

Original research article

ROLE OF NEUTROPHIL TO LYMPHOCYTE RATIO IN COVID 19 PATIENTS

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Abstract

Objectives: To identify association of neutrophil to lymphocyte ratio with disease severity.

Methods: Total 140 Corona Virus RT-PCR positive patients were included in this cross-sectional study. Majority were males with mild severity. Patients were admitted to Bangalore medical college and research institute May 2020 to October 2020. Neutrophil to lymphocyte ratio (NLR) was recorded on admission. NLR cut-off was 3.0. WHO categories for disease severity (asymptomatic, mild, moderate and severe) were used. Demographic profile, symptoms were recorded.

Results: The age of patients ranged from 20 -91years and majority being males. Majority patients (76.5%) were asymptomatic (Mild). Amongst symptoms, fever was the most common symptom. In our study the Mean NLR in mild cases were 2.75+ 1.22, moderate cases showed 13.10+6.40 and in severe cases 28.85+15.66. NLR increased in severe cases compared to mild and moderate severity and was statistically significant ($p<0.0001$).

Conclusion: NLR is a cheap and easily available marker of disease severity.

Keywords: COVID-19, Neutrophil to lymphocyte ratio (NLR), Disease severity (asymptomatic, mild, moderate and severe).

Introduction

The Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome (SARS Cov 2), i.e., from asymptomatic or mild to severe forms causing a significant loss of lives. Therefore, it is fundamental to early identify COVID-19 patients with a higher risk of a poor clinical outcome and predictive markers are of paramount relevance^[1, 2].

Inflammation is caused by infectious diseases, and growing evidence supports its significant role in the progression of various viral pneumonia, including COVID-19 [3]. Severe inflammatory responses contribute to weak adaptive immune response, thereby resulting in immune response imbalance. Therefore, circulating biomarkers that can represent inflammation and immune status are potential predictors for the prognosis of COVID-19 patients [4]. Peripheral white blood cell (WBC) count, neutrophil (NEU)-to-lymphocyte (LYM) ratio (NLR), de-ri-ved NLR ratio (d-NLR, neutrophil count divided by the result of WBC count minus neutrophil count), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) are indicators of the systematic inflammatory response [5]. These parameters are widely investigated.

Recently, several studies have reported that NLR can differentiate between mild/moderate and severe/critical groups and the likelihood of death in patients with COVID-19 infection. Furthermore, a number of studies [6, 7] have suggested that NLR is a reliable predictor of COVID-19 progression and high NLR is associated with high mortality. NLR is calculated as the absolute neutrophil count divided by the absolute lymphocyte count, and 95% of healthy adult subjects have a ratio between 0.78 and 3.53 [8]. In our study we tried see for any association between NLR and disease severity.

Materials and Methods

It is cross sectional prospective study with 140 cases conducted at department of pathology, Bangalore medical college and research institute for a period of 6 months (May -October 2020). Aims & Objective:

1. To study the NLR in Covid 19 patients.
2. To correlate the disease severity with NLR.

Inclusion criteria: All CBC samples of covid 19 positive patients.

Exclusion criteria

- Patients who have declined to participate in the study.
- Patients who lost follow up due to unforeseen causes.
- Pediatric population.

All CBC samples received at central laboratory; Department of pathology was included in the study. EDTA blood samples received was checked for the details of the patient and was processed by Beckman LH 780 analyzer to obtain Neutrophil lymphocyte ratio(NLR) and Clinical severity of the patients is graded as mild, moderate and severe based on established criteria. Statistical tools are applied to look for any evidence of association between platelet indices and clinical severity. Clinical severity: categorized as mild, moderate and severe Patient with mild illness may exhibit variety of signs and symptoms (e.g.: fever, cough, sore throat, malaise, headache etc. They do not have shortness of breath, dyspnoea on exertion or abnormal imaging. Moderate illness is defined as evidence of lower respiratory disease during clinical assessment or imaging with $\text{Spo}_2 \geq 94\%$ on room air at sea-level. Respiratory rate 30 breaths/min or lung infiltrates $>50\%$ [9].

Statistical analysis

Statistical analysis will be performed by SPSS software version. All data of the demographic and clinical characteristics were analysed by descriptive statistics such as mean, standard deviation and percentage. Tables and graph were added wherever applicable. We used Student t-test and ANOVA to determine significant difference between two or more groups. A P value of < 0.05 was considered statistically significant.

Results

Demographic and epidemiological features Overall, 140 laboratory-confirmed covid 19 patients were enrolled in our study, among which 107(76%) patients were mild, 26 (18.5%) was moderate and 7(5%) were severe. In our study, 105(75%) were males, 35(25%) were females, Age ranged from 20-91 years. Majority of the mild severity cases presented as asymptomatic with myalgia, fever and sore throat, Moderate and severe cases presented as cough, fever and breathlessness. One severe case developed septicemia and acute kidney injury. (Table 1)

Table 1: Demographic details with Disease severity

Variables	Mild	Moderate	Severe	P value
Male	77(72%)	24(92%)	4(57%)	0.05
Female	30(28%)	2(7.7%)	3(42.9%)	0.05

Laboratory findings

Laboratory findings are summarized in (table 2). In our study the Mean NLR in mild cases were 2.75+ 1.22, moderate cases showed 13.10+6.40 and in severe cases 28.85+15.66. NLR increased in severe cases compared to mild and moderate severity and was statistically significant (p<0.0001).

Table 2: Association of disease severity with NLR

	Severity	Mean + SD	P Value
NLR	Mild	2.75+ 1.22	0.00001
	Moderate	13.10+6.40	
	Severe	28.85+15.66	

Discussion

COVID-19, an infectious disease caused by SARS-CoV-2, targets the lungs and in severe cases may result in multiorgan failure and death. SARS-CoV-2 binds to the alveolar ACE2 receptors and induces the release of inflammatory factors, which in turn activate the immune system, leading to a cytokine storm ^[10, 11]. Thus, timely and accurate identification of severe COVID-19 cases after diagnosis is important for the immediately treatment of high-risk patients. Significantly lower lymphocyte and higher neutrophil counts have been observed in patients with severe COVID-19 compared to those with mild disease. A study suggested that the NLR could effectively distinguish

between severe and nonsevere COVID-19 cases ^[12]. In this study, we evaluated the accuracy of the NLR in predicting the severity of COVID-19.

The NLR is a simple, economical, commonly used, and rapidly available hematological assay. Lagunas-Rangel conducted a meta-analysis and reported that the NLR, as an indicator of inflammation, predicted the severity of COVID-19; however, the sample size of the study was small ^[13].

The present study was done to document the role of NLR in covid 19 patients and to look for any association between NLR and clinical severity in covid 19 patients. We analyzed the demographic, epidemiological, clinical and laboratory characteristics of 140 patients who were hospitalized.

In a study done by Torre *et al.* he concluded that a high neutrophil to lymphocyte ratio suggests worst survival. Risk stratification and management help alleviate the shortage of medical resources and reduce the mortality of critically ill patients ^[14]. In a study done by Liorprozan *et al.*, He identified a high NLR to be a prognostic factor for poor clinical outcome ^[15].

NLR has been shown to be a reliable indicator to determine disease severity in COVID-19. Many mechanisms have been postulated regarding the response of neutrophils and lymphocytes to corona virus infection. Neutrophils activate the immune system and release reactive oxygen species that can induce cell DNA damage and release the virus from the cells which is then targeted by antibodies. In addition, neutrophils trigger the production of various cytokines and effector molecules. On the other hand, although the viral infection itself triggers lymphocyte response predominantly, the systemic inflammation especially high Interleukin 6 paradoxically decreases the lymphocyte count and resultant cellular immunity. Both these factors result in elevated NLR ^[16, 17]. Hence a higher NLR predicts the severity of inflammation.

Our study has shown that mean NLR value significantly increases as disease severity progresses with lowest NLR recorded in asymptomatic and mild disease. The P value was statistically significant. It's a simple marker giving objective evidence of patients at risk of severe disease and increased mortality.

Conclusion

In our study we highlight the importance of NLR in COVID-19 patients in predicting disease severity and mortality. In a developing country like ours where there are resource limited settings, NLR can be used as an effective marker to predict and stratify COVID-19 patients as per severity and effectively predict the outcome as well, which in turn would lead to efficient resource utilization.

Abbreviations

NLR - Neutrophil to lymphocyte ratio.

WBC - White blood cell count.

CBC - Complete blood count.

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