The Relation between Neutrophil-Lymphocyte Ratio and Inflammatory Markers in Assessing the Severity of COVID-19 Disease

Manasathreya AVK, Rama Devi M

ABSTRACT

Background: The identification of effective laboratory biomarkers together with the clinical presentation is crucial to categorize the severity of the disease. The following biomarkers have been identified: Neutrophillymphocyte ratio (NLR), Inflammatory C-reactive protein (CRP), Serum Ferritin levels, Serum Lactate Dehydrogenase. Cytokine storm is one of the most dreaded complications of COVID19 that can be treated effectively by early identification. The current study is to test and confirm the prognostic value of NLR as an economic and reliable indicator of COVID19.

Methodology: The current study is a retrospective observational study. The data of COVID-19 patients admitted to a tertiary care hospital from the 25th of August, 2021 to the 25th of September, 2021 was analyzed. Patients were categorized into mild, moderate, and severe groups based on ICMR guidelines. The blood reports from the day one of admission were taken into consideration for this study.

Results: The study included 71 patients consisting of 29 males and 42 females, with a male to female ratio of 0.69. In the present study, 52 patients are with mild disease (Males-19; Females-33), 12 (males-4; females-8) are in the moderate category, and 7 (males-1; females-6) patients have severe disease. In mild patients, the mean CRP was 4.01mg/L, the mean serum Ferritin was 214.23mcg/L, and the mean NLR was 3.62. In patients with moderate severity, the mean CRP was 5.86mg/L, the mean serum Ferritin was 383.62mcg/L, and the mean NLR was 5.67. In patients with severe disease, the mean CRP was 22.71mg/L, the mean serum Ferritin was 805mcg/L, and the mean NLR was 15.3.

Conclusion: The study showed that there is a gradual increase in CRP, Serum Ferritin, and NLR with the increase in severity of disease from mild to severe. NLR is gradually increasing with increasing mean CRP and serum Ferritin levels Hence, NLR can be used as a reliable predictor of the severity of the disease instead of CRP and serum Ferritin in places lacking adequate facilities.

Keywords: COVID-19, NLR, S.CRP, S.FERRITIN.

Published Online: April 21, 2022

ISSN: 2736-5476

DOI:10.24018/ejclinicmed.2022.3.2.191

Manasathreya AVK*

Sri Venkateswara Medical College, India.

(e-mail: sachinathreva22@gmail.com)

Rama Devi M. Sri Venkateswara Medical College,

India.

*Corresponding Author

I. Introduction

A novel corona virus (CoV) named '2019-nCoV' or '2019 novel coronavirus' or 'COVID-19' by the World Health Organization (WHO) is in charge of the current outbreak of pneumonia that began at the beginning of December 2019 near in Wuhan City. Corona viruses mostly cause gastrointestinal and respiratory tract infections. Infected patients may present with any of the following; fever, high temperature (>37.3 °C), cough, myalgia, sputum production, headache, haemoptysis, diarrhea, dyspnoea and in some cases, acute respiratory distress syndrome (ARDS), acute cardiac injury or secondary infection. Explore the role of different biomarkers in the disease pathogenesis of COVID-

19 and assess how their levels vary depending on the severity of the disease. By doing so, it gives clinicians a tool to group patients and predicts prognosis and mortality. The biomarkers we review include, C-reactive protein (CRP), IL-6, white cell count (WCC), lactate dehydrogenase (LDH), D-dimer, platelet count, cardiac troponin and renal markers, Neutrophil-Lymphocyte ratio. Cellular-mediated inflammatory response, lymphocytes, neutrophils, and monocytes are increasingly being recognized as having an important role in inflammation. In this context, studies have suggested that NLR can be used as an independent prognostic factor in a variety of diseases including COVID19.

A. Aim

To study the relationship between Neutrophil-Lymphocyte

Ratio (NLR) to serum Ferritin and C-reactive protein in assessing the clinical severity of COVID-19 illness.

II. MATERIALS AND METHODS

The present study is a hospital based retrospective study conducted between August 2021 and September 2021. The study included Patients above 18 years with a history of RT-PCR positive for SARS-CoV-2. Pregnant patients were excluded from the study.

III. METHODOLOGY

Data was collected from medical records of 71 patients with RT-PCR confirmed for COVID-19, who were admitted in COVID19 ward of SVRRGH Tirupati, Chittor district, Andhra Pradesh from August 2021 to September 2021 as per pre-structured pro-forma, and data is analyzed using NCSS 2022 software.

IV. RESULTS

A. Age Distribution

Out of 71 patients, the most common age group affected is 21-30 years (32.39%) followed by the age group of 51-60 years (21.12%). The least commonly affected age group is above 70 years (2.81%). The mean age of the patients is 42.77±17.60.

TABLE I: AGE DISTRIBUTION

Age Group	Frequency(N)	Percentage (%)
<20	4	5.63
21-30	23	32.39
31-40	8	11.26
41-50	8	11.26
51-60	15	21.12
61-70	11	15.49
>70	2	2.81
TOTAL	71	
MEAN \pm S.D:	42.77 ± 17.60	

B. Sex Distribution

This study included 42 females (59.15%) and 29 males (40.84%). Female preponderance was observed with a male to female ratio of 0.69. In male patient the age group 51-60 years was most commonly affected. In female patients the age group 21-30 years was commonly affected.

TABLE II: AGE WITH SEX DISTRIBUTION

Age Group	Male	Female	Total
<20	2	2	4
21-30	5	18	23
31-40	2	6	8
41-50	2	6	8
51-60	10	5	15
61-70	7	4	11
>70	1	1	2
TOTAL	29	42	71

C. Staging of Clinical Severity

In the present study 73% of the study subjects are having mild disease, 17 % were suffered with moderate disease and only 10% are having severe disease (Fig.1).

CLINICAL SEVERITY & NUMBER OF PATIENTS



Fig. 1. Clinical severity of disease.

D. Mean NLR in Relation with Clinical Severity of COVID-19 Illness

In mild patients, the mean NLR was 3.62. In patients with moderate severity, the mean NLR was 5.67. In patients with severe disease, the mean NLR was 15.3 (Fig.2).

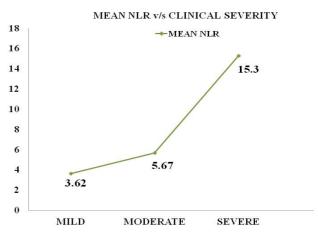
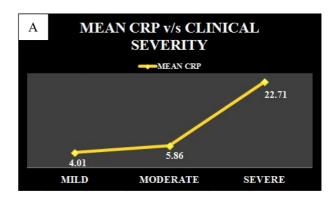


Fig. 2. Relation between clinical severity and mean NLR.

E. Staging of COVID19 with Clinical Severity and Inflammatory Markers

In mild patients, the mean CRP was 4.01mg/L, the mean serum Ferritin was 214.23mcg/L. In patients with moderate severity, the mean CRP was 5.86mg/L, the mean serum Ferritin was 383.62mcg/L. In patients with severe disease, the mean CRP was 22.71mg/L, the mean serum Ferritin was 805mcg/L (Fig.3).



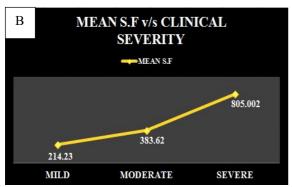


Fig. 3. A) Relation between clinical severity and mean CRP. B) Relation between clinical severity and mean S.Ferritin.

F. Relation between NLR to Serum Ferritin and CRP

In the present study correlation between NLR to CRP and S. Ferritin was assessed and the study showed that there is a positive correlation between NLR; CRP and NLR: S.Ferritin. The correlation coefficient was 0.311 and 0.284 respectively (Fig.4).



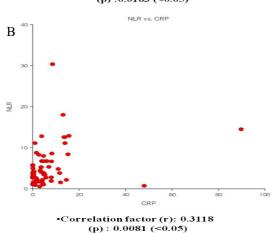


Fig. 4. A) Correlation between mean NLR and mean S.Ferritin. B) Correlation between mean NLR and mean CRP.

V. DISCUSSION

In the present study 71 patients were enrolled. Most common age group affected was 21- 30 years. Female predominance observed (M: F=1: 1.45) in the present study. Mild disease is common followed by moderate and severe illness. Mean NLR, Mean CRP and Mean Serum Ferritin are gradually increases with increasing severity of illness. There is a positive correlation observed between mean NLR to serum mean CRP and mean Ferritin levels in the present study.

Many studies are supportive to the present study observations. We have discussed them below.

A study [1] concluded that NLR is a promising tool for risk stratification and prompt decision making about intensifying the management, further studies for assessing the suitable cutoff points of NLR to utilize the already constrained healthcare resources during the ongoing pandemic are the need of the hour.

Meta analysis by [2] utility of TLC, neutrophils, lymphocytes, and N-L ratio, as significant predictors of COVID-19 outcome found the clinical.

Analysis of hematological profiles by [3] concluded that In severe COVID-19 cases, NLR is significantly higher, and a strong correlation between NLR and CRP.

Reference [4] cross sectional study revealed that NLR and PLR are reliable markers in COVID 19 patients, and even more, they correlated with classical inflammatory markers such as CRP, ESR.

Reference [5] meta analysis revealed that NLR has a high capacity to accurately predict the severity of COVID-19, which can permit laboratory-based differentiation of nonsevere and severe cases.

Reference [6] study of hematological parameters concluded that NLR and LMR can facilitate in categorizing the disease severity and progression in patients, thereby enabling us to make appropriate and informed clinical decisions.

A study by [7] showed that NLR may predict the disease course and severity level of non-mild COVID-19.

A study by [8] concluded that NLR and CRP are a potential, reliable and easy-to-use predictor for COVID-19 prognosis.

Reference [9] study showed that there was significant correlation between increase in NL ratio and disease severity of COVID-19 positive pneumonia.

Reference [10] concluded that NLR was significantly elevated in COVID-19 patients. NLR has been identified as an independent biomarker for COVID-19.

VI. CONCLUSION

The study showed that there is a gradual increase in CRP, S. Ferritin, and NLR with increase in severity of disease from mild to severe. NLR is gradually increasing with increase in mean CRP and mean S. Ferritin. Hence NLR can be used as a reliable predictor of severity of disease in place of S.CRP and S. Ferritin, where there is a lack of adequate facilities for investigations and also it reduces the financial burden to the patients.

LIMITATION

It is a retrospective study.

REFERENCES

- Sarkar S, Khanna P, Singh AK. The Impact of Neutrophil-Lymphocyte Count Ratio in COVID-19: A Systematic Review and Meta-Analysis. Journal of Intensive Care Medicine. 2021: 088506662110456.
- Shetty Ba, Shilpa T, Rajanna A, Ravi K, Rao M, Bhat B. Association of neutrophil-lymphocyte ratio with clinical outcome of COVID-19

- patients: A prospective study. APIK Journal of Internal Medicine.
- [3] Sukrisman L, Sinto R, Priantono D. Hematologic Profiles and Correlation Between Absolute Lymphocyte Count Neutrophil/Lymphocyte Ratio with Markers of Inflammation of COVID-19 in an Indonesian National Referral Hospital. International Journal of General Medicine. 2021;14: 6919-6924.
- [4] Man MA, Rajnoveanu RM, Motoc NS, et al. Neutrophil-to-lymphocyte ratio, platelets-to-lymphocyte ratio, and eosinophils correlation with high-resolution computer tomography severity score in COVID-19 patients. PLOS ONE. 2021; 16(6): e0252599.
- Wang Y, Zhao J, Yang L, Hu J, Yao Y. Value of the Neutrophil-Lymphocyte Ratio in Predicting COVID-19 Severity: A Meta-analysis. Disease Markers. 2021; 2021: 1-10.
- Shivakumar BG, Gosavi S, Rao AA, Shastry S, Raj SC, Sharma A, et al. Neutrophil-to-Lymphocyte, Lymphocyte-to-Monocyte, and Platelet-to-Lymphocyte Ratios: Prognostic Significance in COVID-19. Cureus. 2021; 13(1).
- Qun S, Wang Y, Chen J, Huang X, Guo H, Lu Z, et al. Neutrophil-to-Lymphocyte Ratios Are Closely Associated With the Severity and Course of Non-mild COVID-19. Frontiers in Immunology. 2020; 11: 2160.
- Liu YP, Li GM, He J, Liu Y, Li M, Zhang R, et al. Combined use of the neutrophil-to-lymphocyte ratio and CRP to predict 7-day disease severity in 84 hospitalized patients with COVID-19 pneumonia: a retrospective cohort study. Annals of Translational Medicine. 2020;
- [9] Shenoy GC, Ramaiah M, Kamaraddi S, Somashekar P, Subramanya SK. Comparison of neutrophil-lymphocyte ratio among severe acute respiratory illness COVID-19 positive and negative patients and to correlate with disease severity. International Journal of Advances in Medicine. 2021; 8(8): 1120.
- [10] Nalbant A, Kaya T, Varim C, Yaylaci S, Tamer A, Cinemre H. Can the neutrophil/lymphocyte ratio (NLR) have a role in the diagnosis of coronavirus 2019 disease (COVID-19)? Revista da Associação Médica Brasileira. 2020; 66(6): 746-751.