

Neutrophil to Lymphocyte Ratio in Hospitalized COVID-19 Patients – A Study in a Tertiary Care Covid Centre in Eastern India

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Corona Virus Disease -2019 (COVID-19) has jeopardised human life globally for last more than one year due to its high infectivity and tendency to develop sudden deterioration of cases by complicated pathophysiology. Some cost effective markers are necessary to predict severity so that timely appropriate management can be given. Neutrophil to lymphocyte ratio (NLR) in blood is such a common parameter that has been previously used to predict severity in various conditions like cardiovascular diseases and sepsis. Our objective was to estimate total White blood cell count (TC) and NLR in hospitalised COVID-19 patients and to find out their role to predict severity. This observational cross sectional study was done on hospitalized COVID-19 adult patients where patients were categorized into moderate and severe cases as per guideline of Govt. of India. TC and Differential count were estimated by automated cell counter and NLR was compared in these two groups by unpaired t test to find out their significance. Out of total 175 cases, 49(28%) were categorized as severe while rest 126 (72%) patients were in moderate category of disease. The mean \pm standard deviations of TC ($\times 10^3/\mu\text{l}$) and NLR for moderate disease were 8.85 ± 4.60 and 5.57 ± 6.80 respectively while those for severe disease were 12.78 ± 6.54 and 12.99 ± 12.21 respectively. Both the parameters have statistically significant difference between two groups ($p < 0.001$). TC and NLR were significantly higher in severe cases compared to moderate cases and hence they can be utilised to triage COVID-19 cases at an early stage.

Keywords: COVID-19; Neutrophil to Lymphocyte Ratio; Triage.

COVID 19 (Corona virus disease 2019) is a global health problem and poses a serious threat to the community.¹ The clinical presentation of the disease varies widely with mild cases presenting with cough, fever, shortness of breath, fatigue and muscle ache.² The severe cases develop severe pneumonia and may progress to acute respiratory distress syndrome (ARDS) and multiple organ failure.^{3,4} This fatal nature of severe form of the

disease makes it necessary to delineate markers which would help to identify the patients who have a high risk of mortality.

Peripheral blood neutrophil to lymphocyte ratio (NLR) is an easily available biomarker which may be used to differentiate between moderate and severe cases of COVID 19.⁵ NLR has been previously used to predict severity and outcomes in various conditions like cardiovascular diseases,

chronic obstructive pulmonary disease (COPD), pancreatitis and several solid tumors.⁶⁻⁹ It has been suggested that high NLR is associated with increased mortality in COVID 19.¹⁰

NLR can be readily obtained from the differential count of white blood cells (WBC), which is performed as a routine test in hospitalized COVID 19 patients. Thorough search of literature revealed that there is not much evidence regarding utility of NLR in COVID 19 from the eastern region of India. The present study was undertaken in a dedicated tertiary care COVID centre in this region to estimate NLR in hospitalized COVID 19 patients and also to find out if there is any correlation between the values of NLR and disease severity in among them.

MATERIALS AND METHODS

A hospital based cross sectional study was done in a tertiary care COVID centre in the eastern region of India for a period of one month from the mid of January to the mid of February, 2021. Approval was obtained from the Institutional Ethics Committee.

The patients included in the study were those above 18 years of age who tested positive for COVID 19 by RT-PCR (reverse transcription polymerase chain reaction) test and were admitted either in the COVID ward or the COVID ICU (Intensive Care Unit). Those patients who had haematological malignancies or who were receiving any chemotherapeutic drugs were excluded from the study.

The patients included were categorized into “moderate” and “severe” based on the “Clinical Management Protocol: COVID 19” by the Ministry of Health and Family Welfare and Director General of Health Services, Govt. of India.^[11] When there was presence of clinical signs of pneumonia along with any one of the following: respiratory rate >30 breaths/min, severe respiratory distress, SpO₂ <90% on room air, the patient was classified as “severe”. They were categorized as “moderate” when they suffered from dyspnoea and/or hypoxia, cough, fever, SpO₂ <94% (range 90-94%) on room air, respiratory rate e” to 24 per minute (range 24-30 breaths/min), All relevant data for each patient was recorded.

Blood samples of each patient were

collected from each patient in EDTA vial at admission. These samples were analysed using Sysmex XT-4000i automated haematology analyser. The total and differential counts of WBC of the patients were noted and correlated with differential counts done on stained blood smears and then NLR was calculated for each case. All collected data were meticulously tabulated.

RESULTS

A total of 175 patients were included in the study as per inclusion and exclusion criteria. Forty-nine patients (28%) were categorized as “severe” while the rest (126, 72%) were suffering from “moderate” disease. Age and sex distribution of the patients have been shown in Table 1. The mean age of the patients was 55.9 ± 16.72 years. There was a male preponderance in both moderate (62.69%) and severe (61.22%) categories of COVID 19 patients.

The mean ± standard deviation (X10³/μl) of ANC (absolute neutrophil count), ALC (absolute lymphocyte count) and total WBC count for moderate disease were noted to be 6.57 ± 4.22, 1.96 ± 1.5 and 8.85 ± 4.60 respectively while those for patients with severe disease were 10.53 ± 6.50, 1.07 ± 0.42 and 12.78 ± 6.54 respectively. There were statistically significant differences with respect to all the parameters between moderate and severe COVID 19 patients. ANC and total WBC counts were significantly higher while ALC was significantly lower in cases of severe disease compared to the moderate category. Similarly, NLR was also significantly higher in patients with severe disease when compared with those of moderate disease [Table 2].

DISCUSSION

As COVID 19 continues to wreak havoc in various parts of the world, the search for prognostic indicators of the disease also proceeds. The timely delineation of patients at risk of development of severe disease can save precious lives. This is especially true in developing countries with limited resources. NLR is a cost effective and rapidly available parameter which may be used to predict outcomes in COVID 19 patients.¹²

The role of NLR had been previously

Table 1. Age and sex distribution among COVID 19 patients

Parameter	All patient (n=175)	Moderate (n=126)	Severe (n=49)
Age (Mean±SD)	55.9(±16.72)	55.39(±17.34)	57.22 (±15.1)
No of Male (%)	109 (62.28%)	79 (62.69%)	30 (61.22%)
No of Female (%)	66 (37.71%)	47 (37.3%)	19 (38.77%)

Table 2. Comparison of absolute neutrophil count, absolute lymphocyte count, total leucocyte count and neutrophil to lymphocyte ratio among moderate and severe groups of COVID 19 patients

Study Parameter	Mean ±SD value in Moderate disease group (n=126)	Mean ±SD value in severe disease group (n=49)	p value
Absolute Neutrophil count (X10 ³ /μl)	6.57±4.22	10.53±6.50	<0.001
Absolute Lymphocyte count (X10 ³ /μl)	1.96±1.5	1.07±0.42	<0.001
Total WBC count (X10 ³ /μl)	8.85±4.60	12.78±6.54	<0.001
Absolute Neutrophil count/ Absolute Lymphocyte count ratio	5.57±6.80	12.99±12.21	<0.001

Note - p < 0.05 is statistically significant.

explored in various diseases. The severity of community acquired pneumonia was found to be associated with high NLR levels by Huang Y *et al.*¹³ Disorders of the cardiovascular system, sepsis and malignancies are among the other diseases in which NLR has been found to have a role in predicting outcomes.¹⁴⁻¹⁶

Inflammation is one of the key factors in pathogenesis of COVID 19 infection. In any respiratory infection, there is neutrophilic infiltration in the lungs with damage to the tissues, stasis in the blood vessels and cytotoxicity.¹⁷ A prolonged release of anti-inflammatory cytokines results in extensive apoptosis of lymphocytes and there is lymphopenia.¹⁸ This scenario is reflected in COVID 19 patients who have been found to have high levels of circulating neutrophils. In nearly 40% of COVID 19 patients, lymphopenia has been reported. The imbalance between neutrophils and lymphocytes seems to correlate with progression to complications of COVID 19 like sepsis, acute respiratory distress syndrome and multiorgan failure.¹⁹ In the present study, NLR was found

to be significantly higher in patients with severe disease compared to those with moderate COVID 19 infection.

Ciccullo A *et al.* reported that a higher NLR at the time of admission to the hospital was associated with a more severe course of disease among COVID 19 patients.²⁰ Fu J *et al.* stated that the NLR values can help to discriminate between severe and mild/moderate cases of COVID 19.²¹ Zahorec R *et al.* also opined that NLR may be of assistance in detection of COVID 19 cases and its increasing level is associated with progression to severe disease.²² Similar findings were obtained in the present study. NLR was found to be significantly higher in the patients suffering from severe COVID 19 infection.

There is a tendency of sudden deterioration of clinical status of COVID 19 patients with severe disease. This is one of the reasons that have led to the search for biomarkers which can predict the course of the disease. Decrease in lymphocyte counts and rise of NLR are useful in this aspect.²³ The cause of lymphopenia in COVID 19 is still

obscure. It has been suggested that the virus may directly damage T-lymphocytes which in turn may be responsible for deterioration of the patient's health.²⁴ In the present study, the total leucocyte count was found to be significantly higher in patients with severe infection compared to those with moderate disease. Shi Y *et al.* have suggested that leucocytosis is commonly encountered in severely diseased patients of COVID 19 since damaged cells trigger inflammation in the lungs which is mediated by granulocytes and macrophages.²⁵

Liu J *et al.* concluded in their study that NLR is the most easily applicable predictive factor for classification of COVID 19 patients so that those with chances of progression to severe illness may be triaged.^[20-23] Li X *et al.* stated that NLR is a prognostic indicator in COVID 19 and it reliably predicts severity and risk of mortality in these patients.²⁶ Tatum D *et al.* also recommend use of NLR for accurate prognostication of COVID 19 patients.²⁷ The authors of the present study feel that with limited resources in the hospitals of developing countries, the utility of NLR like biomarkers cannot be overemphasized.

CONCLUSION

NLR is a rapidly available and cost effective parameter which may be used along with regular parameters to predict severity and progression of disease in COVID 19 patients. It is easily estimated from the differential counts of leucocytes, the values of which are obtained from routine haematological tests. Triaging of patients may be done on the basis of NLR. In hospitals of developing countries with limited resources, the use of predictive value of NLR is of utmost importance.

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Conflict of interest

None.

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