

Is NLR or CRP, The Early Inflammatory Marker of Covid-19 Patients

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Abstract

Objective: To evaluate the Neutrophil-Lymphocyte Ratio (NLR) and C-Reactive Protein (CRP) as a Early inflammatory marker in patients admitted to COVID wards and their treatment monitoring.

Methods: A retrospective cohort study was conducted. We extracted data from 76 patients with laboratory-confirmed COVID-19. NLR and CRP values were obtained from blood samples of those patients.

Results: None of the 76 inpatients were lost of any values in this retrospective study. NLR and CRP of all patients were studied. CRP were found positive in 47.4% cases, while NLR was positive in only 3% cases. However, both NLR and CRP were positive in 34.2% cases.

Conclusion: This study showed that CRP proved to rise fast in Inflammatory states but NLR combined with CRP can be considered in Early treatment intervention.

Keywords: COVID-19; Blood cell count; CRP; NLR; Inflammatory marker.

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Introduction

The ongoing worldwide Coronavirus Disease 2019 (COVID-19) pandemic has posed a huge threat to global public health. The pathogen has been identified as a novel single-stranded ribonucleic acid (RNA) beta corona virus named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 represents a spectrum of clinical severity ranged from asymptomatic to critical pneumonia, acute respiratory distress syndrome (ARDS) and even death.¹ Therefore, full monitoring of the severity of COVID-19 and effective early intervention are the fundamental measures for reducing mortality. Accumulating evidence has

suggested that inflammatory responses play a critical role in the progression of COVID-19. Inflammatory responses triggered by rapid viral replication of SARS-CoV-2 and cellular destruction can recruit macrophages and monocytes and induce the release of cytokines and chemokines.² These cytokines and chemokines then attract immune cells and activate immune responses, leading to cytokine storms and aggravations. Several inflammatory markers have some tracing and detecting accuracy for disease severity and fatality. Inflammatory markers such as procalcitonin (PCT), serum ferritin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), NLR (Neutrophil-Lymphocyte Ratio) and interleukin-6 (IL-6) have been reported to be

significantly associated with the high risks of the development of severe COVID-19. However, these tests altogether take a huge price, which is difficult during lockdown Financial crisis. The NLR is simply the number of neutrophils divided by the number of lymphocytes. Under physiologic stress, the number of neutrophils increases, while the number of lymphocytes decreases. The NLR combines both of these changes, making it more sensitive than either alone. CRP is a protein made by the liver. CRP levels in the blood increase when there is a condition causing inflammation somewhere in the body and used to monitor the severity of disease in chronic conditions.

Here we performed an analysis based on the current scientific literature to compare the levels of inflammatory markers, especially NLR and CRP in COVID-19 positive patients. This study will assist clinicians to monitor the severity and prognosis of COVID-19.

Materials and Methods

Study population and data collection

A retrospective review was performed by using a database of 76 Covid 19 positive patients who was admitted in Covid ward in the month of September 2020 in P.D.Hinduja Sindhi Hospital, Bangalore. Only laboratory-confirmed COVID-19 patients with mild/common types on admission were enrolled in this study. A confirmed case of COVID-19 was defined as a positive result on real-time reverse-transcriptase-polymerase-chain-reaction (RT-PCR) assay using nasal or pharyngeal swab specimens. Laboratory assessments consisted of a complete blood count, blood chemical analysis, coagulation testing, assessment of liver and renal function, and measures of electrolytes, C-reactive protein, lactate dehydrogenase. The data of enrolled cases, including demographic information, clinical symptoms or signs, clinical outcomes and laboratory findings only CRP and NLR on admission, were extracted from electronic medical records.

Only results on the day of admission were used for analysis. CRP was done by latex slide agglutination method. Negative CRP is when values are 0-0.6mg/dL. Any value above this reference range is considered Positive. NLR is calculated by dividing Neutrophil and Lymphocyte percentage values. Normal NLR is considered when the Quotient is roughly 1-3. An NLR above 6, confirms that the patient is in stress condition. The study was approved by the Lab Chief and Medical Director.

Statistical Analysis

IBM SPSS Statistics 22.0 were used for statistical analyses. All tests were two-tailed, and P value less than 0.05 was considered statistically significant. The chi-square test or Fisher's exact probability test was used to compare count data.

Results

Demographic profiles and laboratory findings of the participants on admission.

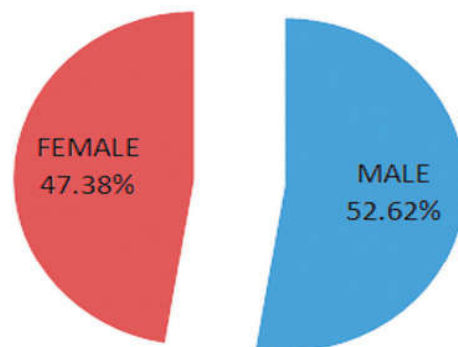


Chart 1: Depicting Sex ratio.

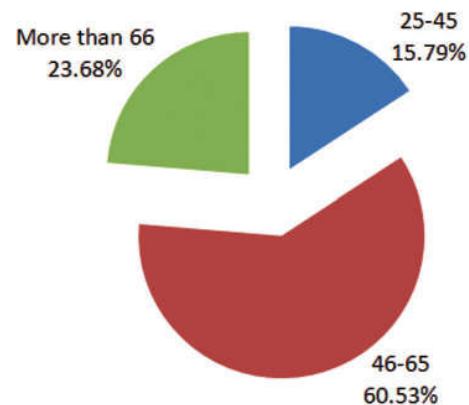


Chart 2: Depicting Age range in Years.

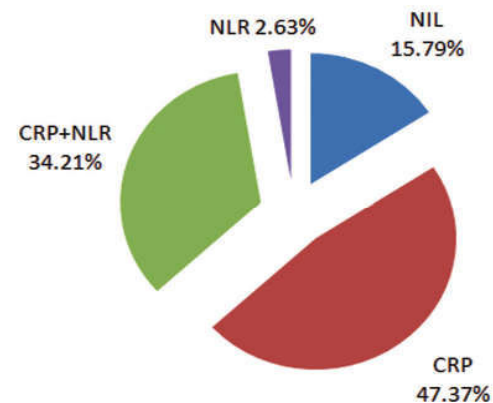


Chart 3: Depicting C-Reactive Protein, Neutrophil-Lymphocyte Ratio results.

Seventy six in patients with COVID-19 were enrolled in this study. The median age of these participants was 55 years (range, 25–85 years). A total of 52.6% of patients were males and 47.3% were females (Chart-1,2). A total of 18 patients were above 65 years of age. Almost 70% of patients had co-morbidities such as Hypertension and Diabetes.

None of the 76 inpatients were lost to follow-up in this retrospective study. Approximately 12 patients (15.7%) did not have either positive CRP or NLR. CRP were found positive in 47.3% cases, while NLR was significant in only 2.63% cases. However 34.2% cases showed a combined CRP and NLR positivity (Chart 3).

Discussion

The present study of 76 cases of COVID-19 patients showed that CRP is gold standard in Covid-19 infected patients as seen in other inflammatory diseases. Although an association between viral infection and lymphocytosis has long been established³ lymphopenia occurring in COVID-19 patients has been reported by previous studies.^{4,5} and this phenomenon was also observed in SARS.⁶ Direct invasion by SARS-CoV viral particles damages the cytoplasmic component of the lymphocyte and causes its destruction; indirect mechanisms such as vascular cell adhesion molecule-1 (sVCAM-1), soluble Fas ligand (sFasL) or intense cytokine storms can induce apoptosis in lymphocytes.⁷ Recently, the NLR has been proposed as a novel predictor of mortality in various diseases, such as heart failure and several types of cancer;^{8,9} however, the use of the NLR in the differential diagnosis of pneumonia is rare.¹⁰

In this study, we found that the neutrophil to lymphocyte ratio is not statistically significant, still NLR when combined with CRP can be used to dictate the severity of SARS-CoV infection in the body. This is inaccordant with other studies.^{11,12}

The CRP was significantly higher in patients infected with SARS-CoV-2, which was consistent with the findings of other study.¹¹ Higher blood CRP levels, as a non-specific inflammation marker, play an instructive role in the acquired immune response as an innate recognition and elevated CRP levels have also been associated with acute dyspnea due to pneumonia and bronchitis.¹¹ Our study showed that CRP ($p < 0.05$) was an independent risk factor predicting COVID-19. Subsequently, we analyzed the diagnostic performance of the parameters mentioned above. NLR and CRP has

good diagnostic efficiency.¹¹ Also when NLR and CRP were combined, the sensitivity and specificity increases. Those, 15.7% cases who showed neither CRP or NLR, where known to have mild symptoms and so can be considered less impact of the virus on the immune system.

Conclusion

In conclusion, the outbreak of SARS-CoV-2 infection has had extensive influence around the world. This study suggests NLR combined with CRP can predict the severity of the disease, in turn early treatment intervention. Also NLR was Not statistically significant, so considering NLR as early inflammatory marker in Covid-19 infection is questionable. Given that this study was limited by its sample size, more comprehensive studies are required to help establish the role of these parameters in predicting COVID-19.

Conflicts of interest: None.

References

1. Guan W, Ni Z, Yu hu, et al. *N Engl J Med* 2020; 382:1708-1720, DOI: 10.1056/NEJMoa2002032.
2. Tay, M.Z., Poh, C.M., Rénia, L. et al. The trinity of COVID-19: immunity, inflammation and intervention. *Nat Rev Immunol* 20, 363–374 (2020). <https://doi.org/10.1038/s41577-020-0311-8>.
3. Naess A, Nilssen SS, Mo R, et al. Role of neutrophil to lymphocyte and monocyte to lymphocyte ratios in the diagnosis of bacterial infection in patients with fever. *Infection*. 2017;45(3):299–307. [PMC free article] [PubMed] [Google Scholar].
4. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *Jama*. 2020;323(11):1061–1069. [PMC free article].
5. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497.
6. Wang JT, Sheng WH, Fang CT, et al. Clinical manifestations, laboratory findings, and treatment outcomes of SARS patients. *Emerg Infect Dis*. 2004;10(5):818–824. [PMC free article].
7. Chan PK, Chen GG. Mechanisms of lymphocyte loss in SARS coronavirus infection. *Hong Kong Med J*. 2008;14(Suppl 4):21–26. [Google Scholar].
8. Durmus E, Kivrak T, Gerin F, et al. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are predictors of heart failure. *Arq Bras Cardiol*. 2015;105(6):606–613. [PMC free article].

9. Dolan RD, Lim J, McSorley ST, et al. . The role of the systemic inflammatory response in predicting outcomes in patients with operable cancer: systematic review and meta-analysis. *Sci Rep.* 2017;7(1):16717. [PMC free article].
10. De Jager CP, Wever PC, Gemen EF, et al. . The neutrophil-lymphocyte count ratio in patients with community-acquired pneumonia. *PLoS One.* 2012;7(10):e46561. [PMC free article] [PubMed] [Google Scholar].
11. Yufei Y, Mingli L, Xuejiao L, et al. Utility of the neutrophil-to-lymphocyte ratio and C-reactive protein level for coronavirus disease 2019 (COVID-19). *Scand J Clin Lab Invest.* 2020;80(7):536-540. DOI:10.1080/00365513.2020.1803587.
12. Liu YP, Li GM, He J, et al. Combined use of the neutrophil-tolymphocyte ratio and CRP to predict 7-day disease severity in 84 hospitalized patients with COVID-19 pneumonia: a retrospective cohort study. *Ann Transl Med* 2020;8(10):635. DOI: 10.21037/atm-20-2372.

