RESEARCH ARTICLE

TO DETERMINE THE MEAN NLR(NEUTROPHIL LYMPHOCYTE RATIO) AND MEAN PLR(PLATELET LYMPHOCYTE RATIO) IN COVID-19 PATIENTS

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ABSTRACT

Objective: *To determine the mean NLR(neutrophil leucocyte ratio) and mean PLR(platelet lymphocyte ratio) in COVID- 19 patients.*

Study design: *Cross Observational Study.*

Place and Duration of Study: *The study was conducted in Medicine unit, Benazir Bhutto Hospital Rawalpindi during the period of May to November 2021.*

Patients and Methods: *A total of 95 patients those who were positive for corona virus by RT-PCR, 20 to 80 years of age, both genders were included. Patients with previous history of asthma, Chronic Obstructive Pulmonary disease, autoimmune disease, ischemic heart disease and chronic liver disease were excluded. The selected patients were given their written informed consent. NLR and PLR were calculated for all the patients on admission versus after 48 hrs. of admission. The data were collected and calculated by the principal researcher on a specially designed proforma.*

Results: *The study included total of 95 patients from 20-80 years with mean age of 46.73 ± 11.16 years. Fifty nine (62.11%) patients were 20-50 years old. Out of total, 39 (41.05%) were male and 56 (58.95%) were females. Mean leucocyte count was 8.05 ± 2.71 x 10^9/L. Mean leucocyte number was 5465 ± 1231 neutrophils/µL. Mean NLR was 5.15 ± 1.26 and mean PLR was 215.88 ± 38.14 in COVID-19 patients. Mean NLR was not significantly associated with changes over time in COVID-19 patients (p =0.21). Mean PLR was significantly associated with changes over time (p= 0.011), showing a statistically meaningful decrease from admission to 48 hours.*

Conclusion: *The study concluded that mean NLR and mean PLR was associated with COVID-19 patients. PLR decreased significantly, consistent with patient improvement. NLR showed a decreasing trend but not significantly, suggesting it may still reflect immune response but not sharply over 48 hours.*

Keywords: *COVID-19, Leucocyte, Lymphocyte, Neutrophil, Platelets*

INTRODUCTION

The novel coronavirus is responsible for causing respiratory infections in more than 30% of the community during the pandemic.[1] This virus has a unique crown like shape under a microscope which gives it a name of corona virus. Now it has been named by the World Health Organization in the first week of March 2019. This virus spread quickly from Wuhan china to all over the globe and currently there were more than 10 million affected people worldwide with greater than 5 million deaths making it a pandemic.[2] This virus spreads from the respiratory tract through air borne droplets and secretions. It has a wide spectrum of presentation. Eighty percent of the individuals are asymptomatic to many being badly affected with severe cardiopulmonary failure leading to high mortality all across the globe. It has an incubation period of 14 days.[3]

The primary means of transmission are respiratory

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droplets and intimate contact; high aerosol concentrations in a sealed setting can also transmit the disease, fecal-oral transfer has not yet been shown.[2] Covid infection can present with a different spectrum of sign and symptoms, like atypical pneumonia, respiratory failure, acute respiratory distress syndrome (ARDS) and hyper-inflammatory responses.[1] Healthcare professionals are searching for an efficient and practical way to handle patients who are afflicted by the virus, given its worrisome pace of transmission.[3] Approximately 30% of these patients progress to severe illness such as ARDS, pneumonitis, septic shocks, DIC are caused by cytokine storm.[4] This cytokine storm is caused by dysregulated inflammation causing worsening of symptoms in COVID 19 patients.[3,4]

Most common hematological abnormalities are thrombocytopenia, leucopenia and lymphopenia.[4] As far as the biochemical markers are concerned the most affected are raised ALT, LDH, D-Dimers, creatinine kinase, serum ferritin and CRP. These factors are related to severity of disease and have an overall poor prognostic value.[5] The lungs are affected as bilateral consolidation and ground glass appearance affecting the lower lungs.[6] According to the literature review the amount and the duration of immunity that a person might develop after the resolution of the disease is also debatable. It is usually short lived and the disease might recur in the near future.[7] The mean Neutrophil to Lymphocyte ratio and Platelet to Lymphocyte ratio were 7.20 ± 4.20 and 204.25 ±148.42 respectively in severe disease Covid-19 patients. Various hematological parameters in COVID-19 are predictors of disease severity and poor prognosis include high TLC, Platelet count, NLR and PLR ratio. These findings are independent high-risk factor that needs urgent and timely management.[8,9] The aim of the article was to calculate the NLR and PLR in acute covid-19 patients as a simple and cost-effective test. The objective of the study was to determine the mean NLR and mean PLR in COVID- 19 patients.

PATIENTS AND METHODS

The Cross observational study was conducted in Medicine unit, Benazir Bhutto Hospital Rawalpindi during the period of May to November 2021 following ethical approval (vide letter no. NO-MU-I/BBH/0024 dated 10/05/2021). The WHO sample size calculator having 95% Confidence Level, Population mean 7.2%, Population standard deviation 4.20%, Absolute precision required 1%. Sample size were calculated as (n)95 cases on that time. The technique was consecutive sampling. Inclusion Criteria having age between 20-80 years, both gender and all patients those who were positive for corona virus by RT-PCR. Exclusion Criteria having Previous history of COPD/ ischemic heart disease, chronic liver disease, autoimmune disease and asthma. After permission from the ethical review committee, COVID-19 positive patients proven by RT-PCR from Oro/nasopharyngeal swab were enrolled. Patients admitted from the A & E department were included in the study. The selected patients were given their written informed consent. NLR and PLR were calculated for all the patients on admission versus after 48 hrs. The data were collected and calculated by the principal researcher on a specially designed proforma. Data were entered and analyzed in SPSS (Version 21). Frequency and percentages were calculated for categorical variables like gender. Mean and standard deviation were calculated for numerical variables like age, lymphocytic count, neutrophil count and platelet count were used as NLR ratio and PLR ratio. Effect modifiers like age and gender were stratified. Post stratification was done by using independent sample t-test. $p<0.05$ was taken as of significance.

RESULTS

Age range was from 20-80 years with mean age of 46.73 ± 11.16 years. Major part of the 59 (62.11%) patients having 20-50 years of age while 36(37.89%) were 51-80 years. Out of the 95 patients, having 39 (41.05%) male and 56 (58.95%) females. Mean leucocyte count was 8.05 ± 2.71 x 10^9/L. Mean leucocyte count was 5465 ± 1231 neutrophils/µL. Mean NLR was 5.15 ± 1.26 and mean PLR was 215.88 ± 38.14 in COVID-19 patients (Table I). Mean NLR was not significantly associated with changes over time in COVID-19 patients (p=0.21). Mean PLR was significantly associated with changes over time (p= 0.011), showing a statistically meaningful decrease from admission to 48 hours. Stratification of NLR & PLR ratio with respect to age is shown in Table II. Stratification of NLR & PLR ratio with respect to gender is shown in Table III.

Table-I: Mean NLR and PLR in COVID-19 patients (n=95)

	On admission	At 48 th hour
NLR ratio	5.15 ± 1.26	4.89 ± 1.54
PLR ratio	215.88 ± 38.14	201.89 ± 36.54

Table II: Stratification of NLR and PLR ratio with respect to age

Age (years)	NLR ratio		*p*-value	PLR ratio		*p*-value
	Mean	SD		Mean	SD	
20-50	5.23	1.61	**0.421**	216.81	38.47	**0.763**
51-80	5.02	1.41		214.36	38.10	

Table 1II: Stratification of NLR ratio and PLR ratio with respect to gender.

Gender	NLR ratio		*p*-value	PLR ratio		*p*-value
	Mean	SD		Mean	SD	
Male	4.99	1.13	**0.317**	219.13	36.39	**0.324**
Female	5.26	1.34		211.23	40.56	

DISCUSSION

Coronavirus is a largest family of viruses, having spectrum of common types of flu/ cold to Middle East respiratory syndrome and severe acute respiratory syndrome.[10] It was discovered as coronavirus disease (COVID-19) of unexplained viral pneumonia in Wuhan, China in December 2019. In January 12, 2020 was recognized by the World Health Organization. COVID-19 was reported to spread throughout the China and even to other countries[11], causing 34,662 confirmed cases of infection by Feb 8,2020.

After one week, individuals with severe sickness frequently developed dyspnea, while the majority of patients infected with the new coronavirus had mild to moderate illness. Patients with severe illness advanced quickly to septic shock, metabolic acidosis, acute respiratory distress syndrome, acute respiratory failure, and coagulopathy. Early detection of critical disease risk factors allowed for timely entry to the intensive care unit (ICU) and the urgent delivery of supportive treatment. Instead, they must get general isolation therapy. Notably, Cao and colleagues have documented a significant frequency of lymphopenia in COVID-19 patients.[11]Furthermore, it has been established that individuals with acute-on-chronic hepatitis B liver failure may benefit from a short-term prognostic assessment based on their baseline neutrophil-to-lymphocyte ratio.[12,13] This study to determine the mean NLR and PLR in COVID-19 patients. Mean NLR was 5.15 ± 1.26 and PLR was 215.88 ± 38.14 in COVID-19 patients. The mean NLR and PLR in patients who had severe disease was 7.20 ± 4.20 and 204.25 ± 148.42 respectively.[8] In this study of 95 cases of COVID-19 patients, the mean NLR showed a slight decrease from admission (5.15 ± 1.26) to the 48th hour (4.89 ± 1.54), but this change was not statistically significant (p =0.21). In contrast, the mean PLR significantly decreased from 215.88 ± 38.14 to 201.89 ± 36.54 over the same time period, with a statistically significant difference (p =0.011). These results suggest that PLR, but not NLR, may be more sensitive to short-term clinical changes in COVID-19 patients.

The majority of patients have minor, self-limiting illnesses, while those with severe or critical conditions have a very bad outlook. Very soon after the COVID-19 pandemic started, it was discovered that individuals with severe or critical conditions had a much greater NLR than those with less severe illness. It has been demonstrated that NLR is a trustworthy measure for assessing COVID-19 illness severity.[14] Numerous theories have been proposed to explain how neutrophils and lymphocytes react to corona virus infection. Reactive oxygen species released by neutrophils stimulate the immune system and liberate the virus from cells, which is subsequently taken up by antibodies. Furthermore, neutrophils initiate the synthesis of several cytokines. However, despite the fact that the viral infection itself primarily causes a lymphocyte response, systemic inflammation particularly elevated Interleukin 6 levels contraryally reduces the number of lymphocytes and subsequent cellular immunity. These two elements both lead to increased NLR.[15] Therefore an elevated NLR indicates the degree of inflammation.

According to the study, the mean NLR value rises noticeably with increasing disease severity, with the lowest NLR values being seen in asymptomatic and moderate cases of the illness. According to a Cochrane Meta-analysis Review of twenty Chinese research, NLR is a reliable prognostic indicator that can distinguish between COVID-19 illness is severe or not.[16] The outcomes are in line with an Italian research that included 74 patients, where the NLR for severe cases was 5.6 compared to 3.0 for non-severe cases.[17] Findings

demonstrating a direct correlation between patient NLR levels and disease severity were also supported by another meta-analysis. Similar results have also been discovered in Pakistani research carried out in several cities by Pervaiz et al. and Asghar et al.[18,19] In comparison to commonly used scoring severity criteria accepted for pneumonia, such as the CURB-65 Score (which evaluates the 30-day mortality of patients with community-acquired pneumonia) and the MuLBSTA Score (which provides early warning about the mortality of patients with viral pneumonia), a Chinese study suggests that NLR is superior in early prediction of severe and critical illness.[16] Additionally, it was discovered that NLR upon admission was a good indicator of illness severity.

There were significant correlations between greater NLR in COVID-19 severity and mortality in two meta-analyses of n = 19 and n = 13 trials.[14,19] Previous research discovered associations between elevated NLR and low-grade inflammatory chronic diseases, including diabetes mellitus, obesity, hypertension, heart and brain atherosclerotic events, and different types of cancer.[20] Even in individuals with comorbidities, NLR may continue to be able to predict the severity of COVID-19. For instance, in hospitalized patients with various cancer types, NLR strongly predicted COVID-19 severity and survival.[21]Severe COVID-19 is at risk due to several underlying illnesses. It has been proposed that COVID-19 patients died at an 8% greater rate for every unit rise in NLR.[22] According to studies, on-admission NLR can be used as a risk classification technique and may be able to predict the COVID-19 outcome. When NLR hits its height a few days after admission, this predictive capacity rises. But when the patient heals from COVID-19 and the inflammation goes down, NLR progressively loses its prognostic power.[23] A full blood count with differentials is necessary for measuring NLR. This is a common, inexpensive, easily accessible and uncomplicated laboratory test. Finally, distinct COVID-19 variations are exhibiting disparate morbidity and death results.[24]

Qu et al. observed 30 COVID-19 patients and discovered a significant difference in PLR between patients who were in critical condition and those who had less severe COVID-19 symptoms.[25] In a cross-sectional research including 93 COVID-19 patients, they discovered a substantial difference in PLR between patients who were critical and those who had less severe COVID-19 symptoms.[26] PLR is now thought to be a sign of inflammation. Studies have evaluated the relationship between PLR and viral, bacterial or malignant diseases as well as diabetes. According to studies, COVID-19 patient's platelet levels dramatically dropped.[27] Thrombocytopenia is frequently observed in patients in critical condition; it typically indicates the onset of intravascular coagulopathy, major organ failure, or physiologic decompensation rather than a main hematologic aetiology.[28]When a virus infects the lung and mechanical breathing damages the endothelium, platelet activation, aggregation, and thrombosis occur in the lung, resulting in massive platelet consumption. This mechanism for thrombocytopenia in severe acute respiratory syndrome is multifactorial.[25] The mechanism of thrombocytopenia in COVID-19 and SARS is similar. Platelet consumption may be the cause of thrombocytopenia in COVID-19. Coronaviruses can potentially cause an auto-immune reaction against blood cells or directly infect components of the bone marrow, leading to aberrant hematopoiesis.[29] However, it's important to remember that SARS and COVID-19 differ significantly from one another.[30]

Future study is required to update the findings relating to systemic inflammatory markers of COVID-19, given the variety of new variants differing morbidity and death outcomes. NLR & PLR were significantly linked with degree of severity as well as mortality rate in COVID-19 patients too.

CONCLUSION

The study concluded that NLR & PLR were significantly linked with COVID-19 patients. The cost-effective recommendation is to use NLR & PLR as a simple, easily available test for admission patients. It is a useful technique for risk categorization and to predict COVID-19 prognosis.

CONFLICT OF INTEREST

None.

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