Section: Medicine

Original Research Article

PROGNOSTIC ROLE OF NEUTROPHIL-TO-LYMPHOCYTE RATIO IN SEPSIS

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ABSTRACT

Background: Sepsis is a life-threatening inflammatory response to infection associated with significant morbidity and mortality. Early diagnosis and risk stratification are crucial. The neutrophil-to-lymphocyte ratio (NLR), an easily accessible and cost-effective inflammatory marker, has been proposed as a potential prognostic tool. This study aimed to evaluate the role of NLR as both a diagnostic and prognostic marker in the early and late phases of sepsis and to compare its performance with the qSOFA score. **Materials and Methods:** This observational study was conducted at Teerthanker Mahaveer Medical College and Research Centre over 12 months. A total of 150 patients diagnosed with sepsis, aged over 18 years, were included. NLR was calculated on Day 1 and Day 5 of admission. Simultaneously, qSOFA scores and relevant biochemical parameters were recorded and compared. The sensitivity of SIRS criteria and qSOFA score in relation to NLR was analyzed. **Result:** The study population was evenly distributed across age groups, with a slight male predominance. NLR was elevated (>9) in all sepsis patients based on SIRS criteria. However, a significant number of non-septic patients also had NLR >9, indicating high sensitivity but low specificity. Patients with NLR >25 showed significantly higher total RBC count and lower absolute lymphocyte count. From Day 1 to Day 5, significant improvements were observed in respiratory rate, temperature, heart rate, WBC count, neutrophil count, and SIRS score, alongside a marked reduction in NLR and increase in lymphocyte count. The qSOFA score also showed significant improvement, except for mental status, which remained unchanged. **Conclusion:** NLR is a sensitive marker for diagnosing sepsis and monitoring treatment response, though not highly specific. SIRS criteria were more sensitive than qSOFA for detecting sepsis. The study supports the clinical utility of NLR as a rapid, low-cost adjunctive tool in the management of septic patients, especially in resource-limited settings.

INTRODUCTION

Sepsis is a potentially-fatal, inflammatory condition incited by the reaction of immune system's for infection characterized by physiological, pathological, and biochemical abnormalities.[1] The current definition of sepsis is a potentially fatal organ failure brought on by an abnormal host reaction to an infection. Sepsis accompanied with malfunction in the circulatory, cellular, and metabolic systems is known as "septic shock," and it is linked to an increased mortality risk.[2]

Sepsis can be the consequence of community-acquired or hospital- acquired infections. More than 80% of sepsis cases are caused by infections of the skin or soft tissues, gastrointestinal tract, genitourinary system, or respiratory tract.[3] 1% of sepsis cases are caused by indwelling devices, endocarditis, meningitis, or encephalitis.[4] Sepsis is most often caused by pneumonia.[5]

Gram-positive [47%] or gram-negative [62%] bacteria are the most frequent pathogens that cause sepsis.[4] Numerous microorganisms are present in the sepsis patients. Fungal, viral, or parasite infections are present in a tiny percentage of sepsis patients. Blood culture examinations are the conventional method for diagnosing sepsis, although they are time-consuming and produce low results. Numerous biomarkers for sepsis diagnosis have been created. One of them is procalcitonin (PCT). Although considered a better marker of sepsis, PCT is relatively high cost and is not readily available in

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many hospitals.[6] The clinical presentation of sepsis depends on the site of the infection. Common presentations are usually nonspecific and include malaise, fever (sometimes hypothermia), tachycardia, tachypnea, or altered mental status. Arterial hypotension can also be present.[7]

A natural reaction of the immune system to systemic inflammation is a rise in neutrophil counts and a corresponding drop in lymphocyte counts in the blood. When compared to a non-inflammatory condition, this shows the dynamic alterations and modulation of apoptosis in a state of systemic inflammation.[8]

In the recently published medical literature, lymphocytopenia & neutrophil-lymphocyte ratio (NLR) has been reported to be superior in predicting bacteremia than conventional infection markers such as leukocyte count, neutrophil count and C-reactive protein (CRP) in emergency patients.[9]

The NLR is a straightforward ratio that can be calculated by dividing the patient's total blood count as the numerator by the total number of lymphocytes, which is the denominator. As a result, every circumstance that modifies the counts will also modify the ratio, which may rise or fall. The ratio shows the person's inflammatory state, or the inflammatory response mediated by cells.

An early diagnosis of sepsis is imperative for decreasing sepsis- related morbidity and mortality. Hence, this study aimed to evaluate neutrophil-to-lymphocyte ratio (NLR) as prognostic marker for early and late phase of sepsis.[10]

Aim

- To evaluate neutrophil-to-lymphocyte ratio (NLR) as prognostic and diagnostic marker in early and late phase of sepsis

Objectives

- To calculate NLR on day 1 and day 5 in all patients.
- To calculate qSOFA score in each patient.
- To compare NLR with qSOFA score.

MATERIALS AND METHODS

Study Design and Place

This observational, hospital-based study was carried out at Teerthanker Mahaveer Medical College and Research Centre.

Study population

Patients aged >18 years admitted to Teerthanker Mahaveer Medical College and Research Centre with the diagnosis of sepsis.

Study period: The period of study was 12 months following approval from College Research Committee and the Institutional Ethics Committee.

Sample size

A total of 135 newly-diagnosed cases of sepsis fulfilling inclusion and
exclusion criteria.

Interpretation of NLR

Some study has identified that the normal NLR value in an adult, non- geriatric, population in good health is between 0.78 and 3.53. NLR may be calculated using either absolute cell counts or percentages, as shown below:

Calculation of NLR:

$$NLR = \frac{\text{Absolute \# Neutrophils}}{\text{Absolute \# Lymphocytes}} = \frac{\text{Relative \% Neutrophils}}{\text{Relative \% Lymphocytes}}$$

RESULTS

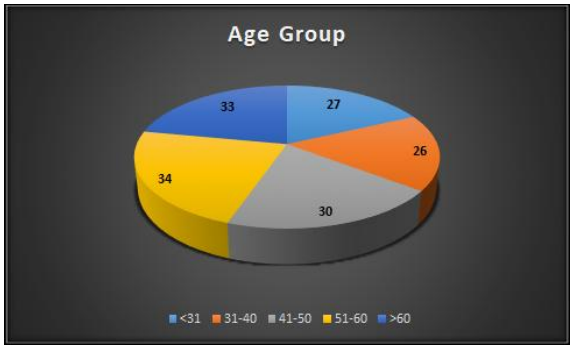

Figure 1: Distribution of Study group based on age-group

The table and figure show homogeneous distribution of our study group in all age-groups.

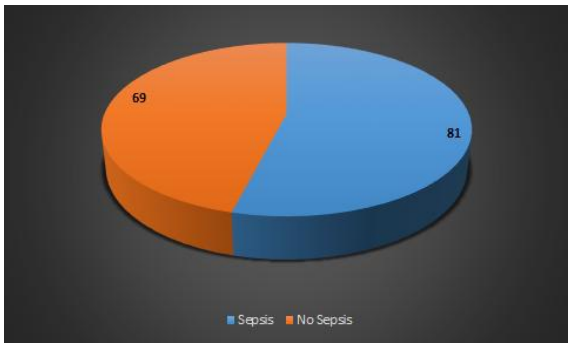

Figure 2: Distribution of Study group based on SIRS at Day 1

Table 1: Distribution of Study group based on age-group.

Age Group	Frequency	Percent
<31	27	18.0
31-40	26	17.3
41-50	30	20.0
51-60	34	22.7
>60	33	22.0
Total	150	100.0

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Table 2: Distribution of Study group based on SIRS at Day 1.

SIRS (Day 1)	Frequency	Percent
Sepsis	81	54.0
No Sepsis	69	46.0

[Table 2] shows slight preponderance of patients with sepsis in our study group.

Table 3: Distribution of Study group based on SIRS criteria and qSOFA score.

SIRS (Day1)	qSOFA (Day1)		Total
	Sepsis	No Sepsis	
Sepsis	38	43	81
No Sepsis	29	40	69
Total	67	83	150

[Table 3] shows the relationship of SIRS criteria and qSOFA score in our study group. It is evident greater number of patients had sepsis based on SIRS criteria rather than qSOFA score (81 vs 67).

Table 4: Distribution of Study group based on SIRS criteria and NLR.

NLRGrp_Day1	SIRSGrp_Day1		Total
	Sepsis	No Sepsis	
9 to 25	35	34	69
>25	46	35	81
Total	81	69	150

[Table 4] shows the relationship of SIRS criteria and NLR in our study group. It is evident all patients with sepsis based on SIRS criteria (81/150) had NLR>9. However, a significant number of patients (69/150) that did not have sepsis also had NLR>9.

Table 5: Distribution of Study group based on Characteristics & qSOFA score of 2 & 3 on Day 1

Characteristic	qSOFA SCORE=2		qSOFA SCORE=3		p-value
	Mean	SD	Mean	SD	
T. Bilirubin	2.27	4.07	1.62	3.52	0.300
SGPT	54.28	74.15	50.70	64.48	0.757
SGOT	65.32	103.42	60.02	69.89	0.720
S. Urea	61.49	54.78	63.14	81.00	0.883
S. Creatinine	1.96	3.50	4.92	19.12	0.168
S. Sodium	137.11	6.23	135.05	16.21	0.289
S. Potassium	4.62	4.70	4.26	1.02	0.541
S. Chloride	103.31	17.81	102.95	11.96	0.887

[Table 5] shows that the difference in the level of various biochemicals based on qSOFA score on Day 2 & Day 3 was not significant. This may be probably related to successful management of patients.

Table 6: Distribution of Study group based on Characteristics with SIRS criteria and qSOFA score

qSOFA Score							
Total Score (SIRS)	2		3		4		p-value
on Day 1	Mean	SD	Mean	SD	Mean	SD	
T. Bilirubin	2.42	4.95	1.79	2.85	1.22	1.43	0.366
SGPT	39.81	52.94	63.63	90.96	64.19	51.18	0.112
SGOT	52.96	65.14	70.95	116.24	72.62	80.61	0.455
S. Urea	66.93	79.00	61.02	60.82	52.04	42.85	0.634
S. Creatinine	4.04	14.78	3.20	13.78	1.35	1.06	0.680
S. Sodium	137.77	5.45	134.17	17.87	136.34	5.45	0.237
S. Potassium	4.17	0.85	4.13	1.07	5.99	8.41	0.061
S. Chloride	104.87	18.44	101.15	12.11	102.87	12.65	0.409

[Table 6] shows the relationship of various characteristics with SIRS on Day 1 with qSOFA score of 2-4. It is evidence from the table the none of the characteristics revealed statistically significant difference.

Table 7: Distribution of Study group based on Characteristics with qSOFA score & SIRS criteria on Day 1 & 5

Characteristic	DAY 1		DAY 5		p-value
	Mean	SD	Mean	SD	
qSOFA SCORE	2.45	0.50	0.11	0.32	<0.001
Respiratory rate >22	25.19	2.12	17.63	1.50	<0.001
Change in mental status	11.80	2.63	11.52	0.86	0.212
Systolic blood pressure <110mmhg	106.35	14.96	127.25	11.80	<0.001

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SIRS	2.71	0.74	0.55	0.50	<0.001
Temp <36 or >38(Celsius)	37.94	1.40	37.04	0.61	<0.001
Heart rate >90 (beats/mint)	98.55	10.13	77.09	7.02	<0.001
WBC Count<4000 or >12000	12359.65	8512.34	7495.65	1690.29	<0.001
Respiratory rate >20(breaths/mint)	25.19	2.12	17.63	1.50	<0.001
Total leukocyte count	12359.65	8512.34	7495.65	1690.29	<0.001
Absolute neutrophil count	11452.73	8011.36	5905.35	1383.75	<0.001
Absolute lymphocyte count	439.74	363.25	1290.48	320.51	<0.001
Neutrophil/Lymphocyte ratio	29.41	11.68	4.62	0.56	<0.001

[Table 7] shows that qSOFA score in our study was significant lower on day 5 with significant improvement in respiratory rate signifying improvement. However, no change in mental status was noted. It is also evident from the table that SIRS score, temperature, heart rate, WBC count and respiratory rate reduced significantly from day 1 to day 5 signifying clinical improvement. Similarly, TLC & absolute neutrophil count reduced while absolute lymphocyte count improved from Day 1 to day 5 signifying improvement in clinical condition.

DISCUSSION

Patients in our research showed a homogenous distribution, had a mean age of 47.49+16.5 years. there was a little male predominance (83 men vs. 67 women). Our study group had slight preponderance of patients with sepsis as per SIRS criteria (81 sepsis vs 69 no-sepsis) with majority (81/150) of patients with NLR>25 without any patient with NLR<9. Sosrohandoyo SU, et al,[6] (2021) also concluded that there is no correlation between NLR and procalcitonin levels, latter being a strong marker for sepsis.

This is similar to our study, where approximately 69/150 (46%) patients without sepsis also had raised NLR. The mean blood levels of potassium, sodium, and chloride were all within normal ranges, however our mean total bilirubin was slightly over normal. Mean SGPT, SGOT, and S. Urea, however, were marginally above the usual range.

In our study, greater number of patients had sepsis based on SIRS criteria rather than qSOFA score (81 vs 67) with NLR>9 in all patients with sepsis based on SIRS criteria. However, a significant number of patients (69/150) that did not have sepsis also had NLR>9.

Rehman FU, et al,[11] (2020) concluded that NLR ratio is not only an inexpensive & rapidly-available marker for sepsis but also has a strong correlation with other expensive markers of inflammation & sepsis.

Based on the qSOFA score on Days 2-4 of our investigation, no significant differences were seen in the levels of several biochemicals and clinical indicators, most likely indicating effective patient treatment.

Lorente L, et al,[12] (2022) found that NLR levels were highly correlated with both the diagnosis of sepsis and the use of SOFA to control mortality during those days. This is consistent with our study's findings, which showed that increased NLR on the first day of sepsis Out of all the features, patients with NLR>25 had a substantially higher total RBC count than those with NLR<25. In the NLR>25 group, the absolute lymphocyte count was also much lower, indicating a severe suppression of the lymphocyte lineage. Significant improvement was noted in respiratory rate on day 5 in our study group without any significant change in mental status. Our study group also revealed that SIRS score, temperature, heart rate, WBC count and respiratory rate reduced significantly from day 1 to day 5 signifying clinical improvement. Similarly, TLC & absolute neutrophil count reduced while absolute lymphocyte count improved from Day 1 to day 5 signifying improvement in clinical condition. Khaled Ali Esmaeil Ali Shalaby et al,[13] (2022) concluded that cut-off value of 10 for NLR can be used as an inexpensive and rapidly available tool for predicting sepsis showing a strong correlation with variety of score for ICU severity including SOFA. In our study where all patient's with sepsis had NLR>9.

CONCLUSION

Based on the observations of our study, we can conclude the following:

- SIRS criteria are more sensitive than qSOFA score for the diagnosis of sepsis and it correlates well the with NLR.
- Patient with sepsis have deranged SGOT, SGPT, S Urea and S. Creatinine, with S. Creatinine being significant higher above the normal range.
- NLR>9 is highly sensitive for sepsis but not specific.
- Total RBC count is significantly higher in patients with NLR>25 than with.
- The absolute lymphocyte count is significantly lower with NLR>25 than with NLR<25.
- SIRS score, temperature, heart rate, WBC count and respiratory rate improves with resolution of sepsis. Similarly, TLC & absolute neutrophil count reduce while absolute lymphocyte count increases with resolution of sepsis.

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