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Neutrophil -To- Lymphocyte Ratio [NLR] as A Promising Prognostic Marker in Critically Ill Septic Patients

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ABSTRACT

Background: NLR is advantageous in regard to simplicity, low cost, and availability compared to many other previously proposed biomarkers, which makes it promising for diagnostic clinicians. Several studies have reported that the NLR is useful in various clinical situations.

Objective: To determine whether NLR obtained from complete blood count (CBC) and with simple calculation can be used to predict mortality in patients with sepsis and septic shock in the ICU in comparison with intensive care unit (ICU) severity scores.

Patients and methods: This prospective trial was carried out on 84 ICU cases with severe sepsis, who were admitted to Specialized Medical Hospital ICUs from June 2020 to June 2021.

Results: There was statistically significantly higher systolic blood pressure (mmHg), mean arterial pressure, rate pressure product *10^3, EF, INR, RBS, PH, HCO_3, L *10^3, platelet count, CRP on admission, ABACHEII score, SOFA score on admission, duration of hospital stay (days), and a statistically significantly lower age (years), diastolic blood pressure (mmHg), heart rate, respiratory rate (RR), GCS, serum creatinine (mg/dl), serum albumin, serum bilirubin, Na, K, total leucocytic count *10^3, N *10^3, in group B NLR >10 vs. group A NLR≤ 10.

Conclusion: Neutrophil to lymphocyte ratio is a cheap and rapidly available predictor of sepsis and has shown a significant correlation with other relatively expensive and non-rapidly existing markers of inflammation and sepsis with comparable efficacy with ICU severity scores [SOFA and APACHE II].

Keywords: ICU, Neutrophil-to-lymphocyte ratio, Sepsis.

INTRODUCTION

Sepsis is a major cause of morbidity and mortality resulting from a devastating host response to the infection, and it affects millions of people worldwide each year. As per the recent advances in the knowledge about the disease and the critical care modalities, the short-term mortality rate in patients with severe sepsis and septic shock remains high accounting for ~30%[(1)].

Despite recent advances in knowledge about the disease and critical care modalities, the short-term mortality rate in patients with severe sepsis and septic shock remains high, accounting for approximately 30% of all cases [(2)].

Although various clinical biomarkers are widely explored, only a few have been currently applied in the clinical practice. Therefore, the search continues for preferable infection markers that may facilitate the prognosis prediction of sepsis in critically ill patients [(3)].

Acute physiological and chronic health evaluation II (APACHE) and sequential organ failure assessment (SOFA) scores are well known mortality predictors in ICU patients with sepsis. SOFA and APACHE II scores are calculated to assess disease severity, treatment response, and risk of mortality in the ICU, and these are not easy to calculate at the bed side in daily practice [(4)].

There are some inflammatory markers, such as the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR), that are used to assess treatment response in sepsis patients for their simplicity [(4)]. Neutrophil to lymphocyte ratio calculated from white cell differential count provides a rapid indication of the extent of an inflammatory process. Immunocompetent white blood cell populations play an important role in the systemic inflammatory response to infection [(5)].

Neutrophilia is well recognized as infection marker whereas the clinician is less familiar with absolute lymphocytopenia (lymphocyte count below 1.0×109/l) as a possible marker in infectious disease management. Combining both parameters seems a logical step and the ratio of neutrophil and lymphocyte counts is increasingly used in several clinical circumstances [(5)].

The neutrophil-to-lymphocyte ratio (NLR), as a readily accessible biomarker, can be calculated based on a complete blood count. Although a growing body of evidence has shown that NLR is proposed as an independent predictor of poor survival in various clinical critical illness circumstances ranging from oncological patients to patients with cardiovascular diseases [(6)].

There is no consensus about the relationship between NLR levels and clinical prognosis in patients with sepsis until now. In the context of infection, researchers in a recent study showed a reversed NLR evolution according to the timing of death [(7)], whereas some other studies suggested that NLR was not associated with mortality in patients with sepsis [(8)].

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The aim of the present study was to determine whether NLR obtained from CBC and with simple calculation can be used to predict mortality in patients with sepsis and septic shock in the ICU in comparison with ICU severity scores.

PATIENTS AND METHOD

This prospective trial was carried out on 84 ICU cases with severe sepsis. Who were admitted to Specialized Medical Hospital ICUs from June 2020 to June 2021.

Inclusion criteria: Age of at least 18 years' old, and patient who were admitted to ICU with sepsis due to one of the following: (a) Community acquired pneumonia. (b) Hospital acquired pneumonia. (c) Ventilator associated pneumonia. (d) Acute pyelonephritis, intra-abdominal infections or primary bacteremia.

Exclusion criteria: Age under 18 years' old, patients who did not provide research authorization, patients with hematological, and non-hematological end stage malignancy, patients with immunosuppressive disease including HIV infection, patients receiving immunosuppressive therapy, and refusal to be enrolled in the study.

Ethical consent:

An approval of the study was obtained from Mansoura University Academic and Ethical Committee. Every patient signed an informed written consent for acceptance of participation in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Sample size:

Sample size was calculated using PASS software [9] [PASS 11. NCSS, LLC. Kaysville, Utah, USA. www.ncss.com.]. In a previous study by **Sari *et al.*** [4], NLR, APACHE II, SOFA and CRP were found be accurate enough for a general description of ICU patients. Based on these assumptions, required sample size was estimated:

NLR in survivors vs non-survivors: A total sample size of 80 (which includes 20 subjects with ICU mortality) achieves 80.2% power to detect a medium to large effect size (d=0.65) between survivors (10.2±7.4) vs non-survivors (20±20) with α-level of 0.050 using one-sided independent-samples t-test.

APACHE II score in survivors vs non-survivors: A total sample size of 40 (which includes 10 subjects with ICU mortality) achieves 96.3% power to detect a large effect size (d=1.40) between survivors (15.82±8.79) vs non-survivors (27.97±8.53) with α-level of 0.050 using one-sided independent-samples t-test.

SOFA score in survivors vs non-survivors: A total sample size of 40 (which includes 10 subjects with ICU mortality) achieves 96.3% power to detect a large effect size (d=2.58) between survivors (5.63 ± 3.63) vs non-survivors (9.68 ± 4.88) with α-level of 0.050 using one-sided independent-samples t-test.

CRP level in survivors' vs non-survivors: A total sample size of 84 (which includes 21 subjects with ICU mortality) achieves 90.2% power to detect a large effect size (d=0.83) between survivors (94.3±87) vs non-survivors (195±146) with α-level of 0.050 using one-sided independent-samples t-test.

Final conclusion: Accordingly, a total sample size of 84 (which includes 21 subjects with the ICU mortality) is required to conduct our study.

Methods:

The primary end point was patient outcome, either death or improvement of the critically ill patient and discharge from ICU.

Patients were divided into two groups: (1) survivors' group: Included 63 patients who developed improvement of the critical illness and discharge from ICU and **(2) non-survivors' group:** Included 21 patients who could not survive and died during their admission at the ICU. The secondary endpoint was either duration of hospital stay or need for mechanical ventilation.

Patients were divided into two groups according to NLR value: **(1) Group A (NLR ≤10):** Included 52 patients and (2) **group B (NLR >10):** Included 32 patients.

All patients were subjected to:

- **Full history taking:** including age, sex, special habits, Charlson comorbidity index**,** vasopressor use, drug abuse
- **Routine physical examination**: including inspection, palpation, percussion and auscultation based on the reported symptoms
- **Laboratory investigations:** Basic investigations including complete blood count, serum creatinine, urine analysis, liver function tests (albumin, SGOT, SGPT, bilirubin, INR, blood sugar level, blood gases, CRP.
- **The NLR** was calculated as the neutrophil absolute value over the lymphocyte absolute value [10]**.** According to the literature, the patients were grouped according to whether their NLR value above or equal to 10, and below 10 [4].
- **Radiological investigations**: including abdominal U/S, ECHO, ECG, chest radiology (chest X-Ray or NCCT chest)

Critical illness stratification by Sequential Organ Failure Assessment (**SOFA**) Score [11].
Critical illness stratification by **APACHE II** score [12, 13].

Statistical analysis

Data were entered and analysed using IBM-SPSS software (IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp). Quantitative data were initially tested for normality using Shapiro Wilk's test with data being normally distributed if P>0.05. Quantitative data were presented as median and interquartile range (IQR) and were compared by Mann-Whitney U test because data were non-parametric. Qualitative data were expressed as number and percentage and were compared by Chi-Square test (or Fisher's exact test). Univariate (Standard) logistic regression was used to predict the likelihood of a diagnosis using only one predictor, standard logistic regression analysis was used to calculate the crude odds ratio (COR) with its 95% confidence interval (95% CI). Multivariate logistic regression was used to create a prediction model of the likelihood of a diagnosis to detect the significant "independent" predictors with their OR (95% CI). P value < 0.05 was considered significant.

RESULTS

This study involved 84 ICU cases with severe sepsis. Their clinical and laboratory data are illustrated in table (1).

Table (1): Clinical and laboratory data of the studied cases (N=84)

Qualitative data	N (%)
Sex	
Male	57 (67.9%)
Female	27 (32.1%)
Age in years	
<60	37 (44%)
60-70	36 (42.9%)
>70	11 (13.1%)
Hypertension	44 (52.4%)
Diabetes	53 (63.1%)
CKD	16 (19%)
CLD	38 (45.2%)
Hospital mortality	
Survivors	63 (75%)
Non-survivors	21 (25%)

This table shows a statistically significantly higher need for mechanical ventilation, in group (B) NLR >10 vs group (A) NLR≤ 10. There was no statistically significant difference in sex, age, hypertension, DM, CLD, CKD and vasopressor use in group (B) NLR >10 vs. group (A) NLR≤ 10 (Table 2).

Table (2): Comparisons of clinical and laboratory data between group (A) NLR ≤ 10 and group (B) NLR >10

Qualitative data	NLR ≤10 N = 52	NLR >10 N = 32	P value
Sex			0.271
Male	33 (63.5%)	24 (75%)	
Female	19 (36.5%)	8 (25%)	
Age (years)			0.132
<60	26 (50%)	11 (34.4%)	
60-70	22 (42.3%)	14 (43.8%)	
>70	4 (7.7%)	7 (21.9%)	
Hypertension	25 (48.1%)	19 (59.4%)	0.314
Diabetes	36 (69.2%)	17 (53.1%)	0.137
CKD	9 (17.3%)	7 (21.9%)	0.605
CLD	21 (40.4%)	17 (53.1%)	0.225
Need for Mechanical Ventilation	9 (17.3%)	19 (59.4%)	**<0.001**
Vasopressor use	19 (36.5)	16 (50%)	0.224

Data are N (%).

This table shows a statistically significantly higher systolic blood pressure (mmHg), mean arterial pressure (mmHg), rate pressure product *10^3, EF, INR, RBS, PH, HCO3, L *10^3, platelet count ($\times 10^3$), CRP on admission, ABACHEII score, SOFA score on admission, duration of hospital stay (days), and a statistically significantly lower age (years), diastolic blood pressure (mmHg), heart rate (beats / minute), RR (bpm), GCS, serum creatinine (mg/dl), serum albumin (g/dl), serum bilirubin (mg/dl), Na, K, total leucocytic count *10^3, N *10^3, in group B NLR >10 vs. group A NLR≤ 10 (Table 3).

Table (3): Comparisons of clinical and laboratory data between group (A) NLR ≤ 10 and group (B) NLR >10

Quantitative data	NLR ≤ 10 N = 52	NLR >10 N = 32	P value
Age (years)	59.5 (34-67)	62 (55.5-67.5)	0.097
Systolic blood pressure (mmHg)	90 (70-110)	75 (60-97.5)	**0.019**
Diastolic blood pressure (mmHg)	50 (40-65)	40 (30-60)	0.112
Mean arterial pressure (mmHg)	66.7 (50-81.7)	51.7 (40.8-72)	**0.033**
Heart rate (beats / minute)	113 (100-120)	111 (102-120)	0.996
Rate pressure product *10^3	9.6 (8.1-11.6)	9 (7.2-9.9)	**0.035**
RR (bpm)	25.5 (22-27.8)	24 (24-27)	0.981
GCS	14 (12.2-15)	13 (12-15)	0.081
EF	57% (52%-65.8%)	53% (46%-58%)	**0.006**
Serum Creatinine (mg/dl)	1.52±0.21	2.12±0.52	0.56
Serum albumin (g/dl)	2.81±0.12	2.61±0.43	0.162
Serum bilirubin (mg/dl)	0.92±0.2	1.12±0.41	0.427
INR	1.01±0.22	1.23±0.2	**0.011**
RBS (mg/dL)	195.35±23.61	185±15.36	**0.022**
PH	6.53±1.23	6.58±1.18	**0.004**
HCO3	12.81±4.15	16.51±4.25	**0.011**
Na	128.35±24.69	125.69±23.78	0.843
K	3.16±0.15	3.52±0.95	0.836
Total leucocytic count *10^3	16.58±3.81	15.23±3.98	0.658
N *10^3	11.32±2.25	13.35±63	0.265
L *10^3	2.85±1.52	1.01±0.09	<**0.001**
Platelet count (×10^3)	198.5±38.65	118.15±28.31	**0.010**
CRP on admission	24 (12-24)	48 (24-96)	**0.005**
ABACHEII score	17 (14-21)	23 (18-28)	**0.001**
SOFA score on admission	4 (2-7)	6 (4-8.75)	**0.014**
CCI	5 (2.25-7)	6 (4-10)	**0.018**
Duration of hospital stay (days)	6 (4-7)	10.5 (9-14)	**<0.001**

Data are median (25th – 75th percentiles).

This table shows a statistically significantly higher CLD proportion in non-survivors vs. survivors. No statistically significant difference in sex, age, hypertension, DM, and CKD proportions in non-survivors vs survivors (Table 4).

Table (4): Comparisons of clinical and laboratory data between survivors and non-survivors

Qualitative data	Survivors N = 63	Non survivors N = 21	P value
Sex			0.500
Male	44 (69.8%)	13 (61.9%)	
Female	19 (30.2%)	8 (38.1%)	
Age (years)			0.537
<60	30 (47.6%)	7 (33.3%)	
60-70	25 (39.7%)	11 (52.4%)	
>70	8 (12.7%)	3 (14.3%)	
Hypertension	32 (50.8%)	12 (57.1%)	0.613
Diabetes	42 (66.7%)	11 (52.4)	0.245
CKD	14 (22.2%)	2 (9.5%)	0.174
CLD	24 (38.1%)	14 (66.7%)	**0.023**

Notes: Data are N (%).

This table shows the results of univariate logistic regression analysis which was run to ascertain the effect of presence of CLD, MAP>50 mmHg, serum creatinine ≤2.2 mg/dl, GCS ≤13, serum albumin ≤ 2.97 g/dl, serum bilirubin ≥1.4 mg/dl, INR > 1.3, serum sodium ≤ 131 mEq/L, NLR > 10, CRP >12, APACHEII score >19, SOFA score >3 on the likelihood of occurrence of in-hospital mortality. All tested variables were statistically significant (Table 5).

Table (5): Predictors of the likelihood of in-hospital mortality (Univariate analysis)

Predictor	P value	COR	95% CI
CLD **Absent** **Present**	**0.026**	 r (1) 3.25	 r (1) 1.1-9.2
MAP **≤50 mmHg** **>50 mmHg**	**0.021**	 r (1) 3.37	 r (1) 1.2-9.4
Serum Creatinine **≤2.2 mg/dl** **>2.2 mg/dl**	**<0.001**	 r(1) 11.25	 r(1) 3.3-38.3
GCS **≤13** **>13**	**0.036**	 r(1) 3.04	 r(1) 1-8.6
Serum Albumin **≤ 2.97 g/dl** **> 2.97 g/dl**	**<0.001**	 r(1) 17.625	 r(1) 4.6-67.8
Serum Bilirubin **≥1.4 mg/dl** **< 1.4 mg/dl**	**<0.001**	 r(1) 9.4	 r(1) 2.96-29.7
INR **> 1.3** **< 1.3**	**0.001**	 r(1) 17.625	 r(1) 2.2-21.4
Serum Sodium **≤ 131 mEq/L** **> 131 mEq/L**	**0.002**	 r(1) 5.128	 r(1) 1.78-14.77
NLR **> 10** **< 10**	**0.002**	 r(1) 5.830	 r(1) 1.95-17.35
CRP **>12** **<12**	**0.049**	 r(1) 4.75	 r(1) 1-22.34
APACHEII Score **>19** **<19**	**<0.001**	 r(1) 46.3	 r(1) 5.79-370.43
SOFA Score **>3** **<3**	**0.007**	 r(1) 2.15-135	 r(1) 2.15-134

r (1) = reference category, COR = crude odds ratio, CI = confidence interval.

This table shows the results of **Multivariate logistic regression analysis,** which was run to ascertain the effect of presence of CLD, MAP>50 mmHg, serum creatinine ≤2.2 mg/dl, GCS >13, serum sodium > 131 mEq/L, NLR ≤ 10. On the likelihood of occurrence of in-hospital mortality (Table 6).

Table (6): Multivariate logistic regression analysis

Predictor	Model 1			Model 2		
	P value	OR	95% CI	P value	OR	95% CI
CLD **Absent** **Present**	0.278	r (1) 2.1	r (1) 0.54-8.4	0.382	r (1) 1.813	r (1) 0.478-6.9
MAP **>50 mmHg** **≤50 mmHg**	0.117	r (1) 3.1	r (1) 0.75-13	-	-	-
Serum Creatinine **≤2.2 mg/dl** **>2.2 mg/dl**	**<0.001**	r (1) 16	r (1) 3.5-73	**0.001**	r (1) 12.337	r (1) 2.69-56.48
GCS **>13** **≤13**	0.106	r (1) 3	r (1) 0.78-12.7	-	-	-
Serum Sodium **>131 mEq/L** **≤131 mEq/L**	-	-	-	0.011	r (1) 6.199	r (1) 1.52-25.28
NLR **≤ 10** **> 10**	**0.031**	r (1) 4.7	r (1) 1.1-19.4	0.004	r (1) 7.874	r (1) 1.9-32.3

This table shows the results of statistically significantly higher proportion of CLD, MAP ≤ 50 mmHg, serum creatinine > 2.2 mg/dl, GCS <13, serum albumin ≤ 2.97 g/dL, serum bilirubin > 1.4 mg/dL, INR > 1.3, serum sodium ≤ 131 mEq/L, NLR > 10, CRP >12, APACHE II score > 19, SOFA score > 3 In non-survivors vs survivors (Table 7).

Table (7): Comparison of predictors frequencies in non-survivors vs. survivors

Predictor :	Survivors N = 63	Non survivors N = 21	P value
CLD	24 (38.1%)	14 (66.7%)	**0.023**
MAP ≤ 50 mmHg	17 (28.3%)	12 (57.1%)	**0.012**
Serum creatinine > 2.2 mg/dl	17 (27.4%)	17 (81%)	**<0.001**
GCS <13	25 (39.7%)	14 (66.7%)	**0.032**
Serum albumin ≤ 2.97 g/dL	16 (25.4%)	18 (85.7%)	**<0.001**
Serum bilirubin > 1.4 mg/dL	16 (25.4%)	16 (76.2%)	**<0.001**
INR > 1.3	20 (31.7%)	16 (76.2%)	**<0.001**
Serum sodium ≤ 131 mEq/L	13 (20.6%)	12 (57.1%)	**0.002**
NLR > 10	10 (15.9%)	11 (52.4%)	**0.001**
CRP >12	42 (66.7%)	19 (90.5%)	**0.034**
APACHE II score > 19	19 (30.2%)	20 (95.2%)	**<0.001**
SOFA score > 3	34 (54.2%)	20 (95.2%)	**0.001**

Notes: Data are N (%)

DISCUSSION

To the best of our knowledge, this was the first study to compare between NLR and ICU severity scores [SOFA and APACHE II]. The majority of previous researches were mainly emphasized on its role only without comparisons.

Cases were divided into two groups according to NLR value Group (A) NLR ≤10, Group (B) NLR >10. Essentially, the need for mechanical ventilation was significantly increased among cases with NLR >10. On the contrary, **Ahmed and Mohammed** [14] have defined two risk groups: the persistently low NLR group, quintile 1 with minimal or no change in NLR; and the persistently high NLR group, quintile 5 with minimal or no change in NLR and with increased NLR. The Kaplan–Meier survival curves were based on the risk groups.

In this study, careful interpretation of the NLR was required. For instance, in contrast to the previous studies, we included neutropenic patients, regardless of precipitating factors. Additionally, there was statistically significantly higher systolic blood pressure (mmHg), mean arterial pressure, rate pressure product *10^3, EF, INR, RBS, PH, HCO_3, L *10^3, platelet count, CRP on admission, ABACHEII score, SOFA score on admission, duration of hospital stay (days), and a statistically significantly lower age (years), diastolic blood pressure (mmHg), heart rate, RR , GCS, serum creatinine (mg/dl), serum albumin, serum bilirubin, Na, K, total leucocytic count *10^3, N *10^3, in group B NLR >10 vs. group A NLR≤ 10.

Of note, CKD was demonstrated to be significantly increased among non-survivors compared to the survivors.

Concerning comparisons of clinical and laboratory data between survivors and non-survivors, GCS, serum creatinine, serum albumin, serum bilirubin, INR, Na, ABACHEII score, SOFA score on admission, CRP on admission as well as NLR were demonstrated to be reliable predictors in differentiation between survivors and non-survivors. In addition, there was statistically significantly higher proportion of CLD, MAP ≤ 50 mmHg, serum creatinine > 2.2 mg/dl, GCS <13, serum albumin ≤ 2.97 g/dL, serum bilirubin > 1.4 mg/dL, INR > 1.3, serum sodium ≤ 131 mEq/L, NLR > 10, CRP >12, APACHE II score > 19, SOFA score > 3 in non-survivors vs survivors. This came in the same line with **Rehman and his colleagues** [15], who have demonstrated that the NLR showed significant associations with all the tested lab parameters of sepsis, such as CRP (p = 0.02), procalcitonin (p=0.01), and SOFA score (p=0.01). Values when analyzed according to culture-positive showed higher values in culture-positive samples but were not statistically significant. Similarly, **Liu and his colleagues** [16] conducted their study on a total of 333 consecutive adult patients with sepsis. They have demonstrated that; median NLR levels were significantly higher in patients who died than in survivors. NLR had a modest power for predicting poor outcome as suggested by area under the curve (AUC) of 0.695±0.036. Multivariate linear regression indicated that increased NLR levels were related to unfavorable outcome independently of the effect of possible confounders. Spearman correlation tests showed that there was a positive correlation between NLR levels and disease severity.

The cause responsible for NLR elevations correlating with poor outcome in patients with sepsis remains unclear, although there are a variety of plausible explanations. One of the most convincing explanations is based primarily on the physiological link between neutrophilia and lymphopenia with systemic inflammation and stress. The evolution of these leukocyte subpopulations may differ based on their respective role in the inflammatory response [16]. Taken together, the sustainability of infection and the incomplete eradication of nidus of infection are responsible for the increase of neutrophils production by the medulla and decrease lymphocytes counts by apoptosis and others mechanisms. Therefore, the resulting increase in NLR may identify patients who are in a state of nonresolution of inflammation, along with concomitant decreased survival rates [16].

By performing univariate logistic regression analysis, the current study revealed thaCLD, MAP, serum creatinine, GCS, serum albumin, serum bilirubin, INR, serum sodium, NLR, CRP, APACHEII score and SOFA score could be used as independent predictors of the possibility of in-hospital mortality. This came in accordance with **Ni and his colleagues** [17] who conducted a single-center, retrospective, cohort study on patients with sepsis admitted to an Academic Emergency Department between January 2010 and January 2015. NLR of patients was analyzed from the hospital's electronic health record (EHR) system. A total of 174 adult patients, of which 80 (46.0%) died in hospital. The primary outcome was in-hospital mortality. Secondary outcome was 28-day mortality. Another study conducted by **Hwang *et al.*** [18] who regarded NLR as a discrete variable, and reported that 1st quartile had the largest in-hospital mortality while 4th quartile the lowest mortality, suggesting an inverse relationship. Another Egyptian study conducted by **Ahmed and Mohammed** [14] concluded that; the initial NLR measured at emergency department admission was independently associated with the 28-day mortality in patients with severe sepsis and septic shock. In addition, the change in the NLR may prove to be a valuable prognostic marker. In **Akilli *et al.*** [19] study, high NLR measured at ED was independently associated with in-hospital mortality and 6-month mortality. In addition, high NLR was also related to a risk of multi-organ failure and sepsis development. More recently, **Riche *et al.*** [7] revealed an association between NLR and risk of death in patients with septic shock. They also suggested that NLR could be used as an indicator of early (before day 5) and late (on or after day 5 after septic shock onset) death. In a study conducted by **Salciccioli and**

his colleagues [8] NLR measured at the time of ICU admission was associated with 28-day mortality in unselected critically ill patients. In subgroup analysis, however, there was no association between NLR and mortality in sepsis patients.

A perfect biomarker for sepsis has not yet been identified, although various tests have been investigated [15, 20, 21]. The NLR has a strength in that it is derived from extremely common laboratory values. Change in NLR as well as initial NLR could be used for identifying patients at high risk of poor outcomes. These values may also provide helpful information about the initial therapeutic response and aid in evaluating host immune responses [22]. However, further clinical studies are required to evaluate the benefit of NLR to sepsis care improvement and the additional role of the NLR compared with other common prognostic markers including lactate and procalcitonin [18].

CONCLUSION

Neutrophil to lymphocyte ratio is a cheap and rapidly available predictor of sepsis and has shown a significant correlation with other relatively expensive and non-rapidly existing markers of inflammation and sepsis with comparable efficacy with ICU severity scores [SOFA and APACHE II]. In addition, initial NLR measured at ED admission was independently associated with 28-day mortality in patients with severe sepsis or septic shock in the ED.

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