Section A-Research paper
ISSN 2063-5346

Original Research Article

" USE OF NEUTROPHILS TO LYMPHOCYTE RATIO AS AN EARLY AND EFFECTIVE MARKER OF SEPSIS IN A TERTIARY CARE HOSPITAL IN CHENGALPATTU DISTRICT – A RETROSPECTIVE STUDY "

Dr.N.Sangeetha[1*], Dr. R.Cresen Cabrina[2], Dr.Saumya Gaur[3] and Dr.A.Kazzali Ahamed[4]

[1]Associate Professor, Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences and Research Center, Chengalpattu, Chinna Kolambakkam, Palayanoor, Maduranthakam, Tamil Nadu.

[2]Post graduate, Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences and Research Center, Chengalpattu, Chinna Kolambakkam, Palayanoor, Maduranthakam, Tamil Nadu.

[3]Assistant Professor, Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences and Research Center, Chengalpattu, Chinna Kolambakkam, Palayanoor, Maduranthakam, Tamil Nadu.

[4]Post Graduate, Department of Surgery, Karpaga Vinayaga Institute of Medical Sciences and Research Center, Chengalpattu, Chengalpattu, Chinna Kolambakkam, Palayanoor, Maduranthakam, Tamil Nadu.

***Corresponding author**
Dr.N.Sangeetha,
Associate Professor,
Department of Pathology,
Karpaga Vinayaga Institute of Medical Sciences and Research Center,
Chengalpattu, Chinna Kolambakkam,
Palayanoor, Maduranthakam, Tamil Nadu.

Received: 06.04.2023 Revised: 21.04.2023 Accepted: 20.05.2023

ABSTRACT

Background : Neutrophil to lymphocyte ratio (NLR) can be easily calculated from the white cell differential count and is considered a good marker for predicting different diseases, including sepsis.

Aim of the study: To study "use of neutrophils to lymphocyte ratio as an early and effective marker of sepsis in a tertiary care hospital in Chengalpattu district – a retrospective study "

Materials and methods: Cross sectional study done in the Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences and Research Centre for duration of 1 year i.e. from January 2022 to January 2023.

Results : Sepsis origin was from the following areas that include pulmonary (50), urinary (30), surgical (20) and abdominal (10), cutaneous (10). In our study
, 80 out of 120 patients had sepsis and the remaining 40 patients had septic shock.

Conclusion : Elevated levels of NLR are seen in early phase of sepsis and thus helpful in making a diagnosis, especially when obtaining microbiological culture possess limitation in terms of time and low-positive rate. Late phase value of this inflammatory biomarker is also helpful in dictating the prognosis.

Key words : Sepsis , Neutrophil to lymphocyte ratio (NLR), organ dysfunction.

INTRODUCTION:

Sepsis is a dysregulated inflammatory response to infection and manifests as a spectrum of illness that ranges clinically from bacteraemia to severe sepsis to septic shock [1]. The Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3) defined sepsis as life-threatening organ dysfunction resulting from dysregulated host responses to infection and defined septic shock as a subset of sepsis in which underlying circulatory, cellular and metabolic abnormalities are profound enough to substantially increase the risk of mortality [1].Sepsis can originate from community-acquired infections or it can be hospital-acquired.The most common site of infection that leads to sepsis is the lung (62%), followed by the abdomen (20%), bloodstream

(15%) and urinary tract 14% [2-3]. The clinical presentation of sepsis depends on the site of the infection. Common presentations include malaise and non-specific signs, such as fever (although hypothermia can be present too), tachycardia, tachypnea or altered mental status. Arterial hypotension can be present, but its absence does not exclude sepsis [4].

The neutrophil/lymphocyte ratio (NLR) was studied in order to provide an easier way to diagnose sepsis. This ratio can be calculated both from the absolute number of neutrophils and lymphocytes and from their relative number. The importance of this report derives from the fact that physiological stress causes an increase in the number of neutrophils and a decrease in the number of lymphocytes. Sepsis stimulates lymphocyte apoptosis, so this ratio is increased in these cases. Septic shock causes a dramatic decrease in lymphocyte counts, so the NLR ratio increases significantly [5].

The neutrophil-to-lymphocyte ratio (NLR), as a readily accessible biomarker can be calculated based on a complete blood count. Although evidence has shown that NLR is proposed as an independent predictor of poor survival in various clinical circumstances ranging from oncological patients [6, 7] to patients with cardiovascular diseases [8], 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 [9], whereas some other studies suggested that NLR was not associated with mortality in patients with sepsis [10]. Consequently, the clinical usefulness of NLR in patients with sepsis is therefore still a matter of on-going controversy and this question deserves further investigation

Objectives: To evaluate the association of NLR with the clinical prognosis in a consecutive series of patients with sepsis.

MATERIALS AND METHODS
Study design: Cross sectional study.
Study setting: Department of Pathology, KarpagaVinayaga Institute of Medical Sciences and Research Centre.
Study duration: 1 year i.e. from January 2022 to January 2023.
Study population: Records of patients admitted with sepsis.
Inclusion criteria:
Age 20 years to 60 years, sepsis due to infections, records of blood sampling within 24 hours from the presentation of signs of sepsis and sepsis due to one of the following infections: community acquired pneumonia, hospital acquired pneumonia, ventilator-associated pneumonia, acute pyelonephritis, intra-abdominal infection or primary bacteraemia.

We formulated a priori criteria to exclude patients according to the following criteria: (1) missing neutrophil and lymphocyte data on ICU admission; (2) missing covariate data for multivariable adjustments; (3) patients with immunosuppressive diseases mainly including cancer and HIV infection or patients with receiving immunosuppressive therapy; and (4) patients who were already in ICU for many days and became septic secondary. Patients were eligible for the final study cohort if they met the inclusion criteria and none of the exclusion criteria.

Exclusion criteria: Records of cases with immunosuppressive diseases mainly including cancer and HIV infection or patients with receiving immunosuppressive therapy. Records of cases who were already in ICU for many days and became septic secondary.

Sampling:
Sampling frame: IPD records from Karpaga Vinayaga Institute of Medical Sciences and Research Centre.

a. **Sampling method:** Convenience sampling.
b. Sample size with calculation methods:
Sample size has been estimated to be based on the formula

$$n = \frac{Z^2\ P\ (1-P)}{d^2}$$

Where n is the sample size,
Z is the level of confidence of 95% (1.96),
P is expected prevalence17.56 (as per previous study), [15]and
d is precision 7. Level of confidence aimed for is 95%.
= 1.96 x 17.56 x 82.44

$(7)^2$
= 114
Rounding off to 120
Which constitutes to n=120. So minimum number of samples needed are120; hence, we include 120 samples for our study.

Study tools:

List of Variables and their measurement methods with standardisation technique:

CLINICAL variables

- Fever (>38.3 °C) or hypothermia (core temperature <36 °C)
- Heart rate > 90 bpm or >2 SD normal value for age
- Tachypnea
- Altered mental status
- Significant edema or positive fluid balance (>20 ml/kg in 24 h)
- Hyperglycaemia (plasma glucose >140 mg/dl or 7.7 mmol/l) without diabetes

PATHOLOGICAL variables

- Leukocytosis (WBC >12,000 cells/microliter) or leukopenia (WBC <4000 cells/microliter)
- Normal WBC with >10 % immature forms
- Plasma C-reactive protein >2 SD above normal value
- ESR

The data will be collected from the record from MRD section with permission from the in charge and the demographic data including age, sex, occupation, personal history, medical history and past history will be collected and entered in a prestructured proforma and the proforma will also include all the investigations including CBC, NLR ratio and ESR.

Blood Measurements

Venous blood (3 mL) was collected from patients presenting to the ICU. The blood was drawn into an EDTA-containing tube (BD Vacutainer, Plymouth, UK) and centrifuged at 3,000 rpm for 15 min and plasma was frozen at −80°C until analysis. Complete blood count was determined using Yumizen H500 Hematology Analyzer. NLR was calculated as a ratio of circulating neutrophil and lymphocyte counts. The normal ranges for the leukocyte in our laboratory are 1.4–6.5 × 10^9/L for neutrophil count and 1.2–3.4 × 10^9/L for lymphocyte count.

Disease Severity and Outcome

To evaluate the severity of sepsis upon presentation, the validated Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated in all enrolled patients on admission. This score ranges from 0 to 71, with higher scores indicating more severe disease.
Furthermore, patients who survived and discharged from hospital were further followed up by telephone calls. The primary outcome of the study was defined as death from any cause within 28 days after admission to the ICU.

Statistical Analysis

Continuous variables were reported as mean values ± standard deviation (SD) or median with interquartile range (IQR), while categorical variables were expressed as count and percentage. The statistical significance of intergroup differences was compared through unpaired Student's *t*-test or Mann-Whitney *U* test for continuous variables and through Pearson's χ^2 test for categorical variables. The ability of the variables to discriminate survivors from nonsurvivors was determined using receiver operating characteristic (ROC) curves. ROC curves showed sensitivity versus 1 − specificity such that area under the curve (AUC) varied from 0.5 to 1.0, with increased values demonstrating higher discriminatory ability. Univariate logistic regression analyses were performed to separately examine the association between unfavourable outcome and each of the indicators. We also conducted forward stepwise multivariate logistic regression models to determine the independent predictors adjusted for the previously specified baseline covariates. Criteria of $P < 0.05$ for entry and $P \geq 0.10$ for removal were imposed in this procedure. Two-sided P value < 0.05 was considered to represent a statistically significant difference. All analyses were performed by the IBM SPSS Statistics software version 19.0 (SPSS, Chicago, Illinois, USA).

RESULTS

In the present study age distribution varied from 20 to 30 years. Majority were noted among 51-60 years constituting 50% (60/120). 41-50 years constituted 33.3% (40/120), 31-40 years occupied 10.8 %(13/120) and 5.8 %(07/120) constituted in 20-30 years. Mean age is 48.85 ± 8.9. Males constituted 68.3 % (70/120) and females 41.6% (50/120).M: F – 1.4:1. According to distribution of socioeconomic status, upper class constituted 8.3% (10/120), upper middle class and lower class constituted 33.3% (40/120) and lower middle class constituted 25% (30/120). According to distribution of occupation, farmer constituted 8.3% (10/120), 33.3 %(40/120) were unemployed, 5% (06/120) were students 25% (30/120) were house wives and 28.3 % (34/120) were business by occupation.

According to distribution of location 62.5% (75/120) were residing in rural areas and 37.5% (45/120) were residing in urban areas. According to past history distribution 20 %(24/120) were having HTN. 16.6% (20/120) were having DM and 25% (30/120) were having both HTN and DM and 38.2 % (46/120) were having no past history. According to personal history distribution 16.6% (20/120) were smokers and 30.8% (37/120) were alcoholics and absent in 52.5 % (63/120).

Fever (>38.3 °C) noted in 75% (90/120) cases and normal temperature in 25% (30/120) cases. Heart rate > 90 bpm seen in 75% (90/120) cases and normal in 25% (30/120) cases.
Tachypnoea seen in 66.6% (80/120) cases and normal in 33.3% (40/120) cases. Altered mental status noted in 25% (30/120) cases and absent in 75% (90/120) cases. Significant oedema or positive fluid balance (>20 ml/kg in 24 h) in 16.6% (20/120) and absent in 83% (100/120).

WBC count of 12,000-20000 cells/microliter seen in 33.3% (40/120) cases and more than 30000 cells/cumm seen in 50% (60/120) cases and < 4000 noted in 16.6% (20/120) cases.
Normal WBC with >10 % immature forms seen in 25% (30/120) cases and absent in 75% (90/120) cases.

Sepsis origin was pulmonary (50), urinary (30), surgical (20), abdominal (10), cutaneous (10), or unknown (5). Most of these patients had sepsis with or without organ failures (80) and the rest (40) were diagnosed with Septic Shock. In our study (40/120) had sepsis, (50/120) had severe sepsis, and the remaining (30/120%) had septic shock.

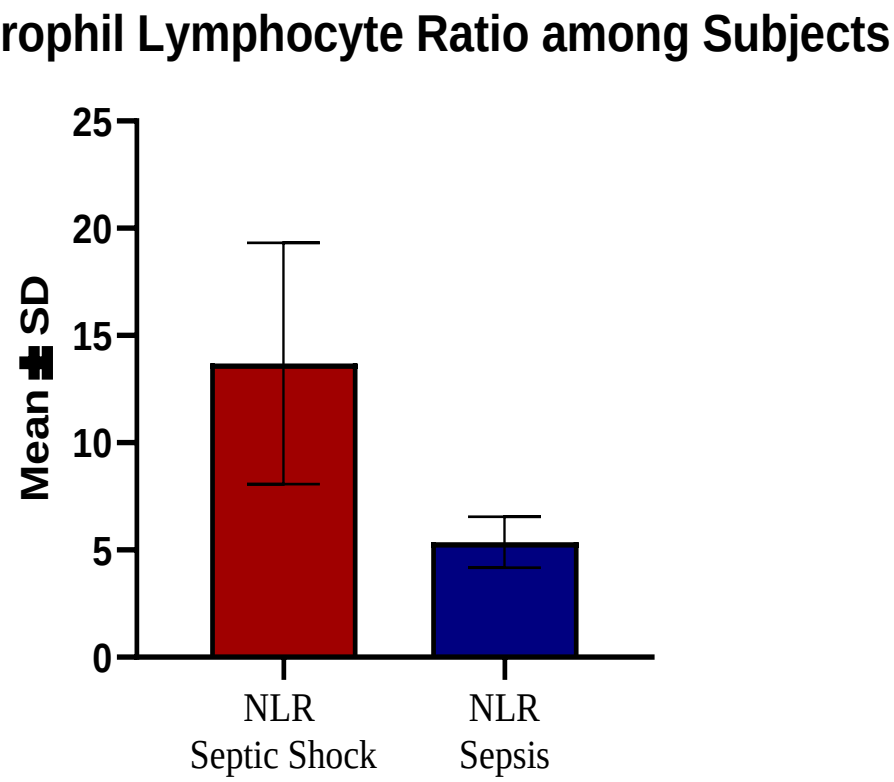
In our study the commonest isolated pathogens from the study cohort were Gram-negative microorganisms with a predominance of Escherichia coli, and blood cultures were positive

Table 1: NLR and Leucocyte distribution among subjects

Parameter	Septic shock	Sepsis	P value
Neutrophil Lymphocyte Ratio Median IQR	18 (6-18) IQR	5 (3-7) IQR	<0.0001 ****
Leucocyte Distribution Mean ± SD	27113 ± 8160	18524 ± 11544	<0.0001 ****

Unpaired t test, P<0.05,*** = significant, ns= not significant. IQR = interquartile range
In our study, Neutrophil Lymphocyte Ratio - Median IQR and Leucocyte Distribution
Mean ± SD showed statistical significance in septic shock patients and sepsis patients with p value <0.0001.

Section A-Research paper
ISSN 2063-5346



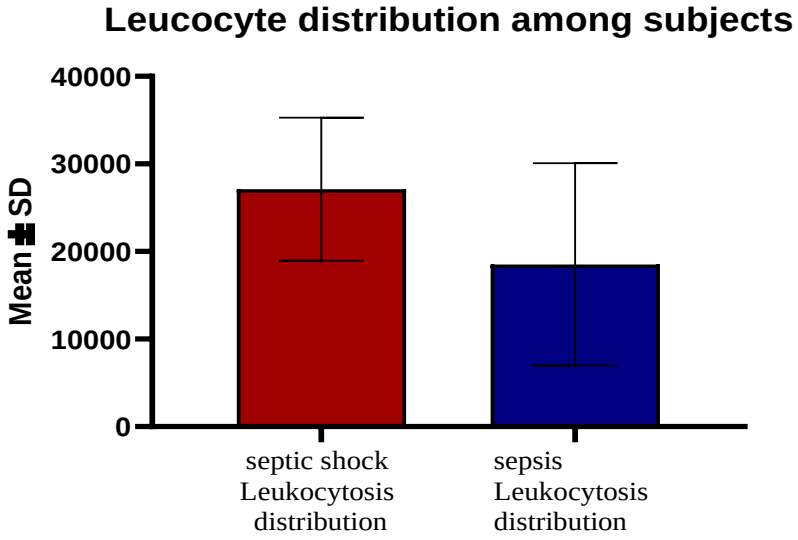


Table 2: >10% Blasts distribution among subjects

Parameter	>10% Lymphoblasts		P value
	yes	no	
Septic Shock	22	18	<0.0001 ****
Sepsis	8	72	

Fisher's exact test, P<0.05,*** = significant, ns= not significant
In our study >10% Lymphoblasts showed statistical significance in septic shock patients and sepsis patients with p value <0.0001.

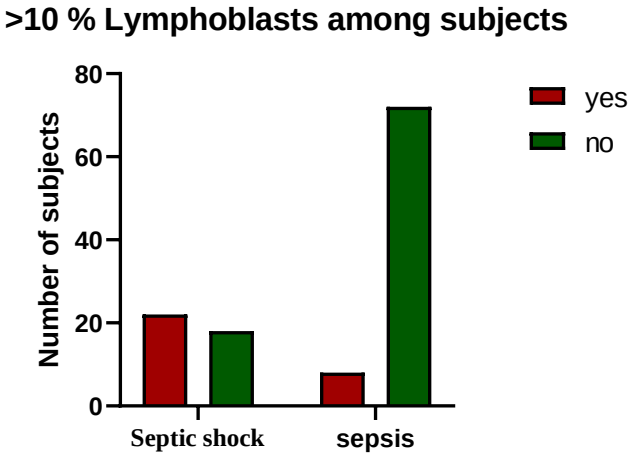


Table 3: Significant oedema distribution among subjects

Parameter	Significant oedema		P value
	yes	No	
Septic Shock	15	25	<0.0001 ****
Sepsis	5	75	

Fisher's exact test, P<0.05,*** = significant, ns= not significant
In our study, significant edema showed statistical significance in septic shock patients and sepsis patients with p value <0.0001.

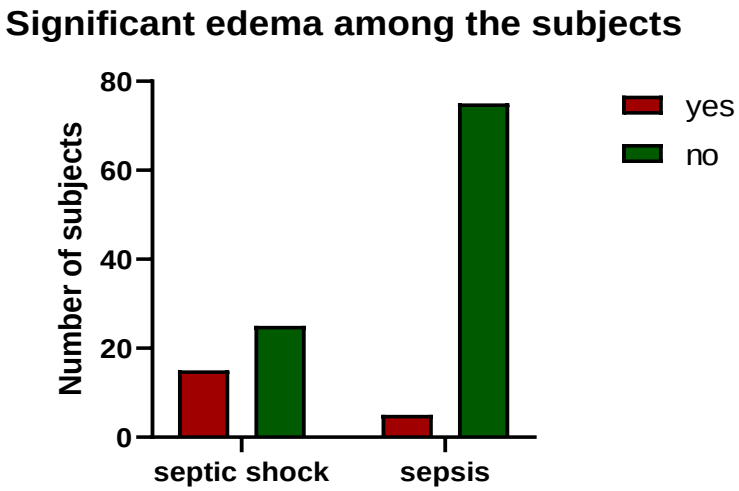


Table 4: Altered mental status among subjects

Parameter	Altered mental status (n)		P value
	yes	No	
Septic Shock	11	29	0.6607 ns
Sepsis	19	61	

Fisher's exact test, P<0.05,*** = significant, ns= not significant

In our Altered mental status does not showed statistical significance in septic shock patients and sepsis patients with p value 0.6607

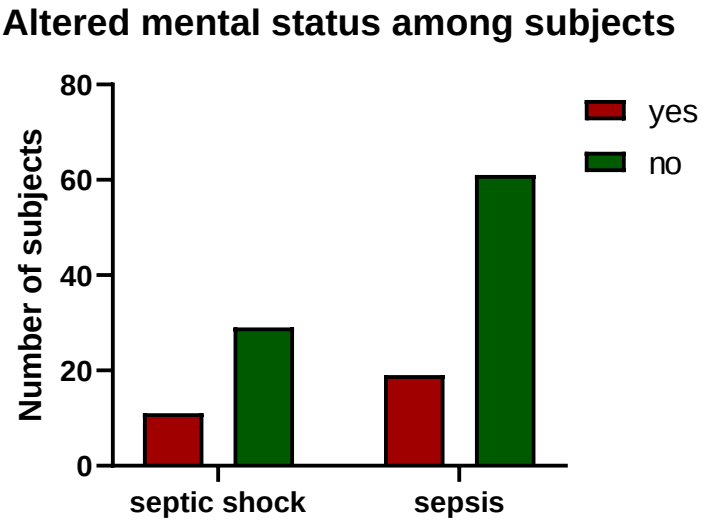


Table 5: Tachypnoea distribution among subjects

Parameter	Tachypnoea (n)		
	yes	no	P value
Septic Shock	35	5	0.0005 ***
Sepsis	45	35	

Fisher's exact test, P<0.05,*** = significant, ns= not significant

In our study, tachypnea showed statistical significance in septic shock patients and sepsis patients with p value 0.0005.

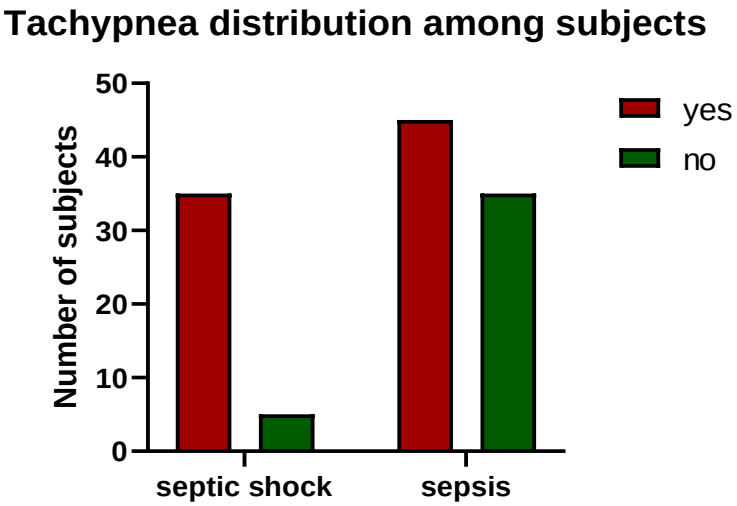


Table 6: Heart Rate among subjects

Parameter	Heart Rate		P value
	Normal	Tachycardia	
Septic Shock	2	38	0.0002 ***
Sepsis	28	52	

Fisher's exact test, P<0.05,*** = significant, ns= not significant

In our study, Heart Rate among subjects showed statistical significance in septic shock patients and sepsis patients with p value 0.0002.

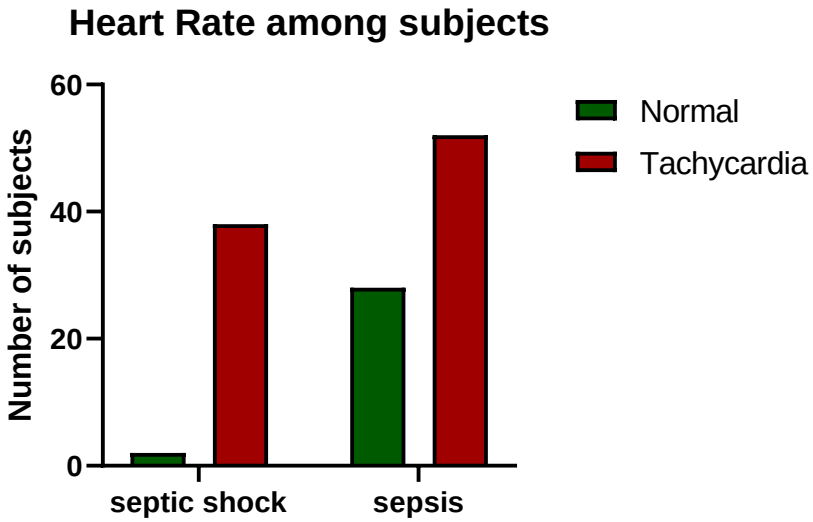


Table 7: Body Temperature among subjects

Parameter	Body Temperature		P value
	Normal	Febrile	
Sepsis Shock	2	38	0.0002 ***
Sepsis	28	52	

Fisher's exact test, P<0.05,*** = significant, ns= not significant
In our study, body temperature among subjects showed statistical significance in septic shock patients and sepsis patients with p value 0.0002.

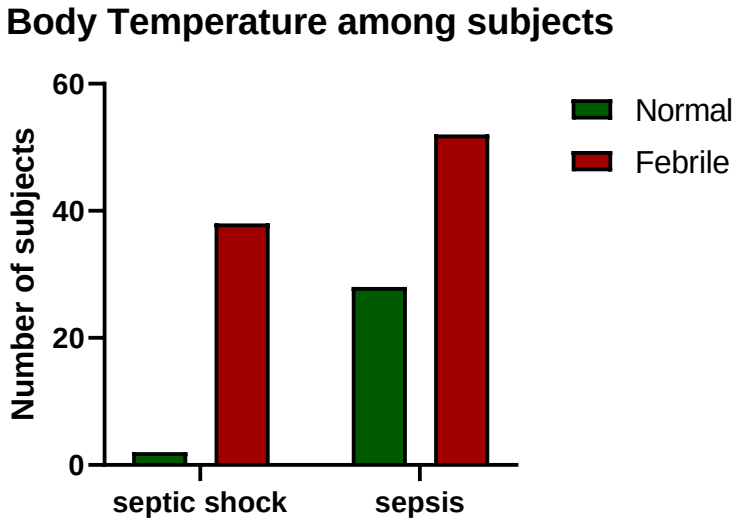
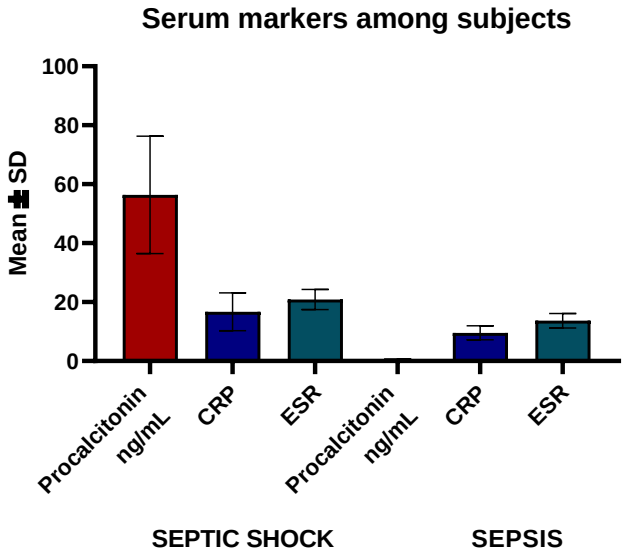


Table 8: Serum markers among subjects

Parameter	Septic shock	Sepsis	P value
	Mean ± SD	Mean ± SD	
Procalcitonin	56.39 ± 19.90	0.5111 ± 0.1923	<0.0001 ****
CRP	16.73 ± 6.401	9.550 ± 2.376	<0.0001 ****
ESR	20.88 ± 3.413	13.68 ± 2.479	<0.0001 ****

Unpaired t test, P<0.05,*** = significant, ns= not significant

In our study, the serum markers such as procalcitonin, CRP and ESR among septic shock and sepsis show

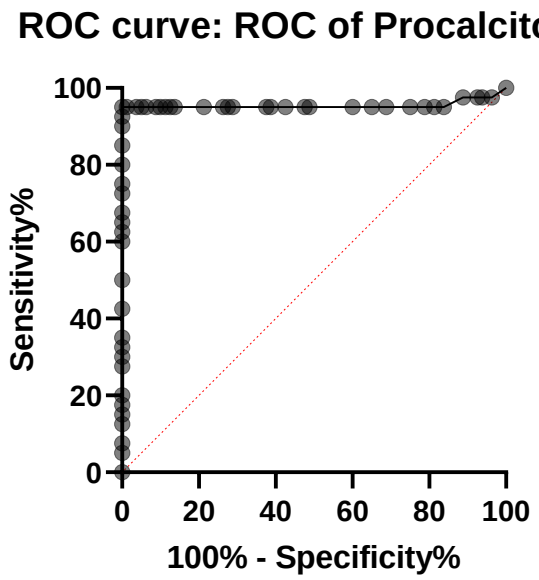


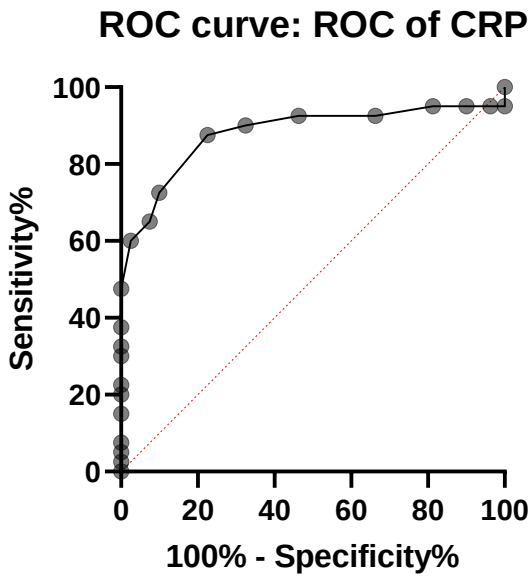
statistical significance with p value <0.001.

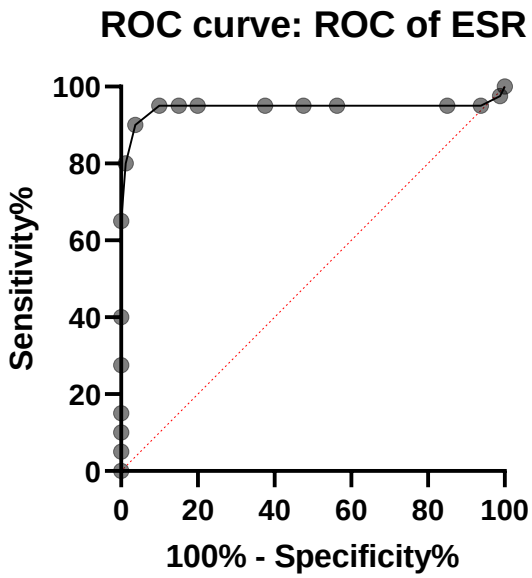
Table 9: Serum markers ROC Curve analysis among subjects

	ROC Curve				P value
Parameter	**Septic shock**	**Sepsis**	**AUC**	**95% Confidence Interval**	
	Mean ± SD	**Mean ± SD**			
Procalcitonin	56.39 ± 19.90	0.5111 ± 0.1923	0.9539	0.8914 to 1.000	<0.0001 ****
CRP	16.73 ± 6.401	9.550 ± 2.376	0.8798	0.8006 to 0.9591	<0.0001 ****
ESR	20.88 ± 3.413	13.68 ± 2.479	0.9442	0.8780 to 1.000	<0.0001 ****

AUC= Area under curve, P<0.05,*** = significant, ns= not significant







DISCUSSION

NLR is an easy parameter to perform, the complete blood count being one of the standard, mandatory tests for any hospitalized patient, so it can be widely used to assess the severity of sepsis or septic shock. NLR was also used to estimate the outcomes of sepsis and septic shock management by Terradas et al. They showed that if the therapeutic management is effective, NLR will usually begin to decrease within a few days. If the NLR value remains high despite initiation of therapy, the prognosis is poor and the mortality risk is high [10.11]. It is likely that if performed daily monitoring of NLR would provide further useful prognostic data.

In our study, Neutrophil Lymphocyte Ratio - Median IQR and Leucocyte Distribution
Mean ± SD showed statistical significance in septic shock patients and sepsis patients with p value <0.0001. >10% Lymphoblasts showed statistical significance in septic shock patients and sepsis patients with p value <0.0001. Distribution of edema showed statistical significance in septic shock patients and sepsis patients with p value <0.0001. Altered mental status does not showed statistical significance in septic shock patients and sepsis patients with p value 0.6607. Tachypnea showed statistical significance in septic shock patients and sepsis patients with p value 0.0005. Heart rate among subjects showed statistical significance in septic shock patients and sepsis patients with p value 0.0002. Body Temperature among subjects showed statistical significance in septic shock patients and sepsis patients with p value 0.0002.

Comparative studies

In the present study age distribution varied from 20 to 30 years. Majority were noted among 51-60 years constituting 50% (60/120). 41-50 years constituted 33.3% (40/120), 31-40 years occupied 10.8 %(13/120) and 5.8 %(07/120) constituted in 20-30 years. Mean age is 48.85 ± 8.9 years. In Xuang et al study [12] mean age was 70.26±15.79 years. In Vasileios Karamouzos, [13] study the mean age of the population was 64.5 (54-78). In Faisal et al [14]study the median age of the participants was 68.40 (19.5 IQR) years in males and 64.0 (18.0 IQR) years in females.

In our study, males constituted 68.3 % (70/120) and females 41.6% (50/120), M: F – 1.4:1.
Similar findings were observed in Xuang et al study [12] and Khaleed et al [15]study where 56.46% and 57 (67.9%) were males.

In our study, sepsis origin was pulmonary (50), urinary (30), surgical (20), abdominal (10) and cutaneous (10). In Xuang et al study[12] noted the commonest locations of infection were lung and abdomen. In Alice et al study [16] pulmonary (42), urinary (27), surgical (18), abdominal (12), cutaneous (10) or unknown (5). In Faisal et al study [14] the most common source of sepsis occurring in 74 (44.0%) patients was pneumonia, followed by urinary tract infection (UTI) in 44 (26.2%), soft tissue/skin infection in 32 (19%), intra-abdominal source in 9 (5.4%) and CNS infection in 9(4.8%) patients. In Rajnees et al study [17]most common comorbid illness was chronic obstructive pulmonary disease present in 18 participants. Among the study cases, the most common site of sepsis was respiratory system (pneumonia). 33(58%) patients had septic shock at the time of enrolment and out of which, 17 survived and 16 expired.

In our study the commonest isolated pathogens were Gram-negative microorganisms with a predominance of Escherichia coli and blood cultures were positive, similar findings were observed in Xuang et al study [12.] In our study (80/120) had sepsis and the remaining (40/120%) had septic shock. In Xuang et al[12]study 137 patients (41.14%) had sepsis, 149 patients (44.74%) had severe sepsis, and the remaining 47 patients (14.11%) had septic shock. In Alice et al study[16] most of these patients had sepsis with or without organ failures (76) and the rest (38) were diagnosed with sepsis shock. There were no significant differences between the two patient samples regarding age or sex.

In our study Neutrophil to Lymphocyte Ratio (NLR) was subsequently calculated by dividing absolute neutrophil count to absolute lymphocyte count. All patients had higher than normal NLR values with an overall average of 8.14± 1.31. The values were significantly higher for patients with septic shock compared with the sepsis group suggesting the potential value of NLR in assessing sepsis severity. In Alice et al [16] all patients had higher than normal NLR values with an overall average of 9.53 ± 2.31. In Eduarda Cristina Martins,et al [18]study the presence of a neutrophil-lymphocyte ratio greater than 5.0, leukocyte count above 12,000 mm^3/mL and band neutrophil percentage above 10% were risk factors for sepsis.

CONCLUSION

Elevated levels of NLR are seen in early phase of sepsis and thus helpful in making a diagnosis, especially when obtaining microbiological culture possess limitation in terms of time and low-positive rate. Late phase value of this inflammatory biomarker is also helpful in dictating the prognosis. In addition to the prognostic value, this marker can also be exploited to discontinue antimicrobials as the patient improves. However, further research is desired with large sample size and in patients of non-infective inflammatory conditions to strengthen the role of this potential marker in sepsis.

REFERENCES

1. Singer M, Deutschman CS, Seymour CW, et al.: The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016, 315:801-810. 10.
2. Vincent JL, Rello J, Marshall J, et al.: International study of the prevalence and outcomes of infection in intensive care units. JAMA. 2009, 302:2323-2329.
3. Karlsson S, Varpula M, Ruokonen E, et al.: Incidence, treatment, and outcome of severe sepsis in ICU treated adults in Finland: the Finnsepsis study. Intensive Care Med. 2007, 33:435-443.
4. Cecconi M, Evans L, Levy M, Rhodes A: Sepsis and septic shock. Lancet. 2018, 392:75-87. 10.
5. Farkas, J.D. The complete blood count to diagnose septic shock. J. Thorac. Dis. 2020, 12 (Suppl. 1), S16–S21.
6. R. Zahorec, "Ratio of neutrophil to lymphocyte counts—rapid and simple parameter of systemic inflammation and stress in critically ill," Bratislavske Lekarske Listy,2001: vol. 102, no. 1, pp. 5–14.

7. M. H. Kang, S.-I. Go, H.-N. Song et al., "The prognostic impact of the neutrophil-to-lymphocyte ratio in patients with smallcell lung cancer," British Journal of Cancer, 2014: vol. 111, no. 3, pp. 452–460.
8. B. Ayc¸a, F. Akln, O. Celik et al., "Neutrophil to lymphocyte ratio is related to stent thrombosis and high mortality in patients with acute myocardial infarction," Angiology, 2015:vol. 66, no. 6, pp. 545– 552.
9. F. Riche, E. Gayat, R. Barth ´ el ´ emy, M. Le Dorze, J. Mat ´ eo, and ´ D. Payen, "Reversal of neutrophil-to-lymphocyte count ratio in early versus late death from septic shock," Critical Care, 2015:vol. 19, article 439.
10. de Jager, C.P.; van Wijk, P.T.; Mathoera, R.B.; de Jongh-Leuvenink, J.; van der Poll, T.; Wever, P.C. Lymphocytopenia and neutrophil-lymphocyte count ratio predict bacteremia better than conventional infection markers in an emergency care unit. Crit. Care 2010, 14, R192.
11. Terradas, R.; Grau, S.; Blanch, J.; Riu, M.; Saballs, P.; Castells, X.; Horcajada, J.P.; Knobel, H. Eosinophil count and neutrophillymphocyte count ratio as prognostic markers in patients with bacteremia: A retrospective cohort study. PLoS ONE 2012, 7, e42860.
12. Xuan Liu, Yong Shen, Hairong Wang, Qinmin Ge, Aihua Fei, and Shuming PaN Research Article Prognostic Significance of Neutrophil-to-Lymphocyte Ratio in Patients with Sepsis: A Prospective Observational Study Hindawi Publishing Corporation Mediators of Inflammation Volume 2016, Article ID 8191254, 8 pages
13. Vasileios Karamouzos, [1] et al Neutrophil to Lymphocyte Ratio and Platelet to Lymphocyte Percentage Ratio as Predictors of In-hospital Mortality in Sepsis. An Observational Cohort Study. Mater Sociomed. 2022 Mar; 34(1): 33–36.
14. Rehman FU, Khan A, Aziz A, Iqbal M, Mahmood SBZ, Ali N. Neutrophils to Lymphocyte Ratio: Earliest and Efficacious Markers of Sepsis. Cureus. 2020 Oct 8;12(10):e10851.
15. Khaled Ali Esmaeil Ali Shalaby, Tarek Elsayed Gouda, Afaf Abdel Hafez Abdel Mageed Neutrophil -To-Lymphocyte Ratio [NLR] as A Promising Prognostic Marker in Critically Ill Septic Patients The Egyptian Journal of Hospital Medicine (January 2022) Vol. 86, Page 242-249.
16. Alice Nicoleta Drăgoescu et al, Article Neutrophil to Lymphocyte Ratio (NLR)—A Useful Tool for the Prognosis of Sepsis in the ICU Biomedicines 2022, 10, 75.
17. Kaushik R, Gupta M, Sharma M, Jash D, Jain N, Sinha N, Chaudhry A, Chaudhry D. Diagnostic and Prognostic Role of Neutrophil-to-Lymphocyte Ratio in Early and Late Phase of Sepsis. Indian J Crit Care Med. 2018 Sep;22(9):660-663.