Benha Journal of Applied Sciences (BJAS) **print: ISSN 2356–9751**
Vol. (8) Issue (3) (2023), (135-146) **online: ISSN 2356–976x**
http://bjas.journals.ekb.eg

A prospective cohort study evaluated the significance of the neutrophil-lymphocyte count ratio in determining if a patient being admitted to an intensive care unit has sepsis

Ahmed.A.Elsaid[1], Essam.Fotouh[2] and Mariam.Mohammed[1]
[1] Critical Care Medicine Dept., Faculty of Medicine, Benha University
[2] Anesthesia and Intensive Care Dept., Faculty of Medicine, Benha University
E-mail: ahmedabdellatif882357@gmail.com

Abstract

Background: Severe infection can become worse by the clinical illness known as sepsis. In critically ill patients, the neutrophil-lymphocyte count ratio (NLCR) assesses inflammation and stress in a straightforward, quick, and affordable manner. Objectives: To test determine neutrophil-lymphocyte count ratio's importance in sepsis diagnosis comparing to other indicators like WBC count, CRP, and neutrophil count. Patients and methods: In 100 patients participated in this prospective cohort study included. Of them, 50 were ICU patients who had sepsis and 50 were not. All patients had thorough history taking, thorough clinical examinations, and standard laboratory tests. confirmation of infection, radiological investigations and inflammatory markers. By dividing the ratio of neutrophils to lymphocytes, or the lymphocyte count divided by the neutrophil count was determined. Results: There were statistically significant variations in SOFA and CRP across the examined groups. In terms of NLCR, Between the groups that were assessed, there were statistically significant differences, with greater mean values seen in the group with sepsis. There was statistically significant data as well relation regarding mortality with significant higher deaths in sepsis group than no sepsis. We showed the validity of NCLR at cutoff value of > 6.65, as sensitivity was 64% and specificity was 60%. But at a cutoff value of > 10.7 to predict mortality, sensitivity was 68.2% and specificity was 67.9%. positive correlations between were statistically significant between CRP and temperature and between NLCR and SOFA. Conclusion: However, the delicateness and precision of the association between higher NLCR and greater mortality in adult septic patients were constrained.

Key Words: Sepsis, Neutrophil lymphocyte count ratio

1. Introduction

Severe infection can become complicated by sepsis, a clinical illness. It is defined by the presence of the three hallmarks of inflammation in tissues far from the site of infection (vasodilation, leukocyte buildup, and enhanced vascular permeability). An infection-induced inflammatory immune response is to blame for its development. Insufficient blood flow or poor organ function are both symptoms of severe sepsis (1).

The ratio of neutrophils to lymphocytes (NLCR) is used to identify subclinical inflammation. It is computed by splitting the sum of lymphocytes by the quantity neutrophils, often from a sample of peripheral blood, though occasionally it can also come from cells that infiltrate tissue, including tumour cells. reduction in lymphocytes and a rise in neutrophils are frequent symptoms of NLCR. Additionally, NLCR might forecast population-wide death. Both overall mortality and particular causes of death, such as heart disease, chronic lower respiratory illnesses, influenza/pneumonia, and renal disorders, were considerably increased by NLCR (2).

Westerdijk.(3) discovered that patients with sepsis had considerably higher NLCR scores than individuals without sepsis. According to Huang et alresearch, .'s NLCR was greater compared to sepsis survivors than in non-survivors and was related with a worse prognosis in patients with sepsis.

The goal of this study is to evaluate the use of the neutrophil-lymphocyte count ratio in the diagnosis of sepsis in comparison to other markers including CRP, WBC count, and neutrophil count.

2. Methods and Patients

This potential group 100 participants in the trial were hospitalised to the Intensive Care Unit Department at Al-Ahrar Teaching Hospital and the Critical Care Department at Benha University Hospitals from September 2021 to February 2022.

There were two groups of patients:

- 50 sepsis-infected ICU patients make up Group 1.
- Group 2: 50 ICU patients without sepsis.

Inclusion criteria:

Patients who met the following requirements might be included: 18 years of age or older with severe sepsis, non-sepsis causes, or septic shock as their initial presentation. Patients with sepsis at the time of admission satisfied the following criteria: requirements:

A: two or more of the following criteria:

- A 38 degrees Celsius or below.
- HR> 90 bpm.
- PaCO2 32 mmHg with RR > 30/min.
- TLC >12000/dL4,000/dL or more than 10% staff cells

B: In the absence of other causes of hypotension, hypotension was defined as (systolic pressure 90 mmHg, or reduced from baseline by >40 mmHg) qqqqq2 2 q2 qand without response to fluid resuscitation.

C: A known infectious source that has been verified by radiological or microbiological analysis. In the absence of infection confirmation, people who, in the opinion of the treating physician, have SIRS and a high clinical suspicion of infection were also deemed to have sepsis.

- Exclusion standards:
- Age under 18 years old.
- Pregnancy or breastfeeding.

Patients having a haematological condition, those receiving
chemotherapy, or those receiving immunosuppressive medicine, such as glucocorticoids, were excluded from the trial.

Patients who had previously been hospitalised to an ICU abroad were also excluded.

Data collection:

The following procedures were applied to all patients:

- Complete history taking, including sex and age (in years) (males and females) and source of admission (emergency department, wards or surgical room).
- Complete clinical examination including mean arterial pressure and Glasgow coma score.
  - ✓ Standard laboratory tests, such as:
  - ✓ A full blood count.
  - ✓ Respiratory rate.
  - ✓ Body temperature.
  - ✓ Heart rate.
- Information on infections that have been confirmed via microbiological testing, including polymerase chain reaction (PCR), positive cultures, and serology.
- Infection-related medical imaging tests (e.g. infiltrate on chest X-ray or abscess on CT).
- Blood samples taken the time of admission to the ICU were tested for inflammatory indicators such as WBC, neutrophil, lymphocyte, and CRP counts are some examples.

Methods:

The present research was conducted using info from the Intensive Care Unit Department at Al-Ahrar Teaching Hospital and critically ill care Department at Benha University medical facility during September 2021 and February 2022. 100 patients who had obvious or impending organ failure, especially cardiac, pulmonary, or renal failure, were included in the research cohort. The need ICU. The intensivist made the decision to admit the patient after consulting with the treating physician. Depending on whether sepsis was present or not, the patients were split into two groups.

To determine the ratio of neutrophils to lymphocytes CBC with automated differential counts, including neutrophils and lymphocytes, was performed at the time of admission (NLCR). the lymphocyte count is calculated by dividing the neutrophil count by which came from the same automated blood samples, the neutrophil-to-lymphocyte count ratio was computed. If the aforementioned laboratory tests were performed more than once within 24 hours, the neutrophil/lymphocyte ratio (NLCR) was computed using the results of the first test. measurements.

Outcome:

Primary outcome measure:

The primary outcome is the link between the NLCR and sepsis's existence.

Additional outcome metrics

Secondary outcome measures were the association between the NLCR and hospital stay duration, ICU stay duration, and ICU mortality. Furthermore, the connections between NLCR and infection location and illness severity (measured by the SOFA score) were established.

The SOFA score, or Sequential Organ Failure Assessment

	SOFA Score				
Variables	0	1	2	3	4
Respiratory Pao_2/Fio_2, mm Hg	>400	≤400	≤300	≤200†	≤100†
Coagulation Platelets $\times 10^3/\mu L$‡	>150	≤150	≤100	≤50	≤20
Liver Bilirubin, mg/dL‡	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular Hypotension	No hypotension	Mean arterial pressure <70 mm Hg	Dop ≤5 or dob (any dose)§	Dop >5, epi ≤0.1, or norepi ≤0.1§	Dop >15, epi >0.1, or norepi >0.1§
Central nervous system Glasgow Coma Score Scale	15	13-14	10-12	6-9	<6
Renal Creatinine, mg/dL or urine output, mL/d‖	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or <500	>5.0 or <200

*Norepi indicates norepinephrine; Dob, dobutamine; Dop, dopamine; Epi, epinephrine; and Fio_2, fraction of inspired oxygen.
†Values are with respiratory support.
‡To convert bilirubin from mg/dL to µmol/L, multiply by 17.1.
§Adrenergic agents administered for at least 1 hour (doses given are in µg/kg per minute).
‖To convert creatinine from mg/dL to µmol/L, multiply by 88.4.

Statistical analysis:

The data was coded, entered, displayed, and analysed using the Statistical Package for Social Science (SPSS) version 26 data base software programme.

Frequencies and percentages were used to represent qualitative data, and the Chi square (X2) test was used to determine if different qualitative variables were related to one another.

Quantitative variables were estimated using mean, standard deviation (SD), and median with range (for data that were not normally distributed), whereas nonparametric data was evaluated using the Mann-Whitney U test. To identify differences between distinct quantitative variables, an independent t-test (t) was used.

Various metrics were correlated using Pearson and Spearman's correlation (r). Always a number between, the correlation coefficient r (-1 and 1) R values that are positive or negative imply a positive or negative correlation between the variables.

the ROC curve's area under serves as a gauge of accuracy. A test that is flawless has an area of 1, whereas a test that is useless has an area of 0.

To assess the validity, the accuracy, PPV, NPV, sensitivity, and specificity were computed at 95% confidence intervals (CI).

When the significant probability (P value) was less than 0.05 and more than 0.001, respectively, the results were declared statistically significant and extremely statistically significant.

3. Results

Table 1 demonstrates there were none statistically significant variations in the study groups' age (years), sex, or gender. admission and duration of ICU (days) ensuring matching of the groups ($p>0.05$).

Significant statistical disparities existed between the tested groups considering, as indicated in table (2), mean arterial pressure, GCS,RR, HR and temperature with higher levels of RR, HR and temperature were detected in the sepsis group and lower levels of mean arterial pressure and GCS also detected in sepsis group ($p<0.001$*).

In terms of CRP, NCLR, and SOFA, between the groups under study, there were statistically significant differences higher mean levels were detected in the group with sepsis (p 0.001*) (table 3).

Table (4) demonstrates that there were statistically significant relation regarding mortality with significant higher died in sepsis group (44%) than no sepsis (22%) ($p<0.05$).

Figure (1) shows the validity of CRP at cut of >36.5,with sensitivity was (80%), specificity= (82%), accuracy of 81%, a negative predictive value (PVP) of 80%, and a positive predictive value (PVP) of 81.6%.

Figure (2) shows the validity of NCLR at cut of >6.65withthe value of Sensitivity was (64%), specificity= (60%), Accuracy was 62%, negative predictive value (PVN) was 62.5%, and positive predictive value (PVP) was 61.5%.

Figure (3) shows the validity of SOFA at cut of >6.5,the value of Sensitivity was (82%), specificity= (82%), Accuracy is 82%, whereas the predictive value for positive (PVP) and negative (PVN) outcomes is 82% each.

Between the groups that were looked at, there were statistically significant differences, as indicated in table (5). in relation to outcome regarding age and HR with older age and higher HR was in the bad outcome group (died) ($p<0.05$*).

There were notable statistical differences between the groups. under study regarding CRP, NCLR and SOFA with higher mean levels were detected in the non-survived group ($p<0.001$*) (table 6).

FIG. (4) displays the validity of NCLR at a cutoff >10.7to predict mortality, with sensitivity was (68.2%), specificity= (67.9%), In contrast to negative predictive value, positive predictive value (PVP) was 62.5%. (PVN)= 73.1%, and accuracy = 68%.

Figure (5) shows the validity of CRP at a cutoff >47to predict mortality with sensitivity was (77.3%), specificity= (53.6%), In contrast to negative predictive value, positive predictive value (PVP) was 62.5%. (PVN)

Figure (6) shows the validity of SOFA at a cutoff >7.5 to predict mortality with sensitivity was (77.3%), specificity= (60.7%), of predictions were positive, while -0.7% were predicted negatively (PVN) = 77.3%, and accuracy = 68%.

The association between CRP and temperature was statistically significant, as indicated in table (7). Additionally, NLCR and SOFA showed a statistically significant positive connection.

Table (1) Demographic differences between the two in the two study groups

Variable	Sepsis group (n=50)	No sepsis group (n=50)	tests	
			t	*P* value
Age (years) Mean±SD	55.62±17.22	58.18±17.72	-0.733	0.466
Duration of ICU (days) Mean±SD	6.26±2.17	6.98±2.44	-1.559	0.122
Variable	No (%)	No (%)	x^2	P value

Sex						
• male	30	60	21	42	3.241	0.072
• female	20	40	29	58		
Admission						
• ER	39	78	39	78		
• wards	9	18	8	16	0.259	0.879
• surgical room	2	4	3	6		

Chi-square test conducted independently (X^2)

Table (2) Comparing vital signs between the groups under study

Variable	Sepsis group (n=50)	No sepsis group (n=50)	tests	
			t	*P* value
Mean arterial pressure				
Mean±SD	69.54±11.31	88.8±17.35	-6.576	<0.001*
GCS				
Mean±SD	12.44±2.56	12.5±2.85	-0.111	<0.001*
RR				
Mean±SD	21.56±4.33	16.84±4.02	5.645	<0.001*
HR				
Mean±SD	99.22±10.2	85.6±8.97	7.092	<0.001*
Temperature				
Mean±SD	38.35±0.77	37.29±0.56	7.915	<0.001*

Independent t-Test

Table (3) Inflammatory markers among the two study groups

Variable	Sepsis group (n=50)	No sepsis group (n=50)	tests	
			Z	*P* value
CRP				
Mean±SD	58.86±22.56	19.75±21.31	-6.840	<0.001*
Median (IQR)	54 (41.75-82.5)	12 (5-22.5)		
NCLR				
Mean±SD	10.93±5.78	8.35±6.32	-2.634	0.008*
Median (IQR)	10.43 (6.3-14.5)	5.9 (3.9-11.9)		
SOFA				
Mean±SD	7.78±1.34	4.98±2.29	-6.130	<0.001*
Median (IQR)	8 (7-9)	4 (3-5)		

Table (4) Comparing mortality rates of the groups examined

Variable	Sepsis group (n=50)		No sepsis group (n=50)		tests	
	No	(%)	No	(%)	x^2	*P* value
Mortality						
• Died	22	44	11	22	5.473	0.019*
• Survived	28	56	39	78		

Figure (1): ROC curve showing the reliability of CRP in predicting sepsis

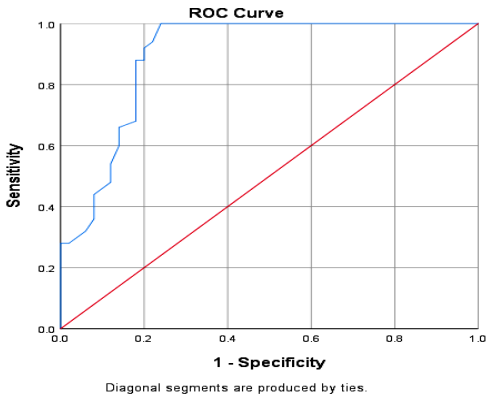

Fig. (2) ROC curve demonstrating NCLR's applicability in predicting sepsis

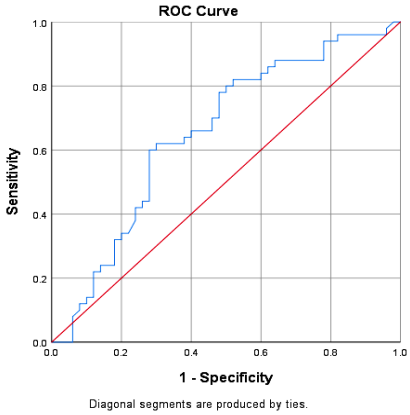

Fig.(3) ROC curve demonstrating CRP's reliability in predicting sepsis

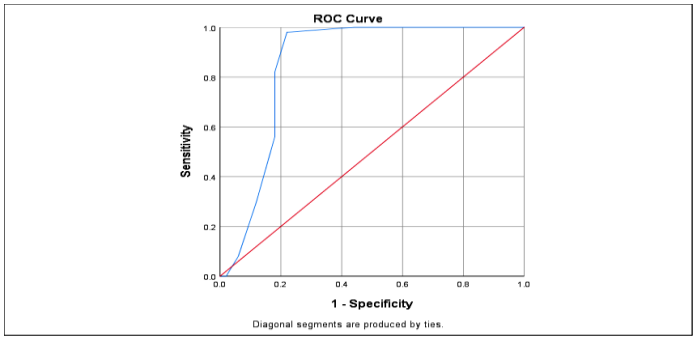

Table (5) Vital signs and laboratory investigations in relation to outcome in the sepsis group (n=50)

Variable	Died group (n=22)	survived group (n=28)	Tests	
			t	*P* value
Age				
Mean±SD	62.91±15.11	49.89±16.82	2.838	0.007*
Mean arterial pressure				
Mean±SD	67.27±12.22	71.32±10.42	-1.264	0.212
GCS				
Mean±SD	12.27±2.35	12.57±2.74	-0.407	0.686
WBC				
Mean±SD	20.32±7.20	18.57±4.80	1.030	0.308
HGB				
Mean±SD	11.92±2.45	12.13±3.12	-0.255	0.800

PLT				
Mean±SD	238.36±96.55	246.39±166.81	-1.007	0.314
RR				
Mean±SD	22.14±4.58	21.11±4.16	0.831	0.410
HR				
Mean±SD	103.14±10.64	96.14±8.85	2.537	0.014*
Temperature				
Mean±SD	38.17±0.90	38.5±0.62	-1.537	0.131
Duration of ICU (days)				
Mean±SD	6.14±2.51	6.36±1.91	-0.353	0.725

Table (6) Inflammatory markers within sepsis analysed groups

Variable	Died group (n=22)	survived group (n=28)	Tests	
			t/z	*P* value
CRP				
Mean±SD	68.86±23.51	51±18.64	-2.621	0.009*
Median (IQR)	76 (47.5-88.25)	46 (36.25-60)		
NCLR				
Mean±SD	14.29±6.03	8.29±3.99	-3.557	<0.001*
Median (IQR)	14.24 (9.9-18.6)	7.7 (4.9-11.3)		
SOFA				
Mean±SD	8.32±1.39	7.36±1.16	2.660	0.011*

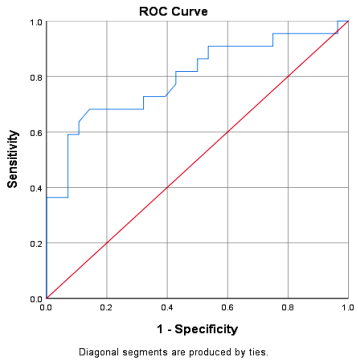

Fig.(4) ROC curve showing the reliability of NLCR in predicting

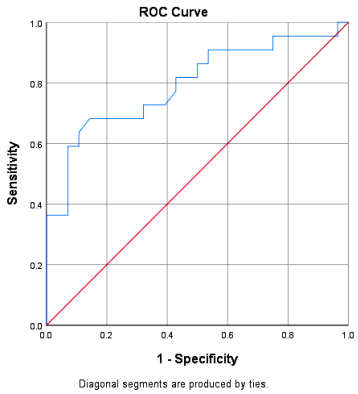

Fig.(5) ROC curve demonstrating NLCR's applicability in predicting mortality in sepsis group

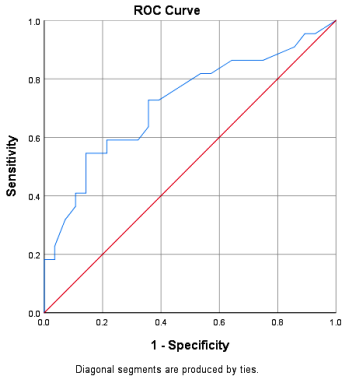

Fig.(6) ROC curve illustrating the validity of SOFA in predicting mortality in sepsis group

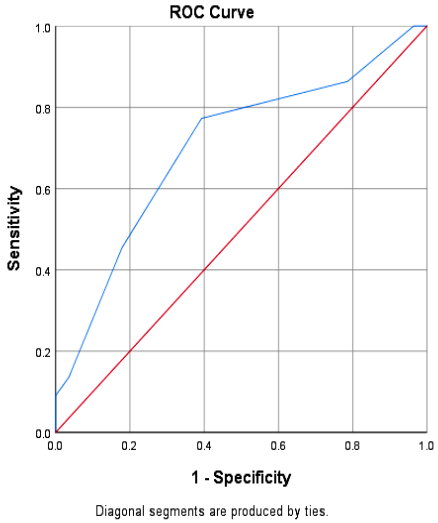

Table (7) Correlation between CRP, NLCR, SOFA and different parameters

Variables		Inflammatory markers CRP	NLCR	SOFA
Age	R	-0.094	0.309*	0.017
	P	0.517	0.029	0.909
Mean arterial pressure	R	-0.222	-0.106	-0.030
	P	0.122	0.464	0.835
GCS	R	-0.079	-0.197	0.006
	P	0.584	0.171	0.966
RR	R	-0.016	-0.023	-0.107
	P	0.911	0.875	0.460
HR	R	0.062	0.021	0.209
	P	0.671	0.886	0.145
WBC	R	0.005	0.208	0.219
	P	0.973	0.147	0.126
Inflammatory markers CRP	R	1.000	0.253	0.173
	P	------	0.076	0.230
NLCR	R	0.253	1.000	0.282*
	P	0.076	------	0.048
Duration of ICU (days)	R	-0.169	0.080	-0.029
	P	0.241	0.582	0.844
Temperature	R	0.286*	-0.192	-0.205
	P	0.044	0.181	0.154

SOFA	R	0.173	0.282*	1.000
	P	0.230	0.048	-----

4. Discussion

Sepsis is a dangerous and sometimes fatal condition characterised by organ malfunction and immunological disorder as a result of the host's reaction to infection. It is infamous for favouring Critical care unit patients (ICU). Sepsis is thought to affect 19.4 million individuals annually throughout the world, however only 14.1 million of these require hospitalisation (5).

Despite the significant advancements in critical care medicine over the years, the death rate of patients who are septic, which is still approximately 30%, has only been slightly decreased. As a result, it's critical for medical professionals to gauge the prognosis of septic patients. Patients with a high mortality risk were found, and it is crucial to precisely predict outcomes in the first stages of sepsis to deliver timely and effective therapies to these patients (6).

Sepsis must be diagnosed as soon as possible in order to lower the high morbidity and death rates in these individuals. However, because the symptoms and indicators used to identify sepsis, such as a shift Fever, tachycardia, and tachypnea in leukocyte count are common but not usually present, sepsis is frequently detected too late (7).

Numerous indicators have already been investigated for the purpose of sepsis early detection. Risk assessment, diagnosis, monitoring, and result categories of these indicators (8). Nobre and Borges (9) emphasised the effectiveness of several of these compounds, including procalcitonin and CD14, although they are expensive and unaffordable for low- and middle-income nations.

According to Yodying et al. (10) NLCR can be used independently to predict poor survival in individuals with cardiovascular disease and tumours. To yet, no agreement has been achieved about the connection between the NLCR level and the clinical prognosis of sepsis patients. Salciccioli et al. (11), but not Djordjevic et al. (12), reported that greater NLCR assessed at the time of ICU admission, but not in patients with sepsis, was significantly related with increased 28-day mortality in either unselected critically ill patients or non-septic patients.

As a result, there is ongoing debate concerning the clinical utility of NLCR in sepsis patients. By comparing the neutrophil-lymphocyte count ratio to other indicators including CRP, WBC count, and neutrophil count, we were able to assess the significance of this measure in the diagnosis of sepsis.

One hundred patients who were hospitalised to the Intensive Care Unit Department at Al-Ahrar Teaching Hospital and the Critical Care Department at Benha University Hospitals between September 2021 and February 2022 made up this prospective cohort research. 50 ICU patients with sepsis and 50 ICU patients without sepsis were separated into 2 groups.

Every patient had a thorough history taken, including their age and sexual orientation and source of admission, complete clinical examination (including mean arterial pressure and Glasgow coma score), routine laboratory investigations (including complete blood picture, respiratory rate, body temperature and heart rate), confirmation of infection (via positive cultures, serology, PCR, or radiographic results) investigations (chest X-ray and CT) and inflammatory markers as well as the WBC, neutrophil, lymphocyte, and CRP counts.

To determine the Neutrophil-to-Lymphocyte Count Ratio, a CBC with automated differential counts, including neutrophils and lymphocytes, was performed at the time of admission (NLCR). the lymphocyte count is calculated by dividing the neutrophil count by which came from the same automated blood samples, the neutrophil-to-lymphocyte count ratio was computed.

Our investigation demonstrated that no statistically significant differences existed variations in age (years), sex, or length of ICU stay between the analysed groups, assuring group matching ($p > 0.05$). Patients that were septic on average were 55.62 years old, while non-septic patients on average were 58.18 years old. Male patients made up 42% of the non-septic patients and 60% of the septic patients.

Additionally, Saeed Ahmed and Mohammed (13), examined the relationships between the outcomes in septic patients and the neutrophil-to-lymphocyte ratio (NLR) or variations in NLR. The population's median age was 65, and 56.4% of the population (n=1787) were men. Ye et al. (14), in a group of adult septic patients, examined the relationship between NLCR and all-cause mortality. They discovered that the cohort as a whole was 67 years old on average. Male patients made up 56% of the population.

No statistically significant difference between the analysed groups was found, according to our study, in terms ofAdditionally, Saeed Ahmed and Mohammed (13), examined the relationships between the outcomes in septic patients and the neutrophil-to-lymphocyte ratio (NLR) or variations in NLR. The population's median age was 65, and 56.4% of the population (n=1787) were men. Ye et al. (14), in a group of adult septic patients, examined the relationship between NLCR and all-cause mortality. They discovered that the cohort as a whole was 67 years old on average. Male patients made up 56% of the population.

There was no statistically different between the groups that were analysed N was found, according to our study, in terms of admission ($p > 0.05$); 78% of septic patients and 78% of non-septic patients were treated as emergency, 18% of septic patients and 16% of non-septic patients were treated in wards and 4% of septic patients and 6% of non-septic patients were treated as surgical admissions. Ye et al.[14] found that

86.1% of patients received medical inpatient care, while 13.9% had surgical hospitalisation.

No statistically significant differences between the analysed groups were found in the laboratory investigations for Hb and PLT count, although there were extremely statistically significant disparities between the studied groups regarding WBCs with higher levels of WBCs were detected in the sepsis group ($p < 0.001$).

The NLR's capability to forecast early sepsis diagnosis and death was examined by Martins et al. (15). Sepsis patients had reduced haemoglobin and hematocrit levels (p 0.05). Sepsis patients had more leukocytes overall than the control group (p 0.05), but there was no difference in platelet concentration between the two groups ($p = 0.29$).

Between the groups that were evaluated in our study, there were statistically significant differences in SOFA with higher mean levels detected in the sepsis group ($p < 0.001$). The median of SOFA score was 7.78 in septic patients and 4.98 in non-septic patients. Also, Ye et al.[14] found that the median of SOFA score was 6.

Additionally, we discovered a statistically significant difference in CRP levels across the examined groups, with higher mean values identified in the group with sepsis (p 0.001). Patients that were septic had CRP medians of 54 and 12, respectively.

In patients with decompensated liver cirrhosis, NLR is a non-invasive marker that can be used to forecast the likelihood of hospital infections (16). With greater mean levels found in the sepsis group (p 0.001), there were statistically significant differences between the analysed groups for NLCR in our investigation. The average of NLCR was 10.93 in septic patients and 7.35 in non-septic patients. Also, Saeed Ahmed and Mohammed [13] found that the original NLR's median value was 8.6, on average in the overall group.

There were statistically significant findings in our investigation. relation regarding mortality with significant higher deaths in sepsis group (44%) than no sepsis (22%) ($p < 0.05$). The NLCR calculated at the time of ICU admission in patients with sepsis and septic shock was linked to death at 28 days, according to research by Hwang et al. (17).

Our investigation showed the validity of CRP at a cutoff value of > 36.5, with sensitivity of 80%, specificity of 82%, positive predictive value of 81.6%, negative predictive value of 80.4%, and accuracy of 81%. However, with a threshold value of > 47 for death prediction, the sensitivity, specificity, positive predictive value (PVP), negative predictive value (PVN), and accuracy were all greater.

The results of our investigation demonstrated the validity of NCLR at a cutoff value of > 6.65, with accuracy of 62%, sensitivity of 64%, specificity of 60%, positive predictive value (PVP) of 61.5%, and negative predictive value (PVN) of 62.5%. However, when predicting death at a threshold value of > 10.7, the sensitivity, specificity, positive predictive value (PVP), negative predictive value (PVN), and accuracy were all 68.2%, 67.9%, and 62.5%, respectively.

In a research by Gürol et al.(18), they suggested a cut-off value series for NLCR corresponding with procalcitonin (PCT) readings as a tool for diagnosing bacteremia or sepsis as well as for decision-making. They found that the cutoff point of 5 for the NLR was linked with a high risk for sepsis. This association had a sensitivity of more than 80% but a low specificity. Numerous conditions, including trauma, surgery, pancreatitis, and rheumatic illnesses, which are frequently linked to sepsis, may play confusing roles in the development of increased NLCR levels.

In our investigation, sensitivity, specificity, positive predictive value (PVP), negative predictive value (PVN), and accuracy were all 82%, demonstrating the validity of SOFA at a cutoff value of > 6.5. However, when a threshold value of > 7.5 was used to predict mortality, sensitivity, specificity, positive predictive value (PVP), positive predictive value (PVN), and accuracy all increased to 77.3%, 60.7%, 77.3%, and 68%, respectively.

In terms of age and HR, there were statistically significant differences between the study groups, with greater age and higher HR in the group with a poor result (death) (p 0.05). Additionally, CRP, NCLR, and SOFA showed highly statistically significant differences between the study groups, with higher mean values in the non-survived group (p 0.001).

According to a research by Bermejo-Martn et al. (19), septic shock patients' prognoses may be adversely affected by low circulating neutrophil counts because these patients are unable to mount efficient innate defences against the encroaching microorganisms. Why the lowest NLCR group did not show the lowest mortality may be explained by increased neutrophil adherence to vascular endothelium, which causes endothelial damage and a drop in circulating neutrophils.In terms of age and HR, there were statistically significant differences between the study groups, with greater age and higher HR in the group with a poor result (death) (p 0.05). Additionally, CRP, NCLR, and SOFA showed highly statistically significant differences between the study groups, with higher mean values in the non-survived group (p 0.001).

Low circulating neutrophil numbers may have a negative impact on septic shock patients' prognoses because these patients are unable to establish effective innate defences against the invading microbes, according to studies by Bermejo-Martn et al. (19). It may be because of enhanced neutrophil adhesion to vascular endothelium, which results in endothelial damage and a decrease in circulating neutrophils, that the lowest NLCR group did not exhibit the lowest mortality. Increased NLCR was linked to poorer outcomes in individuals with tumours of the brain, lung, breast, colon, and pancreatic, according to Patel et al. (20).

In our investigation, the NLCR and SOFA as well as the CRP and temperature showed statistically significant positive relationships.

The connection between the quantities of circulating neutrophils and lymphocytes in the human body is reflected by the NLCR. The ratio can also be utilised to detect systemic inflammation. The NLCR can also contribute to the diagnosis of sepsis and septic shock since a variety of pathophysiologic processes in these conditions may be linked to systemic inflammation (21).

Focusing on newborn sepsis, Heffernan et al.(22) found that a medication that decreased the death of peripheral blood T cells might enhance the prognosis of sepsis.

NLR is a predictive technique that has been employed in critical care medicine. A prospective analysis of severely sick ED patients who needed ICU care was carried out by Akilli et al. (23). Both the in-hospital mortality and the 6-month mortality were independently correlated with high NLR values recorded in the ED. Riche et al. (24), who studied the relationship between the NLR and the probability of mortality in septic shock patients, likewise found a link between high NLR and a risk of multiorgan failure and sepsis development. They added that NLR may be employed as a predictor of early (before to day 5) and late (on or following day 5 after the start of septic shock) demise.

Some of the pathophysiologic mechanisms in severe sepsis and septic shock may be linked to broad immune system activation and dysfunction. The number of circulating neutrophils that move to the damaged area dramatically increases as a result of the quick response of neutrophils to microbial infection. In the innate immune response, neutrophils play crucial functions that include directly killing pathogens by phagocytosis, producing a range of cytokines, and activating T cells (25).

The individuals in the chronically high NLR group may have an ongoing, severe inflammatory process brought on by infection. This syndrome causes a steady rise in neutrophil production in the bone marrow, which massively recruits immature neutrophils into circulation. Complicated sepsis cases also cause a delay in neutrophil death. Another significant element that could be present in such a scenario is lymphocytopenia. It has been discovered that persistent lymphocytopenia is a predictor of death in septic patients and may be a sign of sepsis-induced immunosuppression (26).

In a series of adult patients with sepsis, Liu et al.(27) examined the possible relationship between the NLCR at the time of intensive care unit (ICU) admission and the clinical prognosis. They came to the conclusion that the NLCR was related to 28-day mortality in sepsis patients. The NLCR may assist the doctor in classifying patients into prognosis groups more effectively.

In evaluating the role of the neutrophil-to-lymphocyte ratio as a diagnostic and prognostic marker in sepsis, Kaushik et al.(28) proposed that elevated levels of NLCR are seen in the early stages of sepsis and are therefore helpful in making a diagnosis, particularly in situations where obtaining a microbiological culture presents challenges due to time constraints and a low-positive rate. The prognosis can also be determined by the inflammatory biomarker's late phase value. This marker has predictive significance, but it may also be used to determine when to stop giving antibiotics as the patient gets better.

Ni et al.(29) investigated the relationship between NLCR and in-hospital mortality in sepsis patients. It was discovered that a greater NLCR had lower probabilities of in-hospital mortality as well as bacteremia. Hospital mortality rates were higher for patients with severe/shock or a history of chronic heart failure (CHF). In-hospital mortality was independently predicted by low NLCR. The NLCR and 28-day hospital mortality in sepsis patients, however, did not correlate. The area under curve (AUC) of the NLCR was 0.622 as a predictor of in-hospital survival, and the cut-off value was 9.11 with 0.551 sensitivity and 0.707 specificity. They came to the conclusion that the NLCR, which was assessed in sepsis patients at admission, was a reliable indicator of in-hospital mortality.

In a single-center prospective observational study of septic patients admitted to an intensive care unit (ICU), NLCR values showed a sensitivity of 47%, specificity of 78%, and AUC of 0.631 correlation with presepsin and severity of sepsis as determined by the SOFA score. Additionally, NLCR was considerably greater in septic shock patients (10.31 vs. 2.32), suggesting NLCR may be useful in determining the severity of sepsis, particularly when its value is above 10. (30).

In septic patients, Liu et alresearch .'s (31), showed that NLCR and IL-6 appeared to be separate predictors of 28-day death. Additionally, Jang et al(32) .'s clustering analysis revealed that age, NLCR, and delta neutrophil index (DNI) were the most reliable predictors of sepsis status across all individuals and in distinct clusters.

5. Conclusion

We may draw the restricted but significant conclusion that greater NLCR was linked with increased mortality in adult septic patients.

References

[1] M .Singer, CS .Deutschman, CW .Seymour, M Shankar-Hari, D Annane, M Bauer, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA.vol.315 (8),pp.801–10,2016.

[2] D.Niu,; Huang, Q.; Yang, F.; Tian,W.; Li, C.; Ding, L.; et al. Serum biomarkers to differentiate

Gram-negative, Gram-positive and fungal infection in febrile patients. J. Med. Microbiol.,pp.70: 001360,2021.

[3] K. Westerdijk, KS. Simons, M. Zegers, PC. Wever, P. Pickkers, CPC. de Jager. The value of the neutrophil-lymphocyte count ratio in the diagnosis of sepsis in patients admitted to the Intensive Care Unit: A retrospective cohort study. PLoS ONE 2019; 14(2): e0212861.

[4] Z. Huang,; Fu, Z.; Huang,W.; Huang, K. Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: A meta-analysis. Am. J. Emerg. Med.vol.38,pp. 641–647,2020.

[5] HC. Prescott, CS. Calfee, BT. Thompson, DC. Angus, VX. Liu. Toward Smarter Lumping and Smarter Splitting: Rethinking Strategies for Sepsis and Acute Respiratory Distress Syndrome Clinical Trial Design. Am J Respir Crit Care Med; 194(2): 147-55. 2016

[6] M. Shankar-Hari, GS. Phillips, ML. Levy. Developing a New Definition and Assessing New Clinical Criteria for Septic Shock: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA..vol.315,pp.775-87. 2016

[7] T. Maclay, A. Rephann. The impact of early identification and a critical care–based sepsis response team on sepsis outcomes. Crit Care Nurse.vol.37(6),pp. 88-91,2017.

[8] M. Lora-Andosilla, K. Cantillo-García, D. Borré-Naranjo, M. Buelvas-Villalba, G. Ortiz-Ruiz, C. Dueñas-Castell. Biomarkers in sepsis. In: Ortiz-Ruiz G, Dueñas-Castell C, editors. Sepsis. 3rd ed. New York: Springer-Verlag ,pp.39-50,2018.

[9] V. Nobre, I. Borges. Prognostic value of procalcitonin in hospitalized patients with lower respiratory tract infections. Rev Bras Ter Intensiva.vol.28(2),pp. 179-89,2016.

[10] H. Yodying, A. Matsuda, M. Miyashita, S. Matsumoto, N. Sakurazawa, M. Yamada, et al. Prognostic significance of neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio in oncologic outcomes of esophageal cancer: a systematic review and meta-analysis. Ann Surg Oncol.vol.23,pp.646–654,2016.

[11] JDSalciccioli, DC Marshall, MA Pimentel, MD Santos, T Pollard, LA Celi, et al. The association between the neutrophil-to-lymphocyte ratio and mortality in critical illness: an observational cohort study. Crit Care. vol. 19,pp. 13,2015.

[12] D. Djordjevic, G. Rondovic, M. Surbatovic. Neutrophil-to-Lymphocyte Ratio, Monocyte-to-Lymphocyte Ratio, Platelet-to-Lymphocyte Ratio, and Mean Platelet Volume-to-Platelet Count Ratio as Biomarkers in Critically Ill and Injured Patients: Which Ratio to Choose to Predict Outcome and Nature of Bacteremia? Mediators Inflamm; 3758068,2018.

[13] SA. Saeed Ahmed MAM. and Mohammed. Neutrophil-to-lymphocyte ratio as a prognostic marker in critically-ill septic patients. Research and Opinion in Anesthesia and Inensive Care.vol. 5,pp.279-286,2018.

[14] W. Ye, X. Chen, Y. Huang, Y. Li, Y. Xu, Z. Liang, et al. The association between neutrophil-to-lymphocyte count ratio and mortality in septic patients: A retrospective analysis of the MIMIC-III database. J Thorac Dis; .vol. 12(5),pp.1843-1855,2020.

[15] EC. Martins, L. da Fe Silveirs, K. Viegas, AD. Beck, GF Junior, RV Cremonese, et al. Neutrophil-lymphocyte ratio in the early diagnosis of sepsis in an intensive care unit: A case-control study. Rev Bras Ter Intensiva .vol.31(1) ,pp.63-70,2019.

[16] YJ. Cai, JJ. Dong, JZ. Dong, et al.: Neutrophil-lymphocyte ratio predicts hospital-acquired bacterial infections in decompensated cirrhosis. Clin Chim Acta;vol. 469,pp. 201-207, 2017.

[17] SY. Hwang, TG. Shin, IJ. Jo, K. Jeon, GY. Suh, TR. Lee, et al. Neutrophil-tolymphocyte ratio as a prognostic marker in critically-ill septic patients. Am J Emerg Med; vol. 35(2),pp. 234-9, 2017.

[18] G. Gürol, IH. Ciftci, HA. Terizi, AR. Atasoy, A. Ozbek, M. Köroglu. Are there standardized cutoff values for neutrophil-lymphocyte ratios in bacteremia or sepsis? J Microbiol Biotechnol 2; vol. 25(4) ,pp. 521-5 ,2015.

[19] JF. Bermejo-Martín, E. Tamayo, G. Ruiz. Circulating neutrophil counts and mortality in septic shock. Crit Care; vol. 18,pp. 407, 2014.

[20] S. Patel, S. Wang, M. Snuderl. Pre-treatment lymphopenia and indication of tumor-induced systemic immunosuppression in medulloblastoma. J Neurooncol ,vol. 136,pp. 541-4,2018.

[21] MF Jimenez, RW Watson, J Parodo. Dysregulated expression of neutrophil apoptosis in the systemic inflammatory response syndrome. Arch Surg; 132: 1263-70. 2020

[22] DS. Heffernan, SF. Monaghan, RK. Thakkar. Failure to normalize lymphopenia following trauma is associated with increased mortality, independent of the leukocytosis pattern. Crit Care. Vol. 16,pp. R12. 2018

[23] NB. Akilli, M. Yortanli, H. Mutlu, YK. Gunaydin, R. Koylu, HS. Akca, et al. Prognostic importance of neutrophil-lymphocyte ratio in critically ill patients: short- and long-term outcomes. Am J Emerg Med,pp.32: 1476–1480,2014.

[24] F Riche, E Gayat, R Barthelemy, Le M Dorze, J Mateo, D Payen. Reversal of neutrophil-to-lymphocyte count ratio in early versus late death from septic shock. Crit Care; 19: 439. 2015

[25] YM Joo, MK Chae, SY Hwang, C Jin S-, TR Lee, WC Cha, et al. Impact of timely antibiotic administration on outcomes in patients with severe sepsis and septic shock inthe emergency department. Clin Exp Emerg Med; 1: 35–40. 2014

[26] AM. Drewry, N. Samra, LP. Skrupky, BM. Fuller, SM. Compton, RS. Hotchkiss. Persistent lymphopenia after diagnosis of sepsis predicts mortality. Shock. vol. 42,pp. 383–391,2014.

[27] X. Liu, Y. Shen, H. Wang, Q. Ge, A. Fei and S. Pan. Prognostic significance of neutrophil-to-lymphocyte ratio in patients with sepsis: A prospective observational study. Mediators of Inflammation; Article ID. pp. 8191254 ,2016.

[28] R. Kaushik, M Gupta, M Sharma, D Jash, N Jain, N Sinha, et al. Diagnostic and prognostic role of neutrophil-to-lymphocyte ratio in early and late phase of sepsis. Indian J Crit Care Med;vol . 22,pp. 660-3,2018.

[29] J. Ni, H. Wang, Y. Li, Y. Shu and Y. Liu. Neutrophil to lymphocyte ratio (NLR) as a prognostic marker for in-hospital mortality of patients with sepsis: A secondary analysis based on a single-center, retrospective, cohort study. Medicine; vol.98,pp. 46(e18029), 2019.

[30] A.N. Dragoescu,; V. Padureanu,; A.D. Stanculescu,; L.C. Chiut,; P. Tomescu,; C. Georgmaneanu,; et al. Neutrophil to Lymphocyte Ratio (NLR): A Useful Tool for the Prognosis of Sepsis in the ICU. Biomedicines; vol.10,pp. 75,2021.

[31] S.Liu,; Wang, X.; She, F.; Zhang, W.; Liu, H.; Zhao, X. Effects of Neutrophil-to-Lymphocyte Ratio Combined with Interleukin-6 in Predicting 28-Day Mortality in Patients with Sepsis. Front. Immunol.; vol.12,pp.639735,2021.

[32] J.Y Jang,.; G.Yoo,; T. Lee,; Y. Uh,; J. Kim, Identification of the robust predictor for sepsis based on clustering analysis. Sci. Rep.; vol.12,pp.2336, 2022.