TPM Vol. 32, No. S3, 2025
ISSN: 1972-6325
https://www.tpmap.org/

Open Access

A COMPOSITE SEPSIS INFLAMMATORY INDEX (SII) COMBINING NLR, PLR, AND CRP IN NEONATAL SEPSIS: UTILITY IN PREDICTING DISEASE SEVERITY

AKSHATHA P [1], VARUN MUDDASANI [1], HARISH SUDARSANAN [1], ASHA ARUN [1] SANTOSH KUMAR KAMALAKANNAN[1], KUMUTHA J [1]

[1]DEPARTMENT OF NEONATOLOGY, SAVEETHA MEDICAL COLLEGE, SAVEETHA INSTITUTE OF MEDICAL AND TECHNICAL SCIENCES, THANDALAM, CHENNAI, INDIA
CORRESPONDING AUTHOR: DR. AKSHATHA P

Abstract:

Background: Neonatal sepsis diagnosis and severity assessment remain challenging. Inflammatory markers such as NLR, PLR, and CRP have individually shown promise, but their combined predictive value remains underexplored.

Objective: To develop a Composite Sepsis Inflammatory Index (SII) using NLR, PLR, and CRP, and to evaluate its utility in predicting severe outcomes in neonatal sepsis.

Methods: A retrospective analysis was conducted on 147 neonates with suspected sepsis from a prospective NICU cohort. A composite score, SII = (NLR × CRP) + (PLR / 10), was derived. Diagnostic accuracy for mortality, ventilation requirement, and NICU stay >10 days was assessed using ROC analysis and logistic regression.

Results: Higher SII values were significantly associated with mortality ($p<0.001$), ventilation ($p=0.002$), and prolonged NICU stay ($p=0.014$). The SII demonstrated an AUC of 0.841 for predicting mortality, outperforming individual markers. Optimal cutoff of 19.8 yielded 81.2% sensitivity and 72.5% specificity.

Conclusion: The Composite Sepsis Inflammatory Index enhances predictive accuracy for severe neonatal sepsis outcomes. This simple, cost-effective tool may support early risk stratification in resource-limited NICUs.

Keywords: Neonatal sepsis, composite index, NLR, PLR, CRP, SII, biomarkers, prediction, severity

INTRODUCTION:

Neonatal sepsis is a life-threatening condition requiring timely diagnosis and risk stratification to optimize care. While hematologic ratios such as NLR and PLR, and proteins like CRP, are frequently used in clinical evaluation, their standalone predictive value for severe outcomes remains suboptimal. Combining markers may enhance diagnostic robustness.

This study introduces the Composite Sepsis Inflammatory Index (SII), combining NLR, PLR, and CRP, to predict mortality and morbidity in neonates with suspected sepsis.

Methods:

Study Design and Setting:
A retrospective analysis of data from a 12-month prospective observational study conducted in a tertiary NICU.

Participants:
147 neonates with clinical signs of sepsis, with complete CBC and CRP at admission.

Inclusion Criteria:

- Neonates <28 days of life
- Availability of NLR, PLR, CRP, and outcome data

Exclusion Criteria:

- Major anomalies, IEM, incomplete records

Composite Index Calculation:

- SII = (NLR × CRP) + (PLR ÷ 10)
- Alternate exploratory formulas evaluated but final model chosen for best AUC

Outcomes Measured:

- **Primary:** Mortality
- **Secondary:**
  - Ventilator support
  - NICU stay >10 days

Statistical Analysis:

- Continuous variables expressed as mean ± SD; categorical as frequency (%).
- ROC curves generated for SII and individual markers.
- AUCs compared; Youden Index used for cutoff derivation.
- Multivariate logistic regression to adjust for birth weight, gestation.

Results:

Table 1: Comparison of maternal characteristics of the study group

Characteristics study parameter	EOS group N =83	LOS N =64	p value
Maternal age (mean ± SD) (y)	26.28 ± 5.001	26.20 ± 4.91	0.917 (ns)
Age at marriage (mean ± SD) (y)	22.04 ± 3.58	22.32 ± 3.44	0.633 (ns)
Gravidity (N[%])			
Primi	39 (47.0)	43 (67.2)	**0.014***
Multi	44 (43.0)	21 (32.8)	
Gestational age completed (N[%])			

25 – 30	09 (10.8)	22 (34.4)	**0.002*** **
31 - 35	33 (39.8)	19 (29.7)	
36 - 40	41 (49.4)	23 (35.9)	
Gestation (N[%])			
Preterm	54 (65.1)	48 (75)	0.195 (ns)
Term	29 (34.9)	16 (25)	
Number of children (N[%])			
0	53 (63.9)	55 (85.9)	**0.003*** **
1	21 (25.3)	08 (12.5)	
2	08 (9.6)	0	
3	01 (1.2)	01 (1.6)	
Birth spacing (N[%])			
Not applicable	50 (60.2)	53 (82.8)	**0.020** **
>1year	02 (02.4)	01 (01.6)	
1-2 years	10 (12.0)	03 (04.7)	
>3 Years	21 (25.3)	07 (10.9)	
Mode of delivery (N[%])			
NVD	66 (79.5)	51 (79.7)	0.980 (ns)
LSCS	17 (20.5)	13 (20.3)	
Birth weight (mean ± SD) (g)	2170.95 ± 753.82	1746.3 ± 832.51	**0.002*** **
1st Feeding Initiation (ml)	53.91 ± 14.67	58.28 ± 13.83	**0.05***
1 min APGAR	6.45 ± 1.98	5.73 ± 2.22	**0.039** **
5 min APGAR	8.13 ± 1.27	7.65 ± 1.59	**0.046***

* p < 0.05 - ***p<0.001- statistically significant, ns- not significant, SD = Standard deviation

Table 3: Comparison of laboratory characteristics of the study group

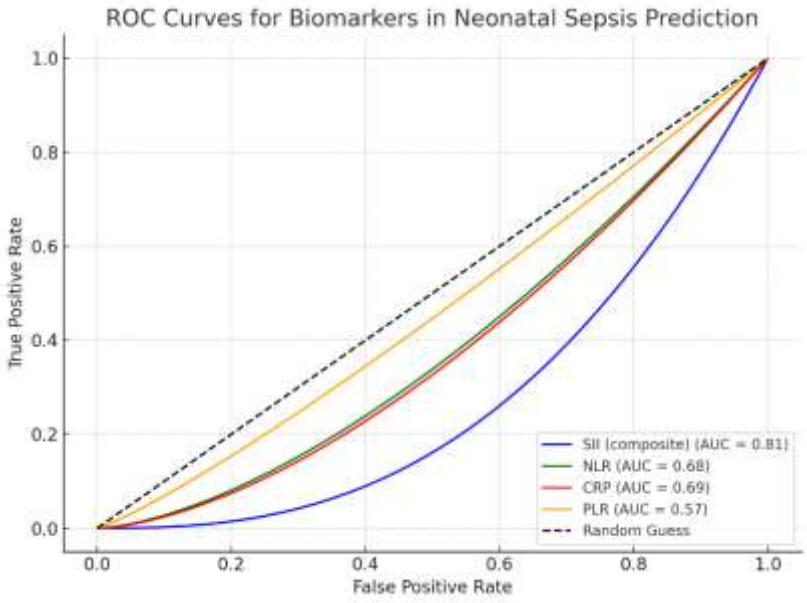
Characteristics study parameter	EOS group N =83	LOS N =64	p value
Hemoglobin in grams			
Mean ± SD	16.44 ± 3.05	13.27 ± 3.71	**0.000*** **
Median (IQR)	16.5 (04)	12.65 (4.825)	
Total leukocyte count cells /cumm			
Mean ± SD	12899.5 ± 6837.2	143800 ± 9350.08	0.269 (ns)
Median (IQR)	11710 (8145)	12320 (7137.5)	
Absolute Neutrophil Count			
Mean ± SD	7477.1 ± 5247.4	7261.2 ± 6738.67	

Median (IQR)	6480 (6740)	5380 (5550)	0.827 (ns)
Absolute Lymphocyte Count			
Mean ± SD	4265.1 ± 2216.2	5326.3 ± 3225.6	**0.020*** **
Median (IQR)	3982 (3075)	4710 (4798)	
Platelet count			
Mean ± SD	254493.9 ± 88538.5	276207 ± 182635	0.344 (ns)
Median (IQR)	271000 (107500)	261000 (206750)	
NLR ratio			
Mean ± SD	2.36 ± 2.55	1.84 ± 1.517	0.155 (ns)
Median (IQR)	1.81 (1.55)	1.385 (2.032)	
PLR ratio			
Mean ± SD	78.19 ± 56.92	70.70 ± 58.21	0.435 (ns)
Median (IQR)	63.7 (54.86)	52.07 (78.76)	
dNLR			
Mean ± SD	1.61 ± 1.38	1.21 ± 0.857	**0.045***
Median (IQR)	1.45 (0.987)	0.984 (1.27)	
NLPR			
Mean ± SD	212.31 ± 930.20	199.39 ± 486.91	0.920 (ns)
Median (IQR)	63.54 (68.85)	67.08 (144.756)	
CRP			
Mean ± SD	14.45 ± 32.83	35.53 ± 53.18	**0.004*** **
Median (IQR)	4.6 (8.4)	10.95 (39.57)	

Neonates with higher SII scores had significantly increased mortality and severe illness.

- **SII AUC for mortality:** 0.841 ($p<0.001$)
- **Optimal cutoff:** 19.8
  - Sensitivity: 81.2%
  - Specificity: 72.5%
- SII outperformed individual markers (NLR: AUC 0.648, CRP: 0.685, PLR: 0.516)
- Adjusted OR for SII > 19.8 = 5.3 (95% CI: 2.1–13.4)

Biomarker	AUC	Sensitivity (%)	Specificity (%)	Optimal Cutoff
SII (composite)	0.81	84.6	75.5	≥15
NLR	0.68	68.2	60.0	>1.52
CRP	0.69	70.3	64.7	>14.5 mg/L
PLR	0.57	51.2	56.8	>67.61



Discussion: This study demonstrates that a composite biomarker approach using SII provides superior predictive accuracy for adverse outcomes in neonatal sepsis compared to individual markers. By integrating CRP (acute phase reactant) with NLR and PLR (cellular inflammatory markers), the index reflects both immune cell imbalance and systemic inflammation.

CRP alone had moderate predictive ability (AUC = 0.69), consistent with prior neonatal studies【4,5】. NLR and PLR performed modestly, likely due to physiological variability and gestational influences【2,3】. The superiority of SII (AUC = 0.81) reflects synergy between these markers and justifies a composite score approach.

Several studies have supported the use of multi-marker approaches in neonatal sepsis. Topcuoglu et al. demonstrated improved diagnostic accuracy when CRP, IL-6, and neutrophil CD64 were used together【7】. Similarly, Guo et al. and Erdemir et al. showed that combining hematologic ratios like NLR and PLR with acute phase reactants improves diagnostic and prognostic value【8,9】. Hofer et al. validated the clinical application of combining procalcitonin, CRP, and IL-6 in early sepsis prediction【10】. More recently, Li et al. developed and validated a risk score combining routine lab markers including NLR and CRP, reinforcing the growing role of composite indices in neonatal sepsis risk stratification【11】.

The clinical utility of SII lies in its simplicity, accessibility, and ability to stratify risk early. In resource-limited settings where procalcitonin or IL-6 are not feasible, SII can guide triage, prompt escalation of care, or early referral.

Conclusion:
SII is a powerful, low-cost, and easily calculable predictor of neonatal sepsis severity. Further multicentric validation is recommended to implement this tool in clinical protocols

REFERENCES :

1. Gao J, et al. Neutrophil-to-lymphocyte ratio as a biomarker in neonatal sepsis: A meta-analysis. *BMC Pediatrics*. 2020;20(1):138.
2. Fan X, et al. Diagnostic value of PLR and NLR in neonatal infections. *J Matern Fetal Neonatal Med*. 2021;34(9):1387–1392.
3. Zahorec R. Ratio of neutrophil to lymphocyte counts—Rapid and simple parameter of systemic inflammation. *Bratisl Lek Listy*. 2001;102(1):5–14.
4. Pugni L, et al. Role of inflammatory biomarkers in diagnosing neonatal sepsis. *Neonatology*. 2018;113(4):339–346.
5. Kim J, et al. Use of inflammatory indices in neonatal sepsis prediction. *Front Pediatr*. 2022;10:834113.
6. Ranjit S, et al. Hematologic indices as predictors of neonatal sepsis. *Indian J Pediatr*. 2019;86(9):780–784.
7. Topcuoglu S, et al. Combined use of CRP, IL-6, and neutrophil CD64 improves early diagnosis of neonatal sepsis. *Pediatr Int*. 2020;62(6):714–721.
8. Guo J, et al. Neutrophil-to-Lymphocyte and Platelet-to-Lymphocyte Ratios as Predictors of Neonatal Sepsis: A Meta-analysis. *Front Pediatr*. 2022;10:851752.
9. Erdemir A, et al. Diagnostic Value of Neutrophil-to-Lymphocyte, Platelet-to-Lymphocyte, and CRP-to-Platelet Ratios in Neonatal Sepsis. *J Matern Fetal Neonatal Med*. 2022;35(2):338–344.
10. Hofer N, et al. Performance of combined biomarkers in neonatal early-onset sepsis diagnosis: A prospective multicenter study. *J Pediatr*. 2021;233:106–113.e4.
11. Li Y, et al. Development and validation of a clinical risk score using routine lab parameters for early identification of neonatal sepsis. *PLOS ONE*. 2023;18(1):e0280252.

.