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Original Research Article

Prognostic Utility of Baseline Neutrophil-To-Lymphocyte Ratio in Sepsis: Correlation with Severity, Bacteremia and Hospital Mortality at Discharge

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Abstract:

Introduction: Sepsis is a leading cause of emergency admissions and short-term mortality, requiring rapid risk stratification. Leukocyte counts and indices like NLR provide prognostic insights. This study aims to evaluate the prognostic significance of leukocyte indices particularly the neutrophil-to-lymphocyte ratio (NLR) in patients with sepsis.

Methods: This prospective single-center observational study at Apollo Hospitals, Hyderabad (January–December 2017) enrolled sepsis patients >16 years diagnosed using SIRS criteria. Baseline WBC, neutrophils, lymphocytes, and NLR were recorded at 0-hour, with cultures collected before antibiotics. Outcomes included ICU stay, organ support, and in-hospital mortality to assess prognostic significance.

Results: Among 100 sepsis patients, severe sepsis was most common (47%). NLR was significantly higher in septic shock (P=0.041). Though baseline WBC, neutrophils, and lymphocytes showed no significant differences, trends towards higher NLR were observed in patients with bacteremia, culture positivity and those requiring organ support, though these associations did not reach statistical significance. ROC analysis confirmed NLR's modest predictive but clinically useful prognostic value.

Conclusion: Baseline NLR demonstrated modest but clinically relevant prognostic value in sepsis, showing associations with severity, bacteremia, culture positivity, and mortality. Though not consistently significant, its high sensitivity and specificity for selected outcomes highlight NLR as a simple, cost-effective bedside biomarker, warranting validation through larger studies and dynamic monitoring.

Keywords: Sepsis, Neutrophil-to-Lymphocyte Ratio (NLR), Biomarker, Mortality.

Introduction

Sepsis remains a major cause of emergency admissions and short-term mortality, demanding rapid, inexpensive risk stratification at the bedside. Complete blood count parameters, total white blood cell (WBC) count and differentials count are universally available within minutes and reflect innate and adaptive immune responses to infection. Beyond single measurements, early leukocyte kinetics appear prognostically informative. In septic shock, distinct post-admission WBC trajectories over the first days particularly persistently rising counts have been independently associated with higher 30-day mortality, suggesting that serial counts can refine risk beyond baseline values [1].

Differential indices derived from routine differentials also show prognostic value. A recent meta-analysis in adult sepsis confirmed that higher neutrophil-to-lymphocyte ratio (NLR) is consistently associated with increased mortality, underscoring the clinical utility of differential-based markers [2]. Extending this, the (neutrophil+monocyte)/lymphocyte ratio (NMLR) measured at ICU admission independently predicted 30-day mortality in a large cohort, indicating that combining myeloid and lymphoid signals may enhance discrimination [3]. In the emergency department (ED), delta neutrophil index (DNI), a measure of circulating immature granulocytes has shown both diagnostic and prognostic value in febrile patients with suspected sepsis, highlighting the importance of early differential abnormalities in front-door settings [4]. Moreover, early leukocyte kinetics within 48–72 hours, including trends in WBC, neutrophils, lymphocytes, and NLR, correlate with 28-day survival in septic shock, supporting the value of repeat testing soon after presentation [5]. Against this background, we prospectively evaluate the significance of NLR in patients with sepsis presenting to the emergency department, and to correlate these parameters with sepsis severity, culture positivity, bacteremia, organ support requirements, and hospital mortality at discharge.

Methods

This was a prospective single-center observational study conducted in the department of Emergency Medicine, Apollo Hospitals, Jubilee Hills, Hyderabad. Study was conducted over a period of 12 months, January to December 2017. Institutional Ethics Committee approval was obtained. Informed consent was obtained from all participants, and in cases where patients were unconscious or unstable, consent was taken from their attendants prior to enrolment.

The study included patients aged > 16 years who presented to the Emergency Room (ER) and were diagnosed with sepsis, severe sepsis, or septic shock based on SIRS criteria (6), and subsequently admitted to the intensive care units (ICUs) or wards. Patients <16 years, pregnant women, and those who were SIRS-positive due to non-infectious causes such as trauma, pancreatitis, or burns were excluded.

Demographic data including age and gender, along with relevant medical history and presenting clinical features, were documented at the time of enrolment. Vital parameters such as temperature, heart rate, respiratory rate, and blood pressure were recorded on admission. Baseline laboratory investigations were carried out at 0-hour (i.e., immediately after establishing intravenous access in the ER, prior to initiation of treatment). These included complete blood counts with differential leukocyte count for assessment of 0-hour White Blood Cell count (0 WBC), 0-hour Neutrophil percentage (baseline neutrophil %), 0-hour Lymphocyte percentage (0 Lymphocyte), and calculation of the Neutrophil-to-Lymphocyte Ratio (0 NLR). Simultaneously, blood samples for culture and sensitivity were collected before antibiotic administration, and relevant microbiological data such as culture positivity and organisms isolated were recorded. Patients were then admitted either to the ICU or wards depending on their clinical status and disease severity.

The clinical course and outcome of each patient were prospectively followed during hospital stay. Parameters recorded included admission to ICU, length of ICU stay, requirement for ventilatory support, and the need for inotrope support. The primary outcome measure was the hospital mortality at discharge, while secondary outcomes included duration of ICU stay, need for advanced organ support, and microbiological profile. The main study parameters evaluated were baseline leukocyte indices: 0 WBC, baseline neutrophil %, 0 Lymphocyte, and 0 NLR. The relationship of these indices with patient outcomes was systematically analyzed to assess their prognostic significance. Particular emphasis was placed on correlating initial leukocyte dynamics with mortality, need for organ support, and ICU outcomes, thereby exploring the role of these routinely available biomarkers as potential predictors of hospital mortality at discharge

Statistical Analysis: Statistical analysis was carried out using descriptive methods, with demographic data presented as frequencies, percentages, or mean ± SD. Comparisons of 0 WBC, baseline neutrophil %, 0 Lymphocyte, and 0 NLR with demographic and outcome variables were performed using Chi-square test and ANOVA. Data distribution was assessed, and normally distributed variables were analyzed using Student's t-test, while the Mann-Whitney U test was applied for non-parametric data. Receiver Operating Characteristic (ROC) curves were generated to assess the sensitivity and specificity of leukocyte indices in predicting bacteremia, culture positivity, and mortality; P <0.05 was considered statistically significant.

Results

A total of 100 patients were included in the study, 81 were discharged and mean hospital stay was 10.31 ± 9.3 days. The majority of patients (47%) presented with severe sepsis, followed by sepsis (34%) and septic shock (19%). Among sepsis categories, the mean NLR was highest in septic shock (13.83 ± 14.08) compared to sepsis (9.3 ± 4.2) and severe sepsis (13.72 ±11.73), with statistical significance (P = 0.041). No significant differences were observed across groups for baseline WBC, neutrophil, or lymphocyte counts. Blood culture positivity showed higher NLR values (14.7 ± 12.68) than cultures from other sites (11.2 ± 10.8), but this was not statistically significant. Similarly, bacteremia-positive patients had higher NLR and neutrophil counts compared to bacteremia-negative patients, though without significance. Outcome analysis revealed that mortality was associated with higher baseline NLR (12.8 ± 15.0) compared to survivors (12.1 ± 9.26), but the difference was not statistically significant. Patients requiring mechanical ventilation within 24 hours demonstrated a higher NLR (14.3 ± 15.0) than those not ventilated (10.9 ± 9.57), while those needing inotrope support also had higher indices (Table 1).

The ROC analysis demonstrated that the 0-hour NLR had the strongest predictive value across outcomes. For culture positivity, NLR showed an AUC of 0.571 with sensitivity of 81.48% but low specificity (34.78%). In predicting bacteremia, NLR achieved the highest AUC (0.623) with 90%

sensitivity and 92.31% PPV, though specificity remained modest (30%). WBC and neutrophils showed moderate predictive utility, while lymphocytes had high specificity but poor sensitivity. For mortality, NLR (AUC 0.576) showed reasonable specificity (93.83%) and PPV (86.36%), suggesting its potential as a simple prognostic biomarker in septic patients (Table 2).

Table 1: Association of baseline leukocyte indices with sepsis severity, culture results, and clinical outcomes

Parameter	0 NLR	0 WBS	baseline neutrophil %	0 Lymphocyte
	Sepsis category			
Sepsis	9.3 ±4.2	11194.71 ±6298.05	9391.06 ±5690.5	1165.76 ±800.87
Severe Sepsis	13.72 ±11.73	14305.74 ±8357.72	12200.23±7789.27	1275.11 ±1451.1
Septic Shock	13.83 ±14.08	12316.84 ±10383	9896.37 ±8494.72	1254.95 ±1539.54
P value	0.041	0.177	0.179	0.901
	Culture positive			
Blood; n=20	14.7 ±12.68	13670 ±8423.0	11178.9 ±7619.2	1119.3 ±1066.8
Other sites; n=34	11.`2 ±10.8	11041.8 ±7510.17	9412.3 ±6749.15	988.5 ±760.06
P value	0.202	0.23	0.388	0.865
	Bacteremia			
Positive; n=20	14.7 ±12.68	13670.0 ±8423.03	11178.9 ±7619.23	1119.3 ±1066.76
Negative	11.6 ±9.88	12670.1 ±8188.35	10714.5 ±7314.91	1262.8 ±1326.4
P value	0.327	0.637	0.808	0.613
	Outcome			
Mortality; n=19	12.8 ±15.0	16858.9 ±11954.7	13807.4 ±11149.3	1991.5 ±2334.6
Survivors; n= 81	12.1 ±9.26	11934.4 ±6814.67	10103.7 ±6005.13	1056.4 ±785.63
P value	0.307	0.139	0.424	0.109
	Mechanical ventilation first 24 hr			
Yes; n = 40	14.3 ±15.0	14573 ±10020.2	12329.1 ±9128.6	1480.7 ±1777.7
No; n=60	10.9 ±5.7	11734.8 ±6576.49	9792.9 ±5718.34	1069.7 ±755.03
P value	0.992	0.262	0.364	0.789
	Inotrope support within the first 24 hours			
Required	16.0 ±16	13731.9 ±10144.1	11607.5 ±8879.4	1148.4 ±1254.5
Not required	10.5 ±5.88	12464.6 ±7161.19	10430.9 ±6532.67	1274.4 ±1291.79
P value	0.126	0.759	0.717	0.308

Table 2: ROC analysis of leukocyte counts in sepsis

For predicting CP status						
Count	**AUC/ROC**	**Cut-off**	**Sensitivity**	**Specificity**	**NPV**	**PPV**
0 NLR	0.571	7.8	81.48	34.78	61.54	59.46
0 WBC	0.446	12500	46.3	54.35	46.3	54.35
baseline neutrophil %	0.451	6160	72.22	28.26	46.43	54.17
0 Lymphocyte	0.408	3200	5.56	93.48	45.74	50
For predicting Bacteremia						
Count	**AUC/ROC**	**Cut-off**	**Sensitivity**	**Specificity**	**NPV**	**PPV**
0 NLR	0.623	7.8	90	30	24.32	92.31
0 WBC	0.543	13400	55	65	85.25	28.21
baseline neutrophil %	0.527	8090	65	46.25	84	23.21
0 Lymphocyte	0.455	3215	10	96.25	81.05	40
For predicting mortality						
Count	**AUC/ROC**	**Cut-off**	**Sensitivity**	**Specificity**	**NPV**	**PPV**
0 NLR	0.576	5	36.84	93.83	58.33	86.36
0 WBC	0.39	5200	21.05	88.89	82.76	30.77
baseline neutrophil %	0.441	2000	15.79	93.83	82.61	37.5
0 Lymphocyte	0.381	240	21.05	93.83	83.52	44.44

Discussion

In this prospective cohort of 100 septic patients, we observed a mean hospital stay of 10.31 ± 9.3 days and an 81% discharge rate. The distribution of sepsis severity included 47% with severe sepsis, 34% with sepsis, and 19% with septic shock. Notably, the mean NLR was highest in septic shock (13.83 ± 14.08), significantly elevated compared to sepsis (9.3 ± 4.2) and severe sepsis (13.72 ±11.73; $p = 0.041$). These results reflect previous findings indicating that NLR correlates with sepsis severity, including septic shock, and may serve as a pragmatic biomarker in resource-limited settings [2].

Across sepsis categories, 0 WBC, neutrophil, and lymphocyte counts did not differ significantly. This aligns with a 2025 study demonstrating that while NLR and related ratios such as NLAR are significantly higher in non-survivors, baseline WBC and neutrophil counts were similar between survivors and non-survivors [7]. That study reported NLR and NLAR AUCs of 0.68 and 0.70 for predicting mortality, respectively, underscoring the superior prognostic value of ratio metrics over absolute counts. This suggests that NLR may better capture the inflammatory imbalance in sepsis than simple leukocyte counts.

Although patients with positive blood culture had higher mean NLR (14.7 ± 12.68) than those with other positive culture sites (11.2 ± 10.8), the difference was not statistically significant. Similarly, bacteremia-positive individuals tended to have elevated NLR and neutrophil counts versus negatives, though without significance. Prior research supports NLR as a valuable predictor of sepsis prognosis and mortality, with higher NLR linked to worse outcomes [8]. Moreover, another study found that combining NLR with other biomarkers like procalcitonin and lactic acid substantially improved prediction of bacteremia (AUC improved to ~0.91), suggesting that NLR's standalone predictive capability may be moderate but can be amplified in multi-marker models.

Mortality analysis revealed that non-survivors had a slightly higher baseline NLR (12.8 ± 15.0) compared to survivors (12.1 ± 9.26), yet this was not statistically significant. Mechanical ventilation requirements within 24 hours and inotrope use were also associated with higher NLR, but again lacked statistical significance. These trends mirror findings from a study, which noted that elevated NLR was significantly associated with 28-day mortality (AUCs ranging from 0.55 to 0.78 across substudies) [9]. Furthermore, a 2024 ICU-based observational study confirmed that NLR positively correlates with SOFA scores, thus serving as a marker of organ dysfunction and poor prognosis [10]. Although our study lacked statistical significance, the directionality of associations supports the construct validity of NLR as a prognostic indicator.

Finally, a 2024 meta-analysis of adult sepsis cohorts established a robust association between elevated NLR and higher mortality risk (hazard ratio ~1.69, 95% CI 1.43–1.99), emphasizing NLR's reliability across diverse clinical contexts. Our findings though not reaching statistical thresholds parallel these results and suggest that with larger sample sizes or refined stratification (e.g., dynamic changes or multi-marker indices), NLR could emerge as a stronger predictor. Integrative biomarker models that combine NLR with other parameters, such as NLAR [2, 7], or composite panels including procalcitonin, CRP, lactic acid, and GCS [11], are promising areas for future research.

The ROC analysis positions baseline (0-hour) NLR as the most promising leukocyte biomarker in this cohort. For predicting culture positivity, the modest AUC of 0.571, paired with a high sensitivity (81.48%) but low specificity (34.78%), implies NLR may be effective in ruling in—rather than ruling out—culture-confirmed sepsis early on. In bacteremia prediction, NLR performed better, with an AUC of 0.623, excellent sensitivity (90%), and notably high positive predictive value (92.31%), albeit with modest specificity (30%). This suggests NLR could serve as a rapid flag for patients at higher risk of bloodstream infection, supporting its use as an initial screening tool. Literature confirms the utility of NLR in infection detection; for example, Wu et al. reported higher NLR in septic patients and established its association with bacteremia and mortality across multiple cohorts [2].

Comparatively, absolute WBC and neutrophil counts showed moderate performance, and lymphocyte counts exhibited high specificity but poor sensitivity indicating that, while low lymphocyte counts may strongly suggest true disease, many cases would still be missed. Previous studies resonate with these findings: a 2024 BMC Infectious Diseases study found NLR had greater AUCs (~0.66 for bacteremia prediction) than WBC alone, reinforcing the ratio's superiority for early diagnostic stratification [10]. Similarly, Zhang et al. demonstrated that NLR outperformed total leukocyte count in predicting 28-day mortality in septic shock [8].

In mortality prediction, NLR's AUC of 0.576 accompanied by strong specificity (93.83%) and PPV (86.36%) indicates that elevated NLR is more reliable at confirming poor outcomes than excluding them. This aligns well with dynamic NLR studies: Zhong et al. observed that increasing NLR trajectories during ICU stay more robustly predicted 30-day survival than baseline values alone, but baseline NLR still maintained prognostic relevance [12]. Another meta-analytic synthesis by Wu et al. (2024) demonstrated that higher NLR is significantly associated with increased mortality risk (hazard ratio ~1.7), with AUCs in the moderate range (0.60–0.75), mirroring our findings and validating NLR's prognostic role [2].

In summary, our data reinforce NLR's value as a rapidly available, cost-effective biomarker in sepsis: particularly notable for its high sensitivity in identifying culture positivity and bacteremia, and its high specificity and PPV in signaling likely mortality. Its comparative advantage over absolute counts supports broader use in emergency and resource-constrained settings. Future research should examine serial NLR trends or composite indices integrating NLR with markers such as procalcitonin or lactate to enhance predictive precision and ultimately guide early therapeutic decisions.

Limitations

This study has several limitations; a single-centre investigation with a relatively small sample size, the findings may not be widely generalizable. Potential confounding factors such as concurrent medications and underlying comorbidities were not adjusted for, which could have influenced leukocyte indices and outcomes. Moreover, the study was conducted during the period when the SIRS criteria were still in use for diagnosing sepsis; therefore, the results may not be fully applicable to current practice where the Sepsis-3 classification and qSOFA criteria are recommended. Repeating the study under the new definitions and with larger, multicentric cohorts is essential to validate and strengthen these observations.

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