Neutrophil to Lymphocytic Count and SOFA Score as Prognostic Marker in Patient With Sepsis

Prasanna Rajbhandari,[1] Yagya Laxmi Shakya,[2] Anup Raj Upreti[3]

[1] Department of General Practice and Emergency Medicine, IOM, TUTH
[2] Department of General Practice and Emergency Medicine, IOM, TUTH
[3] Clinical Pharmacist, Nepal Medical College

ABSTRACT

Introduction: Neutrophil-to-lymphocyte ratio is calculated from the white cell differential blood count, a marker that has been used as a prognostic index when assessing patients suffering from several clinical syndromes, including sepsis. The aim of this study was to find out the relationship between Neutrophil-to-lymphocyte ratio and the commonly used severity score of SOFA in a population of emergency admitted adult patients with sepsis as prognostic marker in a tertiary center.

Methods: This observational analytical study was conducted in the Emergency Department of the Tribhuwan University Teaching Hospital based on data extracted from 155 patients consecutively enrolled, suffering from sepsis of multiple origin. The study period was from June 2017 until August 2017. Neutrophil-to-lymphocyte ratio and SOFA score were calculated as prognostic marker in septic patients upon hospital admission.

Results: Out of 144 patients included in the study, mean age of patients was 51.02 ± 20.96, among which 144 (32.6%) were male and 144 (67.3%) were female, most common source of infection was respiratory system in 45 patients followed by gastrointestinal system in 38 patients , the overall 28 day mortality was observed in 144 (22.92%). There was a strong correlation between SOFA score and NRL (p < 0.05). The sensitivity of NRL was 78.8% and specificity 73.9% at a cut off value of 8.75 and sensitivity of SOFA was 84.8% and specificity 73% at a cut off value of 6.5.

Conclusions: The Neutrophil-to-lymphocyte ratio and SOFA score both proved to be similar as a simple infection marker with discriminatory capacity in predicting prognosis in infectious admissions.

Keywords: neutrophil-to-lymphocyte ratio; prognosis; sepsis; SOFA score.

INTRODUCTION

Sepsis has been called "one of the oldest and most elusive syndromes in medicine". Despite advances in care, existing epidemiologic studies suggest that sepsis remains a huge burden across all economic regions. More than 650,000 cases of sepsis are diagnosed annually. Sepsis occurs in approximately 2 percent of hospitalized patients and up to 75 percent of ICU patients, with a mortality rate of 20 to 50 percent.[1]

Sepsis is a complicated condition and still a big challenge to both the developed and developing world. Various Studies have found that one of the fundamental principles for the appropriate management of sepsis is early and accurate detection of the patients at high risk for death. This is generally dependent on the application of scoring systems. Although various clinical biomarkers are widely explored, only a few have been currently applied in the clinical practice. Furthermore, calculation of SOFA or Neutrophil to lymphocyte ratio could be more economic and easily calculated compare to available scoring system.

Correspondance:

Dr. Prasanna Rajbhandari,
Department of General Practice and Emergency Medicine,
IOM, TUTH
Email: prasnarb@gmail.com
Phone: 9803328287

Hence, the objective of this study is to determine neutrophil to lymphocyte ratio and SOFA score as prognostic marker in patients with sepsis.

METHODS

This was an prospective observational hospital based study conducted at Emergency room of Tribhuvan University Teaching Hospital, Maharajgunj from June 2017 to August 2018, on 155 patients of age >18 years, obtained by purposive sampling, who had presented with suspected infection. Patients with suspected infection with sepsis were taken into study after written/oral consent and followed up by phone calls at 28-day for outcome. Total of 144 patients were enrolled into study after considering the inclusion and exclusion criteria. Ethical clearance was received from Institutional Review Board, Institute of Medicine, Tribhuvan University.

Patients who are greater than 18 years who presented to TUTH emergency and patient diagnosed to have sepsis using qSOFA scores with or without positive blood culturewere included in study and patients with hematological malignancies, who received blood transfusion, left treatment, incomplete information and data and who deny consent were excluded from study.

Sample size was calculated using formula:

Sample size (n) = Z2p(1-p)/d2

Where,

Z= Confidence Interval, 1.96

P= expected proportion in population based on previous studies=10.49%

D= absolute error or precision, 5%

One hundred and forty four patients with suspected infection and hence sepsis suggested by qSOFA score were enrolled into the study after getting formal written consent from patient or legal guardian available at the Emergency room. Sampling was non probability and purposive. Patient's basic demographic information, vital signs on ER arrival, symptoms and underlying diseases, provisional diagnosis and laboratory values required for analysis of Neutrophil to lymphocytic ratio(NLR) and SOFA score were collected, as mentioned in Pro-forma (Annex-1). Outcome of patients were followed by phone calls made at 28-day from the day of ER admission. Collected data were then analyzed. Data collection was done by researcher.

As soon as completion of filling questionnaires, they were checked for correctness and completeness. Data obtained were entered into Microsoft Excel Program. SPSS version 20 was used for analysis. Descriptive statistics (percentage, mean, SD) were used to determine the difference between two groups. Level of significance for all analytical test was set 0.05 and p value < 0.05 was considered significant. Spearman's correlation analysis was done to correlate Neutrophil to lymphocytic ratio and SOFA score. ROC curve was drawn for Neutrophil to lymphocytic ratio and SOFA score to calculate sensitivity and specificity.

RESULTS

Mean and Dispersion of Different Variables

	Mean	S. D	Min	Max
Temperature	99.4333	2.06408	95.00	105.00
Systolic BP	84.51	21.705	60	160
Diastolic BP	52.08	14.622	30	90
Heart Rate	98.23	19.065	58	154
Respiration Rate	25.69	6.600	14	60
Saturation	86.86	8.934	58	99
Glassgow coma scale	14.22	2.012	4	15
Arterial PH	7.3786	.11911	6.80	7.54
Partial pressure of oxygen	81.0322	34.58990	27.00	235.00
Partial Pressure of carbondioxide	25.1549	7.94572	10.90	59.20
Bicarbonate	15.7854	5.15311	2.30	38.10
Blood glucose	7.4271	4.15844	2.40	27.80
Serum Sodium	135.1875	7.32461	114.00	148.00

Serum Potassium	4.0257	.88818	2.30	7.00
Serum Creatinine	204.2256	230.46684	12.00	1033.00
Serum urea	13.0729	11.21660	2.60	49.00
Total count	14105.35	9520.689	1690	45000
Neutrophil	80.22	11.299	45	95
Lymphocyte	16.01	9.388	3	45
Neutrphil lymphocyte ratio	7.9668	5.17203	1.00	31.66
Platelet Count	199437.50	159419.126	13000	831000
Pao2/Fio2 ratio	394.7639	165.82359	129.80	1124.00
Mean Arterial Pressure	63.0895	16.22768	43.00	107.00
Bilirubin	37.2028	53.39321	3.00	421.40
SOFA Score	5.6111	2.88015	1.00	14.00

Table 1. Table showing mean and dispersion of different variables.

Correaltion Between SOFA and NLR

Correlations Between SOFA and NLR				
			SOFA Score	NLR
Spearman's rho	SOFA Score	Correlation Coefficient	1.000	.530**
		Sig. (2-tailed)	.	.000
		N	144	144
	Neutrphil lymphocyte ratio	Correlation Coefficient	.530**	1.000
		Sig. (2-tailed)	.000	.
		N	144	144
**. Correlation is significant at the 0.01 level (2-tailed).				

r=1 , n= 144, p-value= 0.00

Table 2. Table shows the significant correlation between SOFA score and Neutrophil to lymphocyte ratio (P < 0.001).
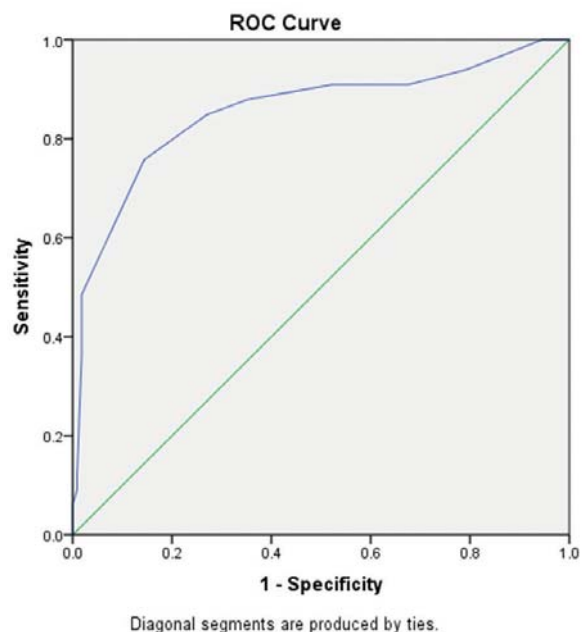
ROC Curve (NLR & Outcome)
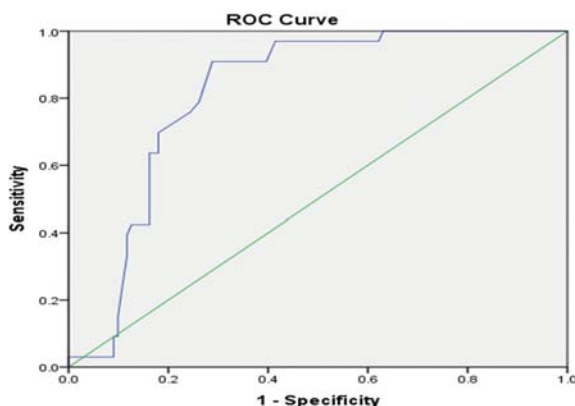
NLR and Outcome

AUC	Std. Error	Sensitivity	Specificity	Cut off Value
0.815	0.36	78.8%	73.9%	8.75

As illustrated by the receiver operating characteristics (ROC) curve, the highest sensitivity and specificity of NLR was found at cut off value of 8.75 with area under the curve of 0.815 which is significant. Area under the curve is related to overall ability of a test to correctly identify normal versus abnormal. The more the value of area under the curve is towards 1, the more accurate diagnostic performance the test has. The area of 0.815means that on average, a patient will have chance of more abnormal test result than 81.5% of control.

ROC curve (SOFA & Outcome)

Diagonal segments are produced by ties.

SOFA and Outcome

AUC	Std. Error	Sensitivity	Specificity	Cut off Value
0.856	0.44	84.8%	73%	6.5

As illustrated by the receiver operating characteristics (ROC) curve, the highest sensitivity and specificity of SOFA was found

at cut off value of 6.5 with area under the curve of 0.856 which is significant. Area under the curve is related to overall ability of a test to correctly identify normal versus abnormal. The more the value of area under the curve is towards 1, the more accurate diagnostic performance the test has. The area of 0.856means that on average, a patient will have chance of more abnormal test result than 85.6 % of control.

DISCUSSION

One of the methods for predicting prognosis in sepsis patients is SOFA score. Neutrophil-to-lymphocyte ratio (NLR) as calculated from the white cell differential blood count is a marker that has been used as a prognostic index when assessing patients suffering from several clinical syndromes, including sepsis.

In my study the male population 47 (32.6%) was less than the female population 97 (67.3%) in total cohort and was not comparable to the study by Glickman et al. and contradicting the theory.[2] Bernato et al has shown that incidence increases with age which holds true in our study too but in contrary, there is female predominance in the older age group.[3]

Regarding the locality of the patients, in my study majority of the patients were from Kathmandu followed by Dhading. The reason behind may be because the site of study was in Kathmandu and for people from Dhading it is nearest possible tertiary center. The most common source of infection was respiratory system (45 out of 144) and the gastrointestinal (38 out of 144), the unknown source (18 out of 144) and genitourinary (17 out of 144) in order. As compared to the Glickman et al where pulmonary system (34%)was the most common one to be affected, and then the genitourinary(14%) and then gastrointestinal system(10%).[2]

In our study the mortality was 22.92 %. The mortality was calculated on the basis of 28 days followup. In contrast, a study done in one of private hospital of Nepal showed overall mortality from sepsis as 39.3%.[4]

Various variables were also taken into consideration during my study. Those variables were temperature (Mean =99.43), systolic BP (mean =84.51), diastolic bp (mean = 52.08), hear rate (mean = 98.23), Respiration rate (mean = 25.69), saturation (mean = 86.86), Glasgow coma scale (mean = 14.22), arterial PH (mean =7.37), partial pressure of oxygen (mean = 81.03), Partial pressure of carbon dioxide (mean =25.15), bicarbonate (mean = 15.78) , blood glucose (mean = 7.42), Serum Sodium (mean = 135.1875),Serum Potassium (mean = 4.0257),Serum Creatinine (mean = 204.2256), Serum urea (mean = 13.0729) Total count (mean = 14105.35) Neutrophil lymphocyte ratio (mean = 7.9668), Platelet Count (mean = 199437.50), Pao2/Fio2 ratio (mean = 394.7639), Mean Arterial Pressure (mean = 63.0895) Bilirubin (mean = 37.202), SOFA Score (mean = 5.6111). One of the study suggest that white blood cell counts, neutrophil counts, and C-reactive proteins did not differ significantly between septicemia and the other bacterial infection groups. (16) Also, in a study done in patients admitted in Critical Care Medicine Department in Alexandria Main University Hospital , the author concluded that NLR values were more strongly significant in patients with sepsis and severe sepsis than the values of classical parameters; such as CRP, WBCs, serum lactate, neutrophelia and lymphocytopenia. Therefore, our study aims to correlate NLR and SOFA score in patients with sepsis.[1]

In our study there was a strong correlation between SOFA score and NLR (P-value< 0.005). The result of my study was supported by one of the prospective observational studies was conducted in the Emergency Department of the University Hospital of Patras, Greece, which concluded that there was a Correlation between neutrophil-to-lymphocyte ratio and severity scores in septic patients upon hospital admission.[5]

Our study calculated the sensitivity of NLR which was 78.8% and specificity 73.9% at the cut off value of 8.75. In the study done done

in patients admitted in Critical Care Medicine Department in Alexandria Main University Hospital, the author concluded the sensitivity and specificity of NLR in the present study were 88.0 and 75.0% respectively.[1] In similar study done by de Jager et al sensitivity and specificity was 77.2% and 63% as a predictor of bacteremia in Emergency care.6 In one of the study done in emergency department in various hospital in U.K. in adult patients presenting with pyrexial illness ,the sensitivity and specificity of NLR for predicting bacteraemia were 70% (64% to 75%) and 57% (55% to 60%), respectively.[7]

Our study also calculated the sensitivity of SOFA which was 84.8% and specificity 73% at the cut off value of 6.5. However, in the prospective observational cohort study done in the emergency department by Baig M A et al. it was concluded that SOFA score was 71% sensitivity and 57% specificity. The limitations of the study were single center study so cannot be generalized with interpersonal variation in measurement of vital sign. Daily calculation of SOFA score and NLC ratio to predict outcome of prognosis is not taken into account.

CONCLUSIONS

SOFA was calculated for each patient and NLR was positively correlated with the sepsis severity prognostic score on admission. NLR is an easily calculated, cost-efficient index that could be used as a tool for clinicians when assessing sepsis patients in the Emergency Department. Although NLR measurement is simple, and rapidly available, future and larger prospective studies are warranted to confirm its definite value as a prognostic index in sepsis patients.

CONFLICT OF INTEREST: None.

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