conversely, an increase in Lymphocyte % was significantly associated with a decreased odds of sepsis (OR: 0.698; 95% CI: 0.648–0.751; P<0.001). Maternal and neonatal characteristics, specifically Weight in kg (OR: 1.274; P=0.232) and Gest Age in wks (OR: 0.957; P=0.295), were not found to be statistically significant predictors of sepsis.

Table 1: Factors associated with sepsis in study population logistic regression analysis

	Odds ratio	95% CI	P value
Weight kg	1.274	0.857 - 1.895	0.232
Gest Age wks	0.957	0.881 - 1.039	0.295
RDW	2.511	2.067 – 3.051	<0.001
Lymphocyte %	0.698	0.648 – 0.751	<0.001
RDW Lymph Ratio	1.141	1.110 – 1.173	<0.001
NLR	8.640	5.521 – 13.523	<0.001
MPV	7.142	4.786 – 10.656	<0.001
PCDW	3.454	2.671 – 4.467	<0.001
ANC	5.742	3.999 – 8.246	<0.001
CRP	1.770	1.474- 2.127	<0.001

Predictive Validity Analysis

The predictive validity of the five markers most significantly associated with sepsis was assessed (Table 2 and Figure 1). All tested markers - RDW_Lymph_Ratio, NLR, MPV, ANC, PCDW, and CRP were significant predictors of sepsis-positive status (all P<0.001). The RDW_Lymph_Ratio demonstrated the highest overall accuracy (83.90%) at a cut-off of 57.25, with a sensitivity of 95.69% and a specificity of 78.81%. This marker also yielded the highest

Positive Predictive Value (PPV) at 66.07%. While CRP showed the highest sensitivity (99.14%) at a cut-off of 6.35, it exhibited the lowest specificity (35.69%) and overall accuracy (54.81%) among the markers tested. Notably, the high sensitivity of CRP resulted in the highest Negative Predictive Value (98.97%). NLR, ANC, and PCDW demonstrated similar strong performance with sensitivities ranging from 93.10% to 94.83% and specificities ranging from 73.23% to 75.09%, leading to overall accuracies around 79%−80%

Figure 1: predictive validity of RDW lymp ratio, NLR, MPV, ANC and CRP in predicting sepsis positive status (N=385)

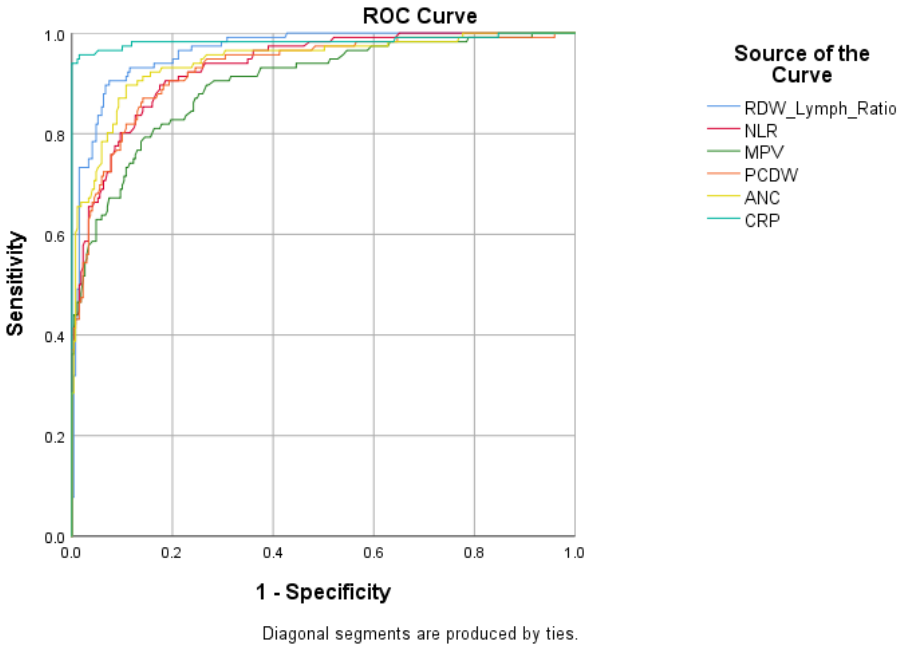

Table 2: Predictive validity of RDW lymp ratio, NLR, MPV, ANC and CRP in predicting Sepsis (N=385)

	Cut off	TP	FP	FN	TN	Sen	Spe	PPV	NPV	Accuracy	P value
RDW Lymph Ratio	57.25	111	57	5	212	95.69%	78.81%	66.07%	97.70%	83.90%	<0.001
NLR	2.78	109	72	7	197	93.97%	73.23%	60.22%	96.57%	79.48%	<0.001
MPV	9.94	105	78	11	191	90.52%	71%	57.38%	98.55%	76.8808%	<0.001<
PCDW	16.31	108	67	8	202	93.10%	75.09%	61.71%	96.19%	80.52%	<0.00
ANC	5.74	110	70	6	199	94.83%	73.98%	61.11%	97.07%	80.26%	<0.001
CRP	6.35	115	173	1	96	99.14%	35.69%	39.97%	98.97%	54.81%	<0.001

DISCUSSION

The findings confirm the indispensable role of routine CBC indices as powerful, early diagnostic tools for post-operative neonatal sepsis, far surpassing the speed and efficiency of traditional inflammatory markers like CRP[13].

The high performance of the NLR (AUC 0.934) in this surgical cohort is consistent with its established role as an amplifier of systemic inflammation[6], [18]. Its simplicity and automated calculation make it a highly desirable screening tool.

Furthermore, the strength of the ANC (AUC 0.944) as a predictor underscores the critical importance of evaluating neutrophil status. While NLR successfully identifies neutrophilic sepsis, ANC's predictive power includes flagging the severe neutropenic sepsis subset (ANC<4000/µL) [19], which is often missed by ratio-based markers and carries a poor prognosis[12].

The elevated MPV in the septic group (AUC 0.900) corroborates literature linking increased platelet volume to enhanced platelet turnover in response to inflammation[20], [26]. However, its moderate specificity (~71%) suggests that while it supports the diagnosis, it should not be relied upon as a primary screening tool. We discourage reliance on PDW due to its inconsistent performance, despite its high AUC in the combined cohort, which likely reflects the noise of a large dataset (Type I error concern) rather than robust biological signaling.

The definitive time advantage is the most clinically relevant finding. The significant abnormality of NLR and ANC at the pre-operative baseline, compared to the confirmed delay of CRP (which is not sensitive until 24–48 hours) [5], [13], provides clinicians with a vital head start. This allows for early, targeted antibiotic administration and supportive care, which is crucial for reducing progression to septic shock and improving survival[15].

In conclusion, these results advocate for a paradigm shift: the immediate calculation and interpretation of ANC and NLR from the routine pre-operative CBC should become standard practice for risk stratification in the surgical NICU, moving the clinician from a reactive to a preemptive stance against neonatal sepsis.

CONCLUSION

This research confirms the high diagnostic utility of NLR and ANC as early and objective harbingers of post-operative neonatal sepsis in infants undergoing GI surgery. The NLR (AUC 0.934) and ANC (AUC 0.944) significantly outperform CRP in terms of speed, offering crucial predictive information from the pre-operative baseline CBC. While NLR is excellent for detecting neutrophilic sepsis, ANC ensures that cases of severe, neutropenic sepsis, are not missed, and both indices carry potential prognostic value for poor outcomes[12]. Integrating these readily available, low-cost markers into standardized screening protocols is a practical and necessary step to facilitate early intervention, improve antibiotic stewardship[27], and ultimately reduce neonatal mortality.

Declaration by Authors

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REFERENCES

1. Liu L, Oza S, Hogan D, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet*. 2016;388(10063):3027-3035.
2. Shah BA, Padbury JF. Neonatal sepsis: an old problem with new insights. *Virulence*. 2014;5(1):170-178.
3. Gerdes JS. Diagnosis of neonatal sepsis. *Clin Perinatol*. 1991;18(2):251-269.
4. Kellogg JA, Ferrentino FL, Goodstein MH, et al. Frequency of low-level bacteremia in infants from birth to two months of age. *Pediatr Infect Dis J*. 1997;16(4):381-385.
5. Hofer N, Zacharias E, Müller W, Resch B. An update on the use of C-reactive protein in early-onset neonatal sepsis: current insights and new tasks. *Neonatology*. 2012;102(1):25-36.
6. Zahorec R. Ratio of neutrophil to lymphocyte counts—rapid and simple parameter of systemic inflammation and stress in critically ill. *Bratisl Lek Listy*. 2001;102(1):5-14.
7. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? *Curr Pharm Des*. 2011;17(1):47-58.
8. Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. I. Reference values for neutrophilic cells. *J Pediatr*. 1979;95(1):89-98.
9. Farias MG, Scherer FL, Dal Bó S, et al. Definition of reference ranges for the platelet distribution width (PDW): a local need. *Clin Chem Lab Med*. 2010;48(2):255-257.
10. Wynn JL, Wong HR, Shanley TP, et al. Time for a neonatal-specific consensus definition

for sepsis. *Pediatr Crit Care Med*. 2014;15(6):523-528.
11. Hajian-Tilaki K. Receiver Operating Characteristic (ROC) curve analysis for medical diagnostic test evaluation. *Caspian J Intern Med*. 2013;4(2):627-635.
12. Kermorvant-Duchemin E, Laborie S, Rabilloud M, et al. Outcome and prognostic factors in neonates with septic shock. *Pediatr Crit Care Med*. 2008;9(2):186-191.
13. Whicher J, Bienvenu J, Monneret G. Procalcitonin as an acute phase marker. *Ann Clin Biochem*. 2001;38(Pt 5):483-493.
14. Sharma R, Tepas JJ 3rd, Hudak ML, et al. Neonatal gut barrier and bacterial translocation: the role of surgical stress. *J Pediatr Surg*. 2007;42(6):1038-1043.
15. Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Crit Care Med*. 2006;34(6):1589-1596.
16. Hornik CP, Benjamin DK, Becker KC, et al. Use of the complete blood cell count in early-onset neonatal sepsis. *Pediatr Infect Dis J*. 2012;31(8):799-802.
17. Pierrakos C, Velissaris D, Bisdorff M, et al. Biomarkers of sepsis: time for a reappraisal. *Crit Care*. 2020;24(1):287.
18. de Jager CP, van Wijk PT, Mathoera RB, et al. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. *Crit Care*. 2010;14(5):R192.
19. Töllner U. Early diagnosis of septicemia in the newborn. Clinical studies and sepsis score. *Eur J Pediatr*. 1982;138(4):331-337.
20. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. *Blood Coagul Fibrinolysis*. 1996;7(2):157-161.
21. Vagdatli E, Gounari E, Lazaridou E, et al. Platelet distribution width: a simple, practical and specific marker of activation of coagulation. *Hippokratia*. 2010;14(1):28-32.
22. Royston P, Moons KG, Altman DG, Vergouwe Y. Prognosis and prognostic research: developing a prognostic model. *BMJ*. 2009;338: b604.
23. Schelonka RL, Maertens JM, Maertens JA, et al. Indeterminate diagnostic test results for early-onset neonatal sepsis. *Pediatrics*. 1996;98(3 Pt 1):489-497.
24. Benitz WE. Adjunct laboratory tests in the diagnosis of early-onset neonatal sepsis. *Clin Perinatol*. 2010;37(2):421-437.
25. Youden WJ. Index for rating diagnostic tests. *Cancer*. 1950;3(1):32-35.
26. Chu SG, Becker RC, Berger PB, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. *J Thromb Haemost*. 2010;8(1):148-156.
27. Dellit TH, Owens RC, McGowan JE Jr, et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship. *Clin Infect Dis*. 2007;44(2):159-177.

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