



Neutrophil Lymphocyte Ratio In Diagnosing Sepsis

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Abstract

Background: Sepsis is a life-threatening condition and is a leading cause of mortality in the World. Early diagnosis and prompt management of sepsis significantly improves the prognosis. Biological markers that have a high sensitivity and specificity, and that is easy to perform and cheap are hence required. NLR is neutrophil lymphocyte ratio. It has a prompt response to infection. The test is quick, cheap and easy to perform.

Materials And Methods: The study was performed in Amrita Institute of Medical Sciences, a tertiary level hospital in South India. 49 patients were taken in our study out of which 35 was in the sepsis group and 14 in non-sepsis group.

Results: The median NLR value in sepsis group on day 1 was 11.71 (5.28, 18.20) and in non-sepsis group was 2.18(1.64, 3.50) and p value was < 0.001. The area under the curve was 1.000 for CRP, 0.867 for NLR, 0.819 for total counts and 0.863 for TC+ NLR.

Conclusion: The median NLR in sepsis group was significantly higher than in the non-sepsis group and thus that NLR is a good marker in identifying sepsis. Also, the levels of NLR showed dynamic variation and hence it can be used as a marker to assess the clinical progression. NLR is a very simple, affordable and easily available biomarker, which can be useful in diagnosis of sepsis and also helps to assess the clinical progression of patient

Keywords: Sepsis, Biomarker, NLR ratio, Infections, Neutrophil, Lymphocyte

Introduction

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection [1]. A recent study estimated that, in 2017 there were 48.9 million cases and 11 million sepsis-related deaths worldwide, which accounted for almost 20% of all global deaths [2].

Individuals with infections, commonly infections of the gastrointestinal system, respiratory tract infections, urinary tract infections, can progress to sepsis. People with comorbid conditions like diseases of the liver, kidney, autoimmune diseases, people living with HIV, are more at risk. Older individuals,

pregnant females and neonates are also at a higher risk of progression to sepsis.

Sepsis if not identified and managed promptly can lead to septic shock, multiple organ dysfunction and death. Identifying sepsis in the early phase is important for adequate management of the condition.

Early (within 6h) and goal-directed resuscitation increases survival in severe sepsis and septic shock [3]. However, sepsis is often diagnosed late because the signs and symptoms used, such as change in leukocyte count, fever, tachycardia, and tachypnoea, are nonspecific and are not always present.

Blood culture is considered as the gold standard for the confirmation of bacteraemia and can isolate and identify the causative agent, but there is time delay, therefore a quick testing of a biomarker is extremely useful for early diagnosis of sepsis [4].

Many biological markers are currently available for the identification of sepsis. The markers most commonly used are CRP and procalcitonin (PCT). CRP and PCT are both useful markers of sepsis but PCT better differentiates infective from non-infective causes of inflammation, more closely correlates with gram negative sepsis severity in terms of shock and organ dysfunction and better predicts outcome when followed in time. However, PCT measurement is more costly and not widespread available [5].

NLR is Neutrophil-Lymphocyte ratio. It is calculated by dividing the number of neutrophils by the number of lymphocytes. The body's response to any physiological stress is by increasing the number of neutrophils and decreasing the number of lymphocytes. During sepsis, neutrophils are systemically stimulated but the migration to the infective foci is impaired. Thus, NLR ratio in times of physiological stress increases. Normal NLR is between 1-3. NLR of 6-9 indicate mild stress and greater than 9 is a sign of severe inflammation. NLR increases rapidly following acute physiologic stress (<6 hours) [6].

This prompt response time may make NLR a better reflection of acute stress than labs which are more sluggish to respond (e.g., white blood cell count or bandemia) [7].

Disadvantage of using NLR as a marker is that any active hematologic disorder can increase the NLR levels. Also, patients on exogenous steroids may have a high NLR ratio.

NLR as a parameter for sepsis is low cost and easy to implement by health services, which reinforces their use in low- and middle-income countries [8].

Materials And Methods

The study was performed in Amrita Institute of Medical Sciences, a tertiary level hospital in South India after approval from the ethics committee. 49 patients were taken in our study. 35 in the sepsis group and 14 in non-sepsis group. Statistics was calculated using SPSS software. CBC was performed

using Sysmex XN 2000 Hematology Analyzer and NLR was calculated based on the obtained CBC.

Results

49 subjects, 35 in sepsis group and 14 in non-sepsis group were taken. 25 (71%) in sepsis group and 5 (35.7%) in non-sepsis group were males. The mean age in sepsis group was 59.74 +/- 13.69 and in non sepsis group was 48.79 +/- 19.47 (Table 1).

In the sepsis group, 18 (51.4 %) of the patients had respiratory focus of infection, 7 (20%) had dermatological focus of infection, 13 (37%) had gastrointestinal focus of infection, 6 (17 %) had neurological focus and 17 (48%) had urinary tract infection. The etiology of the infective agent was also determined and 16 (45.7%) had bacterial cause of infection, 4 (11.4%) had viral cause of infection and 2 (5.7%) had fungal cause of infection. 7 (20%) of the isolated organisms showed multi drug resistance.

In sepsis group the median NLR levels were 11.71 (5.28, 18.20) and in non-sepsis was 2.18(1.64, 3.50) and the p value was <0.001 on day 1 of admission (Figure 1).

The NLR ratio in the sepsis group were then compared in patients with Multiorgan Dysfunction (MODS) and those without MODS. In Sepsis with MODS, the median levels were 12.51 (7.65, 18.28) and in sepsis without MODS median levels were 9.87(4.83,17.12) the p value was 0.337(Figure 2).

The Median NLR levels were then compared at Day 1, 3 and 5 between sepsis with MODS, Sepsis without MODS and Non sepsis. The levels were 12.51(7.65, 18.28) on day 1 and 10.62 (6.60, 18.72) on day 3 and 9.22(4.04, 12.29) on day 5 in sepsis with MODS. The NLR levels were 9.87(4.83, 17.12) on day 1 , 7.40(2.92, 9.64) on day3 and 5.83 (2.46, 8.65) on day 5 in sepsis without MODS. In non-sepsis group, the levels were 2.18 (1.64, 3.50) on day 1 and 2.58 (1.68, 3.50) on day 3 and 2.79 (1.70 , 3.48) on day 5. (Figure 3)

NLR was then compared to other markers like CRP, Total counts and Total counts +NLR in diagnosing sepsis.

The area under the curve was 1.000 for CRP , 0.867 FOR NLR , 0.819 for total counts and 0.863 for TC+ NLR. (Figure 4)

The sensitivity for TC+NLR was 88.6% and the specificity was as 85.7%. The sensitivity and specificity of CRP was 100%. The sensitivity of NLR was 80% and specificity was 85.7%. The sensitivity of total counts was 77.1% and specificity was 78.6%.

The NLR ratio cut-off obtained in our study to diagnose sepsis was 4.94.

Table 1 : General characteristics of the patients in sepsis and non-sepsis groups

	Sepsis	Non Sepsis
MEAN AGE (In Years)	59.74 +/- 13.69	48.79 +/- 19.47
Males Count (% within group)	25 (71.4%)	5 (35.7%)
Comorbidities Count (% within group)		
Diabetes mellitus	22 (62.90%)	2 (14.30%)
Systemic Hypertension	13 (37.10%)	3 (21.40%)
Hypothyroidism	5 (14.30%)	2 (14.30%)
Dyslipidemia	5 (14.30%)	1 (7.10%)
Coronary artery disease	7 (20.00%)	3 (21.40%)
Chronic kidney disease	8 (22.90%)	0 (0.00%)
Chronic liver disease	5 (14.30%)	0 (0.00%)
Cerebrovascular accident	3 (8.60%)	1 (7.10%)
Chronic obstructive pulmonary disease	3 (8.60%)	0 (0.00%)

Figure 1 : Median NLR between sepsis and non-sepsis on day 1

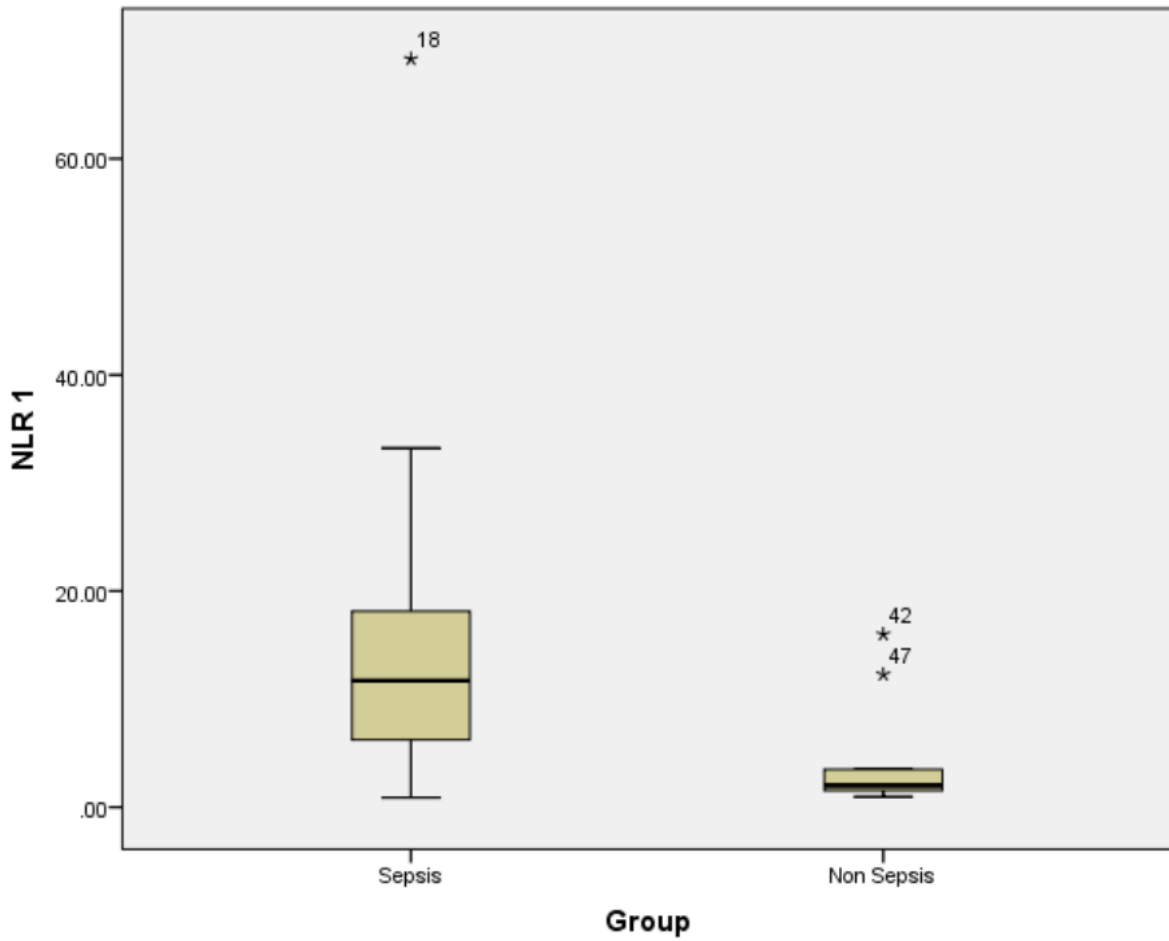


Figure 2 : Median NLR in sepsis with MODS vs sepsis without MODS

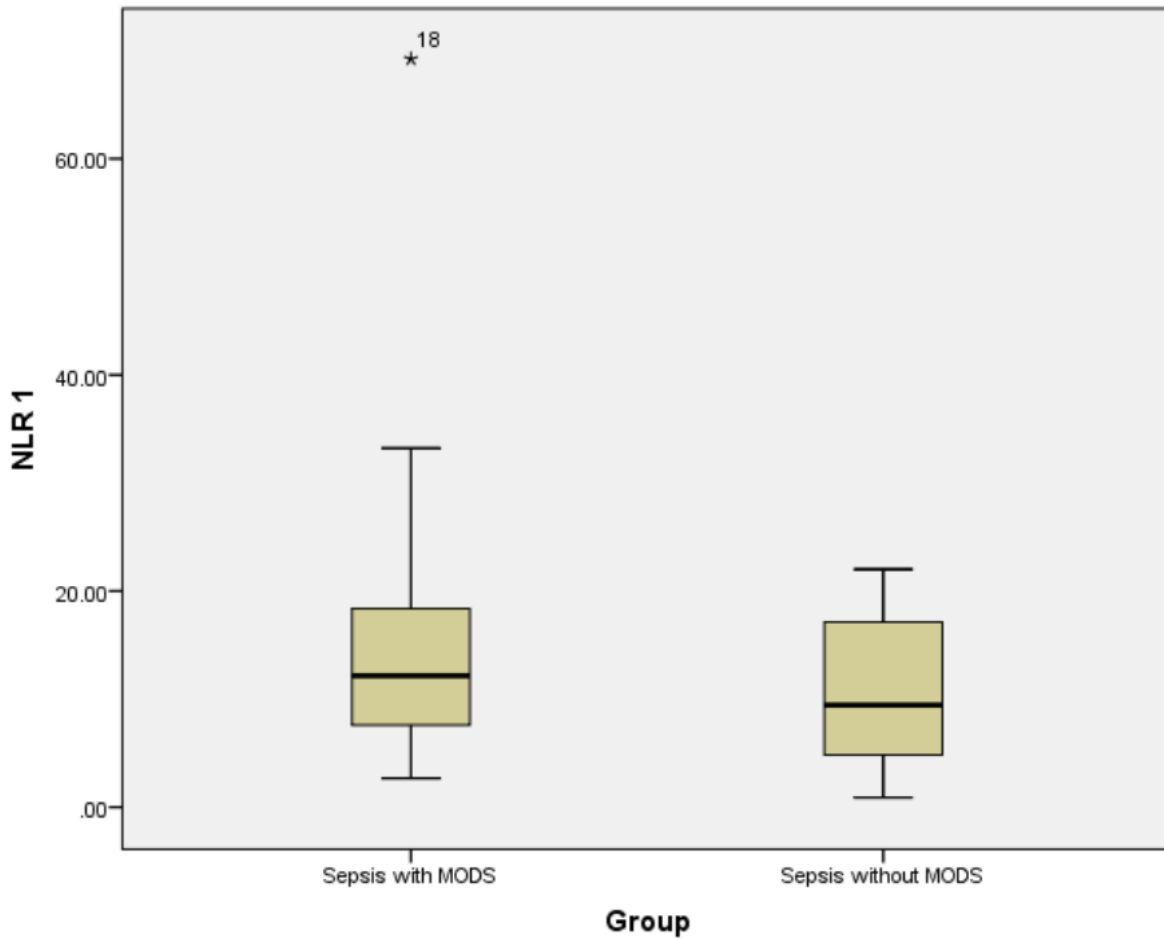


Figure 3 : Median NLR levels between sepsis with MODS , sepsis without MODS and Non Sepsis at Day 1 , Day 3 and Day 5.

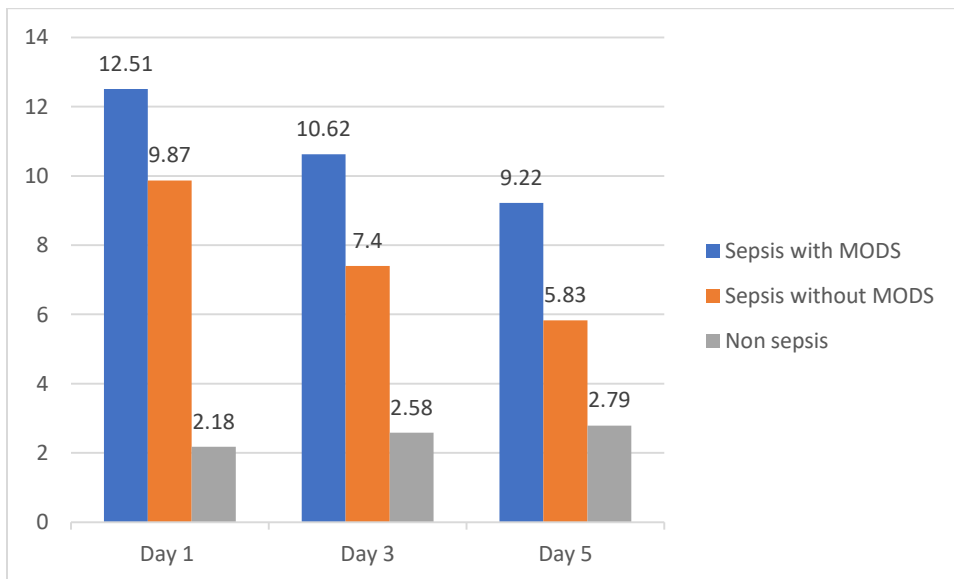
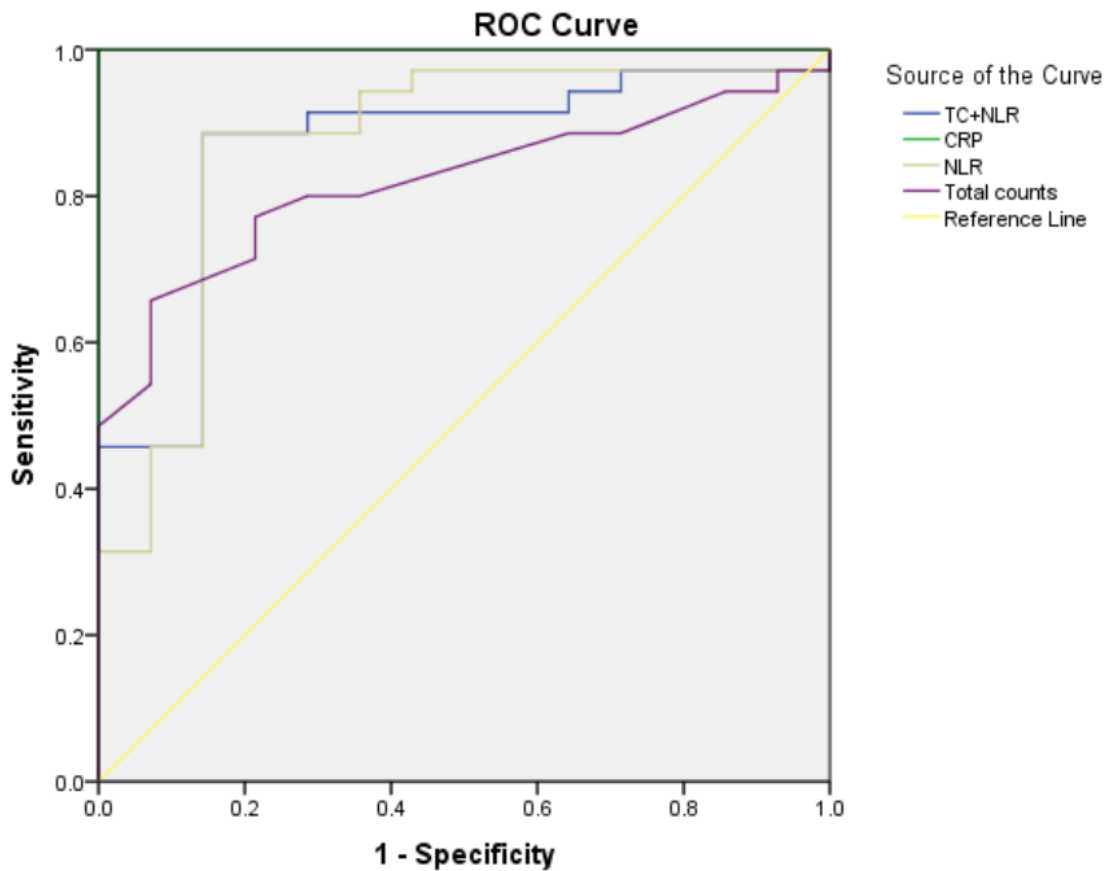


Figure 4 : ROC curve for the different parameters in diagnosing sepsis



Diagonal segments are produced by ties.

Discussion

Sepsis is a leading cause of mortality in the world. Early diagnosis of sepsis is very important and prompt treatment of sepsis can be lifesaving. We have studied the association of NLR ratio in sepsis.

The study consisted of 2 groups, with a total of 49 patients. In the group of patients with sepsis, there were 35 patients and in the non-sepsis group, there were 14 patients. The median NLR ratio in sepsis group was 11.71 (5.28, 18.20) and in non-sepsis 2.00(1.54) and the p value was <0. 001.This shows that NLR is a good marker in identifying sepsis. However, in the sepsis group, the value measured in patients with MODS was 12.16(7.20, 18.54) and in sepsis without MODS the value was 9.87(4.83,17.12) the p value was 0.337. This shows that NLR cannot be used to differentiate those with MODS from those without MODS.

The dynamic variation in value of NLR was seen on Day 1 , Day 3 and Day 5. This shows NLR ratio can also be used to prognosticate sepsis.

NLR was then compared with other parameters and ROC curve was obtained. NLR had a sensitivity of 80% and specificity was 85.7%. NLR along with Total counts showed a sensitivity of 88.6% and the specificity was as 85.7%. Thus, NLR is a very simple, affordable, and easily available biomarker, which can be useful in diagnosis of sepsis and also helps to assess the clinical progression of patient.

Rajnish et al in his study revealed about use of NLR in sepsis [9]. In our study, we showed that the median NLR in sepsis group was significantly higher than in the non-sepsis group and thus that NLR is a good marker in identifying sepsis. Also the levels of NLR showed dynamic variation and hence it can be used as a marker to assess the clinical progression.

Conclusion

Sepsis is most commonly encountered condition and simple and easy diagnosis of sepsis can be very helpful in management. Neutrophil lymphocyte ratio (NLR) is good, cheap and easily available investigation to diagnose sepsis. More elevated is the

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NLR ratio, more severe is the sepsis. This study shows the usefulness of NLR ratio in diagnosing sepsis.

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