



A RETROSPECTIVE STUDY AT A TERTIARY CARE CENTRE IN NORTH INDIA: NEUTROPHIL TO LYMPHOCYTE RATIO AS A PROGNOSTIC MARKER AMONG PATIENTS WITH COVID 19 INFECTION.

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ABSTRACT This retrospective study was done to compare NLR among patients with COVID 19 infection with their clinical outcome. A total of 1888 patients with COVID 19 infection were taken at SRN hospital MLN medical college; a tertiary care centre for COVID 19, Prayagraj (U.P) India. The study was done between 5 May 2020 to 10 October 2020. Blood samples were taken at the time of admission and NLR was calculated. Patients were divided into two groups based on clinical outcome; Survivors and Non survivors. Majority of patients were elderly male among non-survivors. The mean age among non-survivors was 48.3 years and among non-survivors was 59.07 years. The mean NLR among survivor was 15.6 and among non-survivor was 9.5. The NLR cut off >8.6 was identified to predict mortality among COVID 19 patients in ICU according to ROC curve and AUC was 0.768(95% CI, 0.748-0.787, $p < 0.001$).

KEYWORDS : COVID 19, NLR, Inflammatory Biomarker

INTRODUCTION

The 2019-nCoV causes an ongoing outbreak of lower respiratory tract disease called novel coronavirus pneumonia (NCP) by the Chinese government initially. The World Health Organization subsequently recommended as COVID -19. Meanwhile, 2019-nCoV was renamed SARS-CoV-2 by the International Committee on Taxonomy of Viruses¹.

The WHO declared COVID-19 as a global health emergency at the end of January 2020. The epicenter of this ongoing outbreak is in the city of Wuhan in Hubei Province of central China and the Huanan seafood wholesale market was thought to be at least one of the places where SARS-CoV-2 from an unknown animal source might have crossed the species barrier to infect humans¹.

The severe acute respiratory syndrome coronavirus (SARS-CoV), H5N1 influenza A, H1N1 2009 and Middle East respiratory syndrome coronavirus (MERS-CoV) cause acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) which leads to pulmonary failure and result in fatality. These viruses were thought to infect only animals until the world witnessed a severe acute respiratory syndrome (SARS) outbreak caused by SARS-CoV, 2002 in Guangdong, China². Only a decade later, another pathogenic coronavirus, known as Middle East respiratory syndrome corona virus (MERS-CoV) caused an endemic in Middle Eastern countries³.

Transmission of this virus is via droplets as well as through contact with fomites or through faeco-oral route. Most of the patients have mild disease (80%), making it difficult to diagnose during initial period and hence leading to further spread of the virus among susceptible population. Nevertheless, even though the virus is causing mild disease in many, the course of illness may be severe, leading to hospitalization and even death in elderly or those with comorbid conditions⁴.

Inflammation is known to play a significant role in the development of ARDS and has an impact on its prognosis and symptoms⁵. The balance of cytokines and chemokines is responsible for pathogenesis in ARDS. The neutrophil-to-lymphocyte ratio (NLR) is an indicator of systemic inflammation⁶. High levels of neutrophil infiltration may be associated with cytotoxicity, vascular stasis and decreased inflammation in response to changes in the balance of pro-inflammatory and anti-inflammatory cytokines^{5,7}.

Several studies have found to have correlation between NLR and severity of clinical course and outcomes in ICU and it has been suggested that NLR should be considered as a prognostic indicator in severely ill patients⁸⁻¹⁰.

MATERIALS AND METHODS

This study was conducted in Swaroop Rani Hospital, MLN Medical College, Prayagraj, Uttar Pradesh which is a tertiary care centre designated Level 3 for COVID 19. It was a retrospective observational

study. The biochemical parameters of patients presenting to this centre between 5 may 2020 to 8 October 2020 were recorded.

A total of 1888 patients admitted in COVID ICU SRN hospital were taken in this study. Patients were diagnosed to have COVID 19 by RT-PCR at Department of Microbiology MLN medical college, Prayagraj.

The biochemical parameters were compared among survivors and non-survivors.

All patients who were admitted their blood samples were taken for routine investigation. Neutrophil to lymphocyte ratio was calculated at day 1 of admission and was compared among both the groups. The outcome was defined as either patients getting discharged or died during the hospital stay.

Table 1. Comparison of biochemical parameters among survivors and non-survivors

Characteristics	Non survivors (n=358)	Survivors (n=1530)	p-value
Total leukocyte count (cells/mm ³)	22,018 ± 981.4	17142 ± 684.3	0.0001
NLR (mean)	15.6	9.5	
Total bilirubin(mg/dl)	1.62 ± 0.9	0.98 ± 0.81	0.0001
BUN(mmol/l)	52.05 ± 22.3	29.04 ± 24.8	0.0001
Serum creatinine(mg/dl)	2.39 ± 1.08	1.30 ± 0.71	0.0001
Serum Na(mmol/L)	138.6 ± 7.3	138.04 ± 6.1	0.09
Serum K(mmol/L)	4.36 ± 0.77	4.24 ± 0.53	0.005
Serum Ca(mmol/L)	1.05 ± 0.82	0.92 ± 0.11	0.0001

NLR- Neutrophil lymphocyte ratio, BUN – Blood urea nitrogen , Serum Na – serum Sodium, Serum K- serum Potassium, Serum Ca- serum calcium

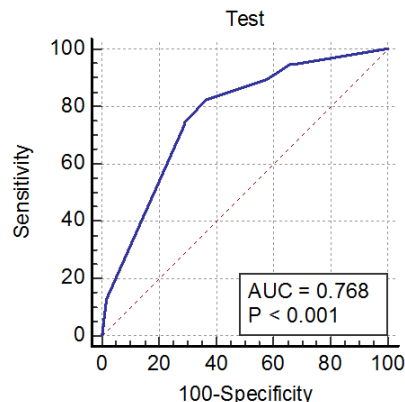


Fig 1. Receiver-operating characteristics (ROC) curve for mortality among COVID 19 patients.

RESULTS

A total of 1888 patients with COVID 19 infection were included in this study. Most of the patients were elderly male who succumbed to COVID 19. The mean age of survivors was 48.3 years and among non-survivors was 59.07 years. Majority of them were males in both survivors and non-survivors 64% and 71% respectively. Mean total leukocyte count was 22,018 cells/mm³ in non-survivor group and 17142 cells/mm³ among survivor group ($p < 0.0001$). The mean NLR among non-survivor was 15.6 and in survivor group was 9.5. A cut-off value of > 8.6 was (sensitivity-82.4, specificity-63.4) identified to predict mortality among COVID 19 patients in ICU according to ROC curve and AUC was 0.768(95% CI, 0.748-0.787, $p < 0.001$) [fig 1] Mean serum creatinine among non-survivors was 2.39 ± 1.08 and among survivors was 1.30 ± 0.71 ($p < 0.0001$).

DISCUSSION

A total of 1888 patients diagnosed with COVID 19 were taken in this retrospective study. Patient's blood samples were drawn at the time of admission and biochemical parameters were determined. Patients were divided into two groups survivors (81%) and non-survivors (19%). NLR for both the groups was calculated at the time of admission. The mean NLR was higher among non-survivors as compared to survivors. The value of NLR > 8.6 at admission was taken as cut-off to predict the mortality in patients infected with COVID 19. Yang et al¹¹ did a study among 93 patients in Wuhan, elevated NLR (hazard risk [HR] 2.46, 95% confidence interval [CI] 1.98–4.57) and age (HR 2.52, 95% CI 1.65–4.83) as independent factors for poor clinical outcome of COVID-19. NLR exhibited the largest area under the curve at 0.841, with the highest specificity (63.6%) and sensitivity (88%). They concluded that elevated NLR and old age can be considered as an independent marker for poor clinical outcomes.

In a similar study done by Liu et al¹² in 115 patients with COVID 19 in Beijing the incidence of critical illness was 9.1% for patients aged ≥ 50 and having an NLR < 3.13 , and 50% patients with age ≥ 50 and NLR ≥ 3.13 were predicted to develop critical illness. They concluded that NLR is a predictive factor for early-stage prediction of patients infected with COVID-19 who are likely to develop critical illness. Patients aged ≥ 50 and having an NLR ≥ 3.13 are predicted to develop critical illness, and they should thus have rapid access to an intensive care unit if necessary. A retrospective study done by Yan et al¹³ among 1004 patients with COVID 19. NLR value of non-survival group (median: 49.06; interquartile range [IQR]: 25.71-69.70) was higher than that of survival group (median: 4.11; IQR: 2.44-8.12; $P < .001$). NLR more than 11.75 was significantly correlated with all cause in hospital mortality (odds ratio=44.351; 95% confidence interval=4.627 -425.088). They concluded that the NLR appears to be a significant prognostic biomarker of outcomes in critically ill patients with COVID-19.

Although many studies have predicted the role of NLR as a prognostic marker in COVID 19 but further validation is required. NLR is a very basic and easily available investigation which can be used to predict the outcomes in patients with COVID 19.

CONCLUSION

Our study showed that NLR was higher among non-survivors at the time of admission. The NLR cut-off > 8.6 was associated with poor outcomes. NLR can be used as a prognostic marker to predict the outcome or severity in COVID 19. NLR is a very basic and easily available investigation which can be used to predict the outcomes in patients with COVID 19. However further studies are required to validate the findings of this study.

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