

## The Predictive Value of Neutrophil to Lymphocyte Ratio in Sample of Iraqi COVID-19 Patients

Dahlia N. AL-Saidi

Department of Laboratory Medical Techniques, AL-Nisour University,  
College. Mayar J. Abd, Ibn Al-Bitar Cardiac Surgery Center

\*Corresponding author: Dahlia N. AL-Saidi, Mobile: 07716914012, Email: dahlia.n.path@nuc.edu.iq

### ABSTRACT

**Background:** The disease of Coronavirus-19 is extremely transmittable and is spreading at a speedy manner. Yet still there are no currently used biomarkers that can simply determine the severity of COVID-19. The neutrophil-to-lymphocyte ratio (NLR) is one of the cutting-edge biomarkers that are used in patients with various diseases. A high NLR is expressed in COVID-19 patients with unfavorable prognosis. Early identification of COVID-19 patients who are at high risk of adverse clinical sequelae is crucial in saving their lives especially in settings of limited medical resources.

**Objective:** This study aimed to investigate the NLR influence on prognosis and the ideal cutoff value in the laboratory-confirmed COVID-19 cases.

**Subjects and Methods:** This is a retrospective cohort study of 100 patients with confirmed COVID-19 that were hospitalized through the period from January 10th till July 20th, 2022, in Dar-Assalam Hospital, Baghdad. Diagnosis was performed by molecular assay from nasopharyngeal swabs. Patients with more than or equal to the cutoff value of NLR had deterioration in their clinical outcome, and classified during hospitalization to mild /moderate to severe condition.

**Results:** 100 patients with COVID-19 were involved in the study. Advanced stages COVID-19 patients had a significant high level of NLR in comparison with earlier stages. NLR can help in the diagnosis and prediction of the prognosis of the disease, primarily mortality prediction.

**Conclusion:** Our work showed that NLR can help in the assessment of COVID-19 severity and can support the decision-making process regarding treatment strategy by the early identification of patients with severe illness.

**Keywords:** Coronavirus disease, COVID-19, Neutrophil to lymphocyte ratio, NLR.

### INTRODUCTION

Coronavirus Disease 2019 (COVID-19) is a systemic and respiratory disease, which requires a fast recognition of patients who are potentially critical<sup>(1, 2)</sup>. In COVID-19, mortality is relating positively with the severity of the disease. Therefore, early recognition of patients who are susceptible to poor outcomes is of an eminent value<sup>(3)</sup>.

Different studies reached the conclusion that the neutrophil/lymphocyte ratio (NLR) offers a strong predictive evaluation of COVID-19 patients' disease severity and mortality. Additionally, the NLR ratio is a rapid and simple prognostic marker in multiple clinical conditions including COVID-19 disease<sup>(4, 5, 6)</sup>. We investigated in this study the NLR influence on prognosis and the ideal cutoff value in the laboratory-confirmed COVID-19 cases.

### PATIENTS AND METHODS

A retrospective study of 100 adult patients with confirmed COVID-19 infection was done. Patients were admitted from January 10th till July 20th, 2022, in Dar-Assalam Hospital, Baghdad. They were analyzed retrospectively for identification of the NLR cut-off point on admission to enable severity of disease prediction. Respiration rate of less than 30 breaths per minute, arterial blood oxygen partial pressure, or oxygen concentration of less than 300 mm Hg, in addition to mean oxygen

saturation of less than 94% when breathing room air were all considered as the positive indicators of severe COVID-19.

#### Exclusion criteria:

Patients who were pregnant, receiving palliative care, or receiving chemotherapy for a solid cancer or hematological condition were not included. Patients under the age of 18.

Basic information including sex, age and history of comorbid diseases were collected through a questionnaire and interviews with the patients or their family members. The diagnosis of COVID-19 was made by RT-PCR molecular analysis of the nasopharyngeal swab.

The calculation of NLR ratio was done by depending on the absolute neutrophil and lymphocyte count. Blood examinations involved complete blood cell counts, serum biochemical tests and coagulation study were done once the patient was admitted to the hospital. Risk factors linked to severe COVID-19, such as age, malignancy, liver disease, hypertension, diabetes, COPD, and the intensive care unit admission and the requirement for ventilator support were collected. Patients with NLR that is equal to or greater than the threshold value (2.69) based on the neutrophil and lymphocyte data assessed at hospital admission were classified as being in the exposed group.

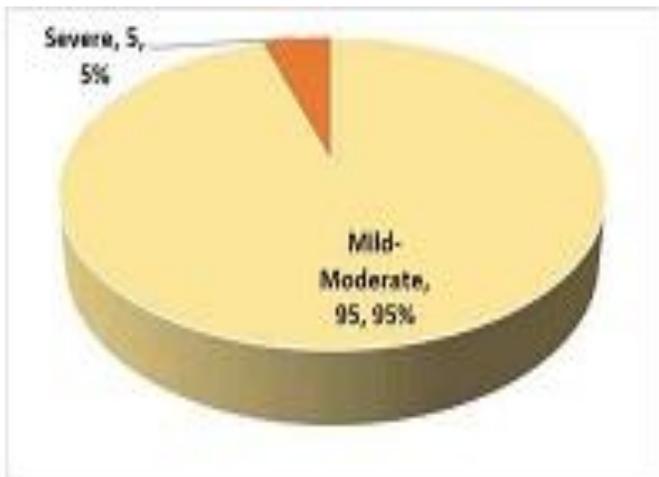
**Ethical approval:** The study was approved by the Ethics Board of *AL-Nisour* University, and an informed written consent was taken from each participant in the study. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Statistical analysis:** All statistical analyses were performed using SPSS 27 software (IBM SPSS Statistics, version 27.0, Armonk, NY: IBM Corp) and The Mann-Whitney U test. P value  $\leq 0.05$  is considered as statistically significant.

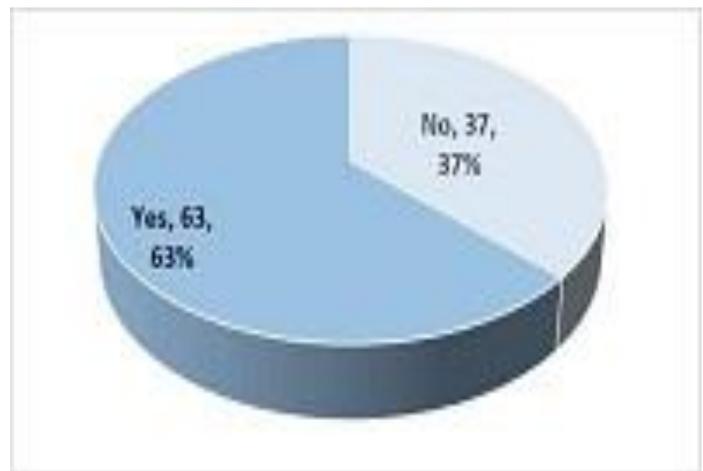
**RESULTS**

A 100 COVID-19 confirmed patients were involved in this study, with 95 patients categorized as mild-moderate cases and only 5 were severe cases (Figure 1).

Male patients represented 56 % of the cases, while females represented 44%. The mean age for female patients was 48.5 years ranging from (18-71) years and 50.6 years for male patients ranging from (19-72) years as shown in table (1). A percentage of 63.6% of patients had a history of at least one comorbidity (Figure 2).



**Figure (1):** Cases distribution according to severity of the disease.



**Figure (2):** Cases distribution according to presence of comorbidity.

**Table (1):** Demographic and inflammatory parameters in COVID-19 patients involved in this study

Parameter		Female (n=44)	Male (n=56)	P value
Age (years)	Mean $\pm$ SD	48.5 $\pm$ 14.43	50.61 $\pm$ 14.61	0.473*
Neutrophils (x10 <sup>9</sup> /L)	Mean $\pm$ SD	6192.96 $\pm$ 769.37	7046.61 $\pm$ 150.33	<b>0.036*</b>
Lymphocytes (x10 <sup>9</sup> /L)	Mean $\pm$ SD	2805.68 $\pm$ 89.19	2847.32 $\pm$ 89.2	0.808*
N/L ratio	Mean $\pm$ SD	2.26 $\pm$ 0.54	2.62 $\pm$ 0.2	<b>0.018**</b>

\* Unpaired t test, \*\* Mann Whitney test.

All the patients (100 %) involved in the analysis had NLR measured at hospital admission. At time of hospital admission, the median NLR was 2.4, and the range was (1.25-8.17). Patients with severe disease had higher NLR value (median: 4.58) than those with mild-moderate COVID-19 infection (median: 2.38, P: 0.016) (Table 2). When NLR is evaluated on hospital admission it has a great influence in categorizing the disease according to severity and can help in prediction of clinical outcome. The cutoff value of NLR is 2.69.

**Table (2):** Comparison of inflammatory parameters between mild-moderate and severe cases with COVID-19

Parameter		Mild-Moderate (n=95)	Severe (n=5)	P value*
Age (yr)	Mean $\pm$ SD	49.41 $\pm$ 4.74	54.8 $\pm$ 8.07	0.424
Neutrophils (x10 <sup>9</sup> /L)	Mean $\pm$ SD	6564.21 $\pm$ 1987.09	8700 $\pm$ 874.83	<b>0.034</b>
Lymphocytes (x10 <sup>9</sup> /L)	Mean $\pm$ SD	2867.37 $\pm$ 28.7	2100 $\pm$ 60.23	0.095
N/L ratio	Mean $\pm$ SD	2.33 $\pm$ 0.57	5.02 $\pm$ 1.76	<b>0.016</b>

\* Mann Whitney test

## DISCUSSION

In this study, we verified that the NLR cutoff value of 2.6 that was obtained upon hospital admission as a measure of great help in disease classification according to severity, which can aid in predicting the disease's subsequent clinical course. NLR of < 2.6 in patients with confirmed COVID-19 had a chance of excluding disease worsening and serious clinical outcomes helping in providing the appropriate treatment and maximizing the use of the restricted resources<sup>(7)</sup>. The peripheral blood NLR has a prognostic significance in cardiac diseases, vascular disorders, autoimmune diseases, cancers, and infectious diseases<sup>(8, 9, and 10)</sup>.

An increased NLR may be a sign of both the patients' immunological health and the severity of COVID-19. The NLR has been shown to be effective in identifying severe cases and predicting the COVID-19 patients' death in several studies<sup>(11, 12, and 13)</sup>.

The present study confirms the results of the earlier studies and boosts the effect of NLR in disease classification into mild-moderate and severe cases in addition to prediction of disease serious clinical outcomes. The NLR cutoff value in this study is of 2.6 above which significant clinical events happened and the patient's condition deteriorated. This result may lead to a more precise clinical decisions made by physicians caring for patients with COVID-19 upon hospital admission, particularly in areas with limited medical supply. Immediately after hospital admission, NLR was evaluated, and only five patients (5%) were found to be in the severe category with median of 4.58 for the NLR. This result goes with another study which finds only 20 patients (5.9%) to be within the NLR's sensitivity range of 5.0-8.0<sup>(14)</sup>

## CONCLUSIONS

In conclusion, the NLR measured upon hospital admission in this research of 100 COVID-19 patients was highly valuable in predicting the later disease worsening and significant clinical outcomes.

## REFERENCES

1. **Todor S, Bîrluțiu V, Topîrcean D et al. (2022):** Role of biological markers and CT severity score in predicting mortality in patients with COVID-19: An observational retrospective study. *Exp Ther Med.*, 24 (5): 698.
2. **Zhao X, Zhou L, Kou Y et al. (2022):** Activated neutrophils in the initiation and progression of COVID-19: hyperinflammation and immunothrombosis in COVID-19. *Am J Transl Res.*, 14 (3): 1454-1468.
3. **Bennett S, Tafuro J, Mayer J et al. (2020):** Clinical features and outcomes of adults with COVID-19: a systematic review and pooled analysis of the literature. *Int J Clin Pract.*, 75: e13725.
4. **Xu X, Han M, Li T et al. (2020):** Effective treatment of severe COVID-19 patients with tocilizumab. *Proc Natl Acad Sci U S A.*, 117 (20): 10970-10975.
5. **Yildiz H, Yombi J, Castanares-Zapatero D (2021):** Validation of a risk score to predict patients at risk of critical illness with COVID-19. *Infect Dis (Lond)*, 53 (1): 78-80.
6. **Liu J, Liu Y, Xiang P et al. (2020):** Neutrophil-to-lymphocyte count predicts critical illness patients with 2019 coronavirus disease in the early stage. *J Transl Med.*, 18: 206.
7. **Liu Y, Du X, Chen J et al. (2020):** Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. *J. Infect.*, 81: e1-e6.
8. **Huguet E, Maccallini G, Pardini P et al. (2019):** Reference values for neutrophil to lymphocyte ratio (NLR), a biomarker of cardiovascular risk, according to age and sex in a Latin American population. *Curr Probl Cardiol.*, doi: 10.1016.
9. **Wang X, Qiu L, Li Z et al. (2018):** Understanding the multifaceted role of neutrophils in Cancer and autoimmune diseases. *Front Immunol.*, 9: 2456.
10. **Yao X, Li T, He Z et al. (2020):** A pathological report of three COVID-19 cases by minimally invasive autopsies. *Chinese journal of pathology*, 49(5):411-417
11. **Liang W, Liang H, Ou L et al. (2020):** Development and validation of a clinical risk score to predict the occurrence of critical illness in hospitalized patients with COVID-19. *JAMA Intern Med.*, 180: e202033.
12. **Yan X, Li F, Wang X et al. (2020):** Neutrophil to lymphocyte ratio as prognostic and predictive factor in patients with coronavirus disease 2019: a retrospective cross-sectional study. *J Med Virol.*, 92 (11): 2573-81.
13. **Tatum D, Taghavi S, Houghton A et al. (2020):** Neutrophil-to-lymphocyte ratio and outcomes in Louisiana Covid-19 patients. *Shock*, 54 (5): 652-8.  
**Zeng Z, Feng S, Chen G et al. (2021):** Predictive value of the neutrophil to lymphocyte ratio for disease deterioration and serious adverse outcomes in patients with COVID-19: a prospective cohort study. *BMC Infect Dis.*, 21: 80.