ORIGINAL RESEARCH PAPER

Pathology

ROLE OF NEUTROPHILS-TO-LYMPHOCYTE RATIO (NLR) AND PLATELET-TO-LYMPHOCYTE COUNT RATIO (PLR), AS A PROGNOSTIC INDICATOR IN COVID-19 PATIENTS – A CROSS SECTIONAL STUDY

KEY WORDS:

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ABSTRACT

Objectives- 1. To monitor the Neutrophil lymphocyte ratio (NLR) and Platelet lymphocyte ratio (PLR) in admitted COVID positive patients.
2. To use Neutrophil lymphocyte ratio (NLR) and Platelet lymphocyte ratio (PLR) as prognostic factors for predicting severity of COVID 19 cases.
Materials and Methods- A cross- sectional study will be conducted during August 2020 to September 2020 among blood samples taken from Covid positive cases admitted in SIMS, Shivamogga. A single center study on 500 COVID positive patients who had been hospitalized will be conducted. The demographic, clinical details and CBC which was determined using SYSMEX CELL COUNTER at admission will be collected. NLR and PLR will be calculated. **Results-** Patients with severe disease have higher NLR as well as lower lymphocyte count NLR and PLR were shown positively proportional to disease severity suggesting that NLR levels were positively Proportional to disease severity. In addition, neutrophil count was positively correlated with disease severity while lymphocyte count was inversely proportional to disease severity. **Conclusion-** The conclusions of this study support that elevated NLR is an independent prognostic biomarker for COVID-19 patients. NLR and PLR have proven to be reliable markers in several diseases that go with systemic inflammation. As shown, they have a higher value in COVID 19 patients.

INTRODUCTION

Coronaviruses (CoVs) are single-chain, enveloped RNA viruses. They do not contain the RNA polymerase enzyme; however, they encode this enzyme in their genome. They are defined as CoV due to the protrusions on their surface (Latin: corona=crown)[1]. The pathophysiology of the high pathogenicity of this unusual highly contagious SARS-CoV2 could not be fully understood yet. Inflammation plays an important role in infectious diseases. Accumulating evidence has shown the importance of inflammation in the progression of viral pneumonia, including in coronavirus disease 2019 (COVID-19) cases[2]. Of note, a high incidence of lymphopenia in COVID-19 patients has been reported by Cao and his colleagues[3]. Studies have found that one of the fundamental principles for the appropriate management of sepsis is early and accurate detection of the patients at high risk for death [1]. This is generally dependent on the application of scoring systems. The neutrophil-to-lymphocyte ratio (NLR), as a readily accessible biomarker can be calculated based on a complete blood count.(1) Although a growing body of evidence has shown that NLR is proposed as an independent predictor of poor survival in various clinical circumstances ranging from oncological patients to patients with cardiovascular diseases , there is no consensus about the relationship between NLR levels and clinical prognosis in patients with sepsis until now. In the context of infection, researchers in a recent study showed a reversed NLR evolution according to the timing of death , whereas some other studies suggested that NLR was not associated with mortality in patients with sepsis .Consequently, the clinical usefulness of NLR in patients with sepsis is therefore still a matter of ongoing controversy and this question deserves further investigation[1].

In addition, the baseline neutrophil-to-lymphocyte ratio (NLR) has been confirmed as a potential short-term prognostic indicator for patients with acute-on-chronic hepatitis B liver failure[4]. Thus, we wondered that whether NLR might be a potential predictor for critical illness of COVID-19. To test this hypothesis, we included many variables including NLR along with epidemiological history, comorbidity, and other laboratory tests.

The platelet to lymphocyte ratio (PLR) is an easily obtainable ratio from complete blood count (CBC) panels. Recently, it has been proposed as a better indicator of inflammation when compared to white blood cell count (WBC) alone. Increased PLR has been observed in patients with chronic inflammatory conditions like autoimmune diseases, rheumatic disorders, cancers, and diabetes.[1–5] Various studies have indicated a correlation between elevated PLR and mortality in acute pulmonary embolism, advanced cancers, and gynecologic malignancies [6,7,8,9,10,]

AIMS AND OBJECTIVES

To monitor the Neutrophil lymphocyte ratio (NLR) and Platelet lymphocyte ratio (PLR) in admitted COVID positive patients and their use as prognostic factors for predicting COVID 19 severity

MATERIALS AND METHODS

The study included all patients with confirmed SARS-COV 2 infection consecutively hospitalized between August 12, 2020, till September 5th, 2020. COVID-19 diagnostics were confirmed using real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay to test nasal and pharyngeal swab specimens according to WHO guidance.

Inclusion Criteria:

Blood samples taken from all the covid positive cases admitted in SIMS, Shivamogga during the study period.

Exclusion Criteria:

All the blood samples from Non covid cases will be excluded.

Study design

A Retrospective study was conducted during August 2020 to September 2020 (12th August and 5th September 2020) among blood samples taken from Covid positive cases admitted in SIMS, Shivamogga. A single center study on 500 COVID positive patients who had been hospitalized were conducted. Demographic, clinical, and laboratory data were taken from the patients at admission and extracted from electronic

medical records. Laboratory tests were collected from all the patients and were recorded. The demographic, clinical details and CBC which was determined using SYSMEX CELL COUNTER at admission were collected. NLR ratio was calculated as the absolute count of neutrophils divided by the total count of lymphocytes. The PLR was defined as the absolute count of platelets divided by the absolute count of lymphocytes.

Blood examinations involved measuring complete blood cell count and differential values. All laboratory tests were done in the hospital laboratory with standard procedures. The laboratory reference values of white blood cells, neutrophils, and lymphocytes, were 3.50–9.50, 1.8–6.3, and 1.10–3.20, 103/ul,respectively.

The study was approved by the Hospital Ethics Committee

DATA ANALYSIS METHODS: Data was entered in Microsoft Excel and analysed.

RESULTS

Patients with COVID-19 had lower statistically significantly lymphocyte Neutrophils ,and NLR, PLR were higher.

During the study period, there were 500 consecutive patients with complete neutrophil and lymphocyte data available, and all of these patients had complete data available for the primary outcome. Of the 500 patients, 269 patients with no oxygen support,164 patients under oxygen support and 67 patients were in ICU.

NLR cut off value obtained = 3.84
PLR Cut off value obtained = 140

Below table showing (table 1) patients with High NLR and PLR ratio

Table 1. Patients with disease shoeing high NLR and PLR

Number of patients (500)	High NLR (>3.84)	High PLR (>140) i
	Number, (%)	Number, (%)
Non o2 support-269	63, (23.4)	92, (34.2)
O2 support164	131, (79.4)	97, (59.1)
ICU-67	45, (67.1)	41, (61.1)

Patients with severe disease have higher NLR as well as lower lymphocyte count NLR and PLR were shown positively proportional to disease severity suggesting that NLR levels were positively

Proportional to disease severity. In addition, neutrophil count was positively correlated with disease severity while lymphocyte count was inversely proportional to disease severity.

DISCUSSION

NLR was able to accurately stratify patients in terms of short-term mortality. These findings remained robust after adjusting for several potential covariates, suggesting that increased NLR was independently associated with unfavorable outcome in patients with sepsis. In our opinion, the strength of the NLR is the possibility of implementing this parameter simply by using already available biomarkers (neutrophil count and lymphocyte count). Therefore, this ratio is easy to integrate in clinical practice and cost effective.

In a study conducted by Ahmet Nalbant et al and Jingyuan Liu et al[3]) showed that NLR and PLR was significantly elevated in COVID-19 patients. They considered a cut-off for this readily available test and showed that patients with NLR ≥2.4 were 20.5 times more likely to have COVID-19 compared to patients whose NLR was ≤2.4.

In another prospective observational study done by Xuan Liu et al[1]. they sought to evaluate the potential association of NLR on intensive care unit (ICU) admission with the clinical prognosis in a consecutive series of adult patients with sepsis. PLR was initially suggested as an excellent candidate marker for determining the severity and mortality of COVID-19. First, PLR is an established marker of inflammation. Inflammation plays a considerable role in the pathophysiology of COVID-19, with cytokine storm as a hallmark condition in severe disease and poorer prognosis. Thus, elevated PLR value suggests an overactive inflammatory response and subsequently, worse prognosis. Second, PLR is sensitive to natural and acquired immune response.

Third, PLR is an inexpensive and readily available measurement that can be used in resource-limited settings.[7,8,9] Therefore, our systematic review aims to review the validity of the PLR level on admission as a prognostic indicator in COVID-19 patients. Our analysis, which included a total of 500 COVID-19 patients, showed that high PLR value was associated with severe COVID-19. Six out of the seven included studies demonstrated similar results with increased PLR on admission found in severe cases of COVID-19 compared to those with mild or moderate diseases. This suggests that elevated PLR on admission among severe COVID-19 patients reflects a higher degree of the cytokine storm. This evidence can be useful for providing specialized treatment to patients with severe COVID-19, as they might require more prolonged hospital admissions.[8]

To date, there is no universal laboratory reference value for PLR, especially for COVID-19 patients. Of all the included studies, only two studies attempted to determine the optimal cut-off PLR value. Yang et al. reported the optimal cut-off PLR value as 180 with AUC of 0.784, specificity of 44%, and sensitivity of 77%.11 Meanwhile, Sun et al. suggested a cut-off PLR value of 226.67 with AUC of 0.746, specificity of 80.90%, and sensitivity of 59.26%.[8]

CONCLUSION

In conclusion, The COVID-19 epidemic may spread rapidly by human-to-human. The clinical manifestations of this disease can vary even in patients with the same viral infection; the severity of the condition may be related to the number of immune cells. Disease severity is an independent predictor of poor outcome. The conclusions of this study support that elevated NLR is an independent prognostic biomarker for COVID-19 patients. NLR and PLR have proven to be reliable markers in several diseases that go with systemic inflammation. As shown, they have a higher value in COVID 19 patients, NLR and PLR ratios are easy to calculate which is novel, rapid & used as a prognostic factor in the early screening of critical illness in confirmed COVID 19 patients and may help the physician to stratify patients in to prognostic categories at its early stage. These ratios can be easily implemented even in primary health centers to monitor the patients and predict the severity.

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