


Original Research Article

# Neutrophil to lymphocyte ratio and C-protein level as markers to predict deterioration in stable COVID-19 patients

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## Abstract

The new Corona virus disease (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2). It is a highly communicable infectious disease [1]. Clinical manifestations of COVID-19 vary from asymptomatic to ARDS leading to death, it is important to differentiate between severe and non-severe cases. Early warning signs can be identified by several laboratory tests which are often expensive, time taking. Neutrophil-lymphocyte ratio (NLR), C-reactive protein (CRP) are two simple tests that can be used as markers for clinical outcome in COVID-19 patients. The aim and objectives of the study were to correlate patients clinical severity and CRP, NLR levels and to assess direct correlation between CRP levels and NLR. 101 patients who fulfilled the inclusion criteria were taken into the study. Patients are divided into mild, moderate severity based on WHO criteria and CBP, CRP were sent on the 6<sup>th</sup>/ 7<sup>th</sup> day of illness. Among the 101 patients, 93 were in mild group, 8 were in moderate group. The study group included subjects who aged between 18 years to 80 years of age. Plasma CRP levels were higher in moderate cases than in mild cases, and this difference was significant ( $p < 0.001$ ). The mean NLR of moderate severity were significantly higher than those of mild cases ( $p=0.00003$ ). Results showed that NLR was positively correlated with CRP levels. NLR and CRP are potential, reliable and easy-to-use predictors for deteriorating covid-19 infection. The integration of NLR and CRP may lead to improved predictions and help to triage patients at the time of hospital admission.

## Key words

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Neutrophil to lymphocyte ratio, C-protein, Markers, Covid-19.

## Introduction

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The new coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a highly communicable infectious disease. It has rapidly and widely spread worldwide [1-3], and was declared a pandemic in March 2020 by World Health Organization [4].

Clinical manifestations of COVID-19 vary. Patients develop variable signs and symptoms, ranging from asymptomatic to acute respiratory distress syndrome, leading to death, so it is important to differentiate between severe and non-severe cases [2].

Generally, severe patients are treated in the intensive care unit, while mild patients are isolated at home or hospitalized in the usual isolation ward. However, a small subset of non-severe patients will develop into severe cases.

Clinically, if early warning signs of severe COVID-19 infection can be identified, timely intervention and treatment may help reduce the mortality, improve the cure rate, shorten the hospital stay and reduce the consumption of resources.

A rising neutrophil count and a falling lymphocyte count indicate the intensity of the inflammatory response and damage to the immune system, respectively [5]. Several studies have reported their findings that NLR can be used as an early warning signal of severe COVID-19 infection [6], and considered as an independent marker for poor clinical outcomes and mortality in COVID-19 infection [7-11].

In response to infections, the liver synthesizes significant quantities of acute-phase proteins (APPs), such as CRP [12, 13]. Qin, et al. observed higher CRP levels in severe COVID-19 patients than in non-severe cases, suggesting that

this biomarker can be monitored to evaluate disease progression [14].

NLR and CRP are potential, reliable and easy-to-use predictors for deteriorating covid-19 infection. Studies that correlate the CRP and NLR levels in covid-19 are very limited. This study sheds some light on this correlation

## Aim and objectives

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- To identify cases of primary infection of Covid-19
- To correlate patients clinical severity and CRP, NLR levels
- To assess direct correlation between CRP levels and NLR

## Materials and methods

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It was a retrospective observational study of 101 patients with diagnosis of Mild – moderate SARS COV-2 Infection treated on OPD basis in Malla Reddy Hospital, Hyderabad, Telangana. Study period was from January 2021 to January 2022.

## Inclusion Criteria

- Age > 18 years who came to our hospital OPD with mild/moderate severity of COVID-19 infection.
- Patients with Real-time fluorescent reverse transcription-polymerase chain reaction (RT-PCR) of respiratory samples (nasal/ oropharyngeal swab) positive for SARS-CoV-2.

Mild disease – included patients with upper respiratory tract symptoms (and/or fever) without shortness of breath or hypoxia

Moderate disease - characterized by any one of:

1. Respiratory rate > 24/min, breathlessness
2. SpO<sub>2</sub>: 90% to < 93% on room air

### Exclusion Criteria

- Patients who were already hospitalized
- Patients tested negative on RT PCR for covid-19

101 patients who fulfilled the inclusion criteria were taken into the study. Patients were divided into mild, moderate severity and on day 6/7 of illness CRP, CBP was sent and values were compared between both groups.

### Statistical analysis

All the data were collected in approved proforma and data were entered in MS EXCEL 2007 and was subjected to statistical analysis.

Descriptive data were analyzed using percentages and central tendency. Paired t test

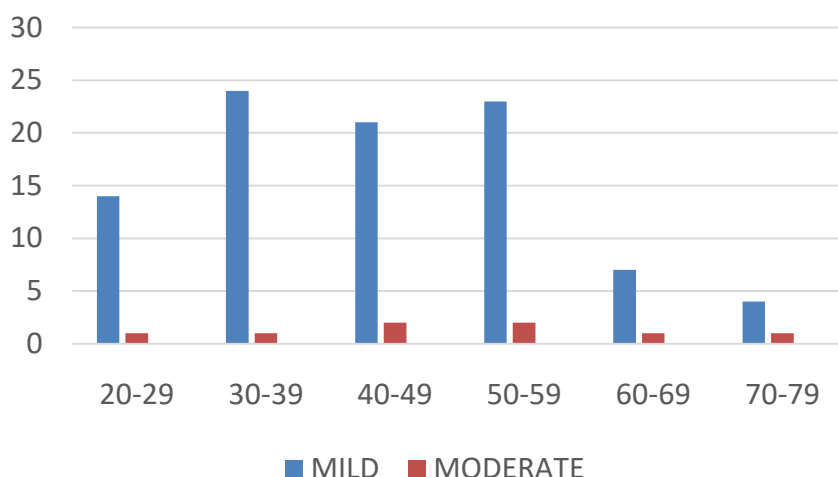
was applied for mean values. P value < 0.05 was considered as statistically significant.

### Results

In our study, we had taken a total number of 101 patients who had fulfilled the inclusion criteria. Among them 93 were in mild group and 8 were in moderate group. In the mild group 48 were male and 45 were female. In the moderate group 5 were male and 3 were female.

The study group population age was from 18 years to 80 years of age and the majority of patients were in the age group 30-39 (**Figure - 1**). The mean age of the study population was 45.9 in the mild group and 57.5 in the moderate group.

**Figure – 1:** Age wise distribution.



**Table – 1:** Mean values.

	Neutrophil	Lymphocyte	NLR	CRP
Mild Group	59.97	31.34	2.46	14.71
Moderate Group	71.03	20.78	5.98	17.5

The mean CRP value of the mild group was 14.71 and of moderate group was 17.5.

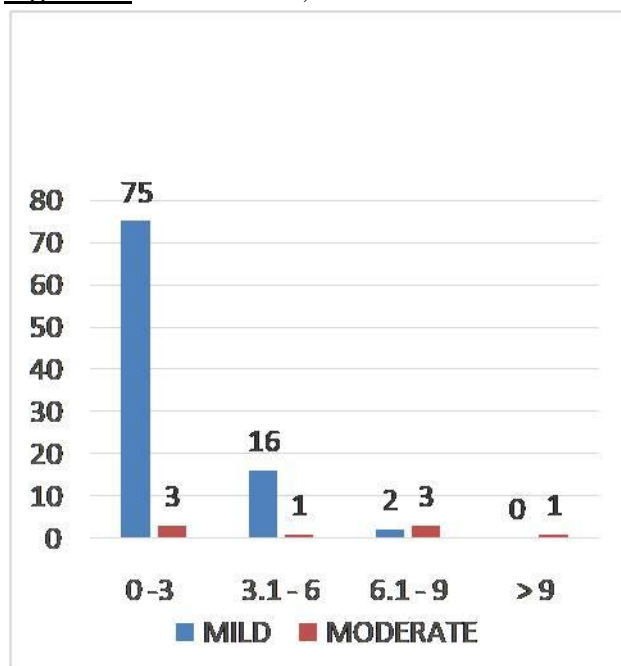
respectively and of moderate group was 71.03 and 20.78 respectively (**Table - 1**).

The mean N:L ratio of the mild group was 2.46 and of moderate group was 5.98.

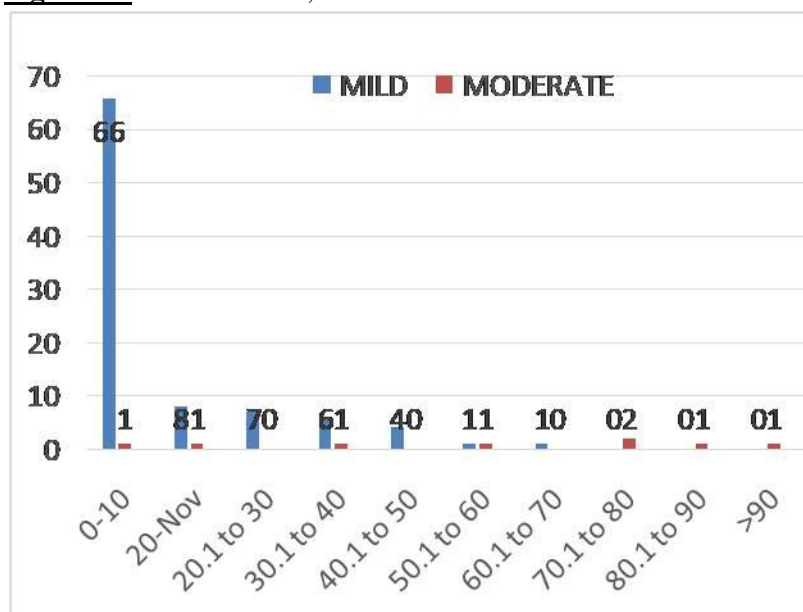
The mean values of WBC, Neutrophils, NLR, CRP were higher in moderate group than those of in mild group.

The mean values of neutrophil and lymphocyte of the mild group were 59.97 and 31.34

**Figure – 2:** NLR in Mild, Moderate Cases.



**Figure – 3:** CRP IN Mild, Moderate cases.



The mean NLR of moderate severity were significantly higher than those of mild cases ( $p = 0.00003$ ) (**Figure - 2**).

Plasma CRP levels were higher in moderate cases than in mild cases, and this difference was significant ( $p < 0.001$ ) (**Figure - 3**). Results showed that NLR was positively correlated with CRP levels.

## Discussion

The COVID-19 disease spectrum varies from no symptoms to severe disease and death. Clinical observation has found that some patients with mild disease progress to severe disease within a short period of time with a high risk of mortality. The specific pathological mechanism is unknown. Some believe that the sudden aggravation of the condition is because of the rapid emergence of ARDS and subsequent

multiple-organ dysfunction in the later period which may be related to the "cytokine release storm" [15].

A notable laboratory finding in regard to COVID-19 was reduced absolute lymphocyte count with a normal or slightly decreased white blood cell count, which was different from the findings in patients with other beta-coronavirus infections, such as Middle East respiratory syndrome [16]. In clinical practice, it has been observed that in some non-survivors, the absolute value of lymphocytes decreases progressively while the white blood cell count gradually increases over time, resulting in a "divergence" between the absolute value of neutrophils and lymphocytes, which gave us the idea that the neutrophil-to-lymphocyte ratio, namely, the NLR, may be correlated with the progression and prognosis of this newly emerged disease.

The use of CRP in COVID-19 case management has been proposed as early marker for predicting severe COVID19. Aji found that CRP threshold value of 26.9 mg/L may serve as optimal cutoff and every one-unit increase in CRP may lead to 5% increased risk for getting severe COVID-19 [17].

In our study the mean age of the study population was 45.9 in the mild group and 57.5 in the moderate group. Similar to the study done by Yue-Ping Liu, et al. [18] where the median age of the participants was 53 years (range, 20–91 years).

Our study included 101 patients out of which 93 were in mild group and 8 were in moderate group. The mean NLR, CRP levels of moderate severity were significantly higher than those of mild cases and this difference was significant ( $p < 0.001$ ). This correlates with the study done by Seyed Dawood Mousavi-Nasab, et al. [19] in which COVID-19 cases comprised 14 (20%) patients with severe disease and 56 (80%) with non-severe infection. The mean values of WBC, NEU, LYM, and NLR of the severe patients were significantly higher than those of the non-

severe patients. Plasma CRP levels were higher in severe cases than in non-severe cases, and this difference was significant. The results showed that NLR was positively correlated with CRP levels.

Similar findings were noted in the study done by Linda Rotty [20] who recruited 40 COVID-19 patients out of which 20 patients were having mild disease and 20 patients were having severe COVID19 disease. Findings showed that NLR value was significantly higher in severe COVID19 disease group compared to mild COVID-19 group with  $p$  value of 0.002. Similar finding was also found in analysis of CRP ( $p = 0.000$ ). The Spearman correlation test showed significant correlation between NLR and CRP level ( $p = 0.001$ ) with correlation coefficient of 0.506.

The findings of this study indicate that the integration of NLR and CRP may lead to improved predictions and is recommended as a valuable early marker to assess prognosis and evaluate the severity of clinical symptoms in COVID-19 patients.

### **Limitations**

The current study encompasses a short sample size. Thus, it may lack generalizability. Furthermore, the retrospective nature of this study and the consequent missing clinical data was another limitation. Therefore, subsequent clinical studies with larger sample sizes and multiple CRP, NLR level measurements, especially at different treatment times, should be performed to confirm our findings.

### **Conclusion**

NLR can be used as an early warning signal for deteriorating severe COVID-19 infection and can provide an objective basis for early identification and management of severe COVID-19 pneumonia. This marker is especially important in our setting, where lack of resources often prevents costly testing.

Also, the present study suggests that patients with higher CRP levels should be carefully monitored throughout their disease course.

Therefore, health care institutions should also pay close attention to the mild patients, identify progressors early, and provide appropriate treatment to reduce mortality.

Studies that correlate the CRP and NLR levels in covid-19 are very limited. This study sheds some light on this correlation.

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