

NEUTROPHIL TO LYMPHOCYTE RATIO (NLR) CAN BE A PREDICTOR OF THE OUTCOME AND THE NEED FOR MECHANICAL VENTILATION IN PATIENTS WITH COVID-19 IN PAKISTAN

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ABSTRACT

Objective: The aim of our study was to depict whether a neutrophil to lymphocyte ratio can predict the outcome and need for mechanical ventilation in COVID-19 patients. It also defined the trends of the symptoms and hematological/biochemical parameters in COVID-19 patients in Pakistani population.

Material & Methods: The descriptive cross-sectional study was conducted in the corona virus isolation ward at a tertiary referral facility, Jinnah Hospital, Lahore. A total 31 patients were enrolled in study after applying an inclusion and exclusion criteria over a period of one month. COVID-19 confirmed cases via RT-PCR of nasopharyngeal swab included, after taking informed consent to use their data in the study. Peripheral blood in EDTA vial was taken and immediately sent to the hospital laboratory. Detailed history along with clinical examination was done for every patient.

Results: The mean age of patients was 40.03±15.7 years in which 61.30 % (n=19) belong to the 20-45 years age group and 38.70 % (n=12) were having age of 45-70 years. 74.20% (n=23) were males and 25.80 % (n=8) were females. 28 Patients (90.32%) presented with NLR <3.13 and 3 Patients (9.6%) presented with NLR >3.13 along with lymphopenia. 2 out of 3 patients with NLR > 3.13 were predicted to develop critical illness with age more than 50 years. Outcome in the form of either recovery with home discharge or complications in the form of respiratory failure was observed at the 3rd day of hospital admission. Based on risk stratification of NLR according to age, we prioritized the patients and helped in guiding treatment decisions.

Conclusion: It is concluded that Neutrophil to Lymphocyte ratio can be used as a predictor to the use of supportive protective mechanical ventilation. High NLR > 3.13 associated with mortality in COVID-19 patients and with a rapid access to intensive care. Among metabolic profiles, there is a propensity of hyponatremia and normal upper limit of serum potassium levels in COVID-19 patients.

Key Words: Neutrophil, lymphocyte, Predictor, Outcome, Mechanical ventilation.

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INTRODUCTION

Coronavirus is an enveloped RNA virus responsible for many zoonotic infections. There are multiple outbreaks of the virus observed as SARS (Severe acute respiratory distress syndrome) in 2002 and MERS (Middle east respiratory syndrome) in 2012 in some areas of the world and in Arabian countries like UAE, Jordan, and even in China [1]. The novel SARS-CoV-2 is responsible for causing coronavirus disease (COVID-19) and emerged as a pandemic in December 2019, first time in the city of Wuhan, Hubei province of China [2]. COVID-19 disease has a various spectrum of illness, affecting people by rapid transmission via respiratory droplets. It has marked variation of presentation with asymptomatic conditions to life threatening

respiratory failure leading to morbidity and mortality [3].

80,000 cases were reported in China, among them 5% patients presented with critical disease having respiratory failure, septic shock and even multi organ failure. Although COVID-19 is routinely diagnosed by taking nasopharyngeal swabs (NPS) along with throat swabs but it can also be isolated from bronchial secretions and saliva. Patients are categorized as mild, moderate, severe and critical depending upon the oxygen requirements, clinical features as fever more than 39°C, presence of hyperinflammation with raised CRP, ferritin and d-dimers levels and radiological finding of lung fields involvement. Certain other inflammatory cytokines like CRP and IL-6 were observed in their bloodstream in response to COVID-19 [2].

Neutrophils and lymphocytes are the part of earliest body defense mechanism and are released in bloodstream in response to acute inflammation. Their

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count/ratio not only predicting prognosis in various disorders but also the development of the disease as well [3]. Raised neutrophil to lymphocyte ratio is found associated with various malignancies.

Neutrophil to lymphocyte ratio can be obtained from a peripheral blood sample with less harm to the patient, reduce health care workers exposure and is easy to perform with minimal expertise and low cost. As COVID-19 is a viral infection disease, so there is a propensity of low lymphocyte count with a disturbed neutrophil to lymphocyte ratio. The data is scarce about neutrophils and lymphocytes ratio in COVID-19 patients. A study in China had proposed various predictors for mortality in COVID-19 that included age, myocardial involvement and release of various inflammatory markers in the blood [4,5,6,7]. Another study from China suggested that a raised neutrophil to lymphocyte ratio with a low lymphocyte count predicts for the severity of disease [3,8,9]. So complete blood count is a relatively cheap test from which neutrophil to lymphocyte ratio can easily be calculated in order to anticipate the need of mechanical ventilation and helps in predicting the outcome even on presentation. Therefore, the present study was performed to check the impact of Neutrophil and lymphocyte ratio with disease progression along with the status of biochemical/hematological parameters in COVID-19 patients

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted in the corona virus designated isolation ward at Jinnah Hospital, Lahore over a period of one month from 6th March 2020 to 6th April 2020. Thirty-one patients admitted via corona triage center and medical emergency room with confirmed RT-PCR for COVID-19, were recruited in our study. Patients were informed about the study and informed consent was taken from each patient. All patients received standard treatment as per hospital policy with modification in accordance to disease severity. Patients with any blood disorders, hematological malignancies, solid organ malignancies, chronic viral hepatitis like hepatitis B, hepatitis C were excluded from the study. 3 ml peripheral blood sample was taken in EDTA and serum vial and immediately sent to laboratory for estimation complete blood count (CBC) parameters including, hemoglobin, Total Leukocyte Count (TLC), differentials white cell count for neutrophils, lymphocytes, eosinophils and platelets count via using sysmex automated hematological analyzer. All information was recorded

and saved on a pre-designed proforma. Statistical analyses were performed using the SPSS-17 software. Stratification for age, gender, duration and stage of disease was recorded to address the effect modifiers. The data of various variables represented as mean and standard deviation. The mean and standard deviations were calculated for variables including, age, duration of illness serum sodium, potassium, ALT, AST levels while frequencies and percentages were used for qualitative variables like gender and symptoms.

RESULTS

The study group comprised of 31 patients (23 males (74.2%) and 8 females (25.8%); median age (40.03± 15.7), having positive RT-PCR detection for COVID-19 with nasopharyngeal swab. The demographic and clinical features of corona patients are shown in table-1. 15 patients (48.4%) had history with acquisition via a foreign travel whereas, 16 patients (51.65%) had direct contact with a previously diagnosed COVID-19 patient.

Table-1: Demographic information of patients.

Parameter	Corona subjects (n=31)
Gender	Male 23 (74.2%) Female 8 (25.8%)
Age (years)	Median age (40.03± 15.7)
Residency	Lahore 16 (51.6%) Outside from Lahore 15 (48.4%)
Travel History	Travel abroad 15 (48.4%) Local transmission 16 (51.65%)
Contact History with COVID-19 Patients	No 18 (58.1%) Not known 5 (16.1%) Contact with COVID-19 patient 8 (25.8%)

Mostly patients 67.7% presented with fever whereas other symptoms having variable frequency including cough 54.8%, sore throat 35.5%, breathing difficulties 32.3%, flu 25.8%, gastrointestinal symptoms including diarrhea and abdominal pain was 16.1%. None of the patients showed any neurological symptoms like seizures, polyneuropathy and immune mediated thrombocytopenic purpura. The clinical features and symptoms of patients shown in table-2.

Table-2: Clinical features and symptoms of COVID-19 patients.

Parameters	COVID-19 subjects (n=31)
Fever	67.7%
Flu	25.8%
Sore Throat	35.5%
Breathing difficulty	32.3%
Cough	54.8%
Diarrhea	16.1%
Abdominal Pain	16.1%
Myalgias	48.4%

The hematological and biochemical parameters were recorded and shown in table-3.

Table-3: Hematological and biochemical parameters of patients.

Parameters	Corona subjects (n=31)
Oxygen saturation (%)	96.67 ±4.415
Hemoglobin (g/dl)	13.74±0.985
Total Leucocyte Count (10 ³ /μL)	8.41±4.44
Neutrophil (%)	67.34±9.97
Lymphocyte (%)	29.45±8.76
Platelet (10 ⁹ /L)	272.29±114.8
AST (IU/L)	35.93±15.31
ALT (IU/L)	35.64±8.24
Urea (mg/dL)	21.70±18.87
Creatinine (mg/dL)	1.06±0.334
Serum Sodium (mmol/L)	138.70±4.45
Serum Potassium (mmol/L)	4.28±0.32
Neutrophil Lymphocyte ratio (NLR) cut-off 3.13	NLR <3.13 (28 Patients) 90.32% NLR >3.13: (3 Patients) 9.6%: Age <50 years: 1 patient (33.33%) Age >50 years: 2 patients (66.66%)

Out of 31 patients, 90.32% having NLR < 3.13, remained stable with normalization of the biochemical parameters like AST, ALT, and even total leukocyte count and had an uneventful hospital stay leading to discharge from the healthcare facility at 3rd day of admission. 3 patients having NLR> 3.13 out of which two patients had rapid progression of disease in the form of respiratory failure leading to death and both having age more than 50 years. One patient with NLR> 3.13 remained stable on room air with age more than 50 years, without absence of any comorbidity. However, serum sodium levels tend to remain on the lower side with a serum potassium on the upper limit during illness.

COVID-19 patients of less than 50 years age without any comorbidities with NLR of >3.13 had a favorable outcome with complete recovery at 3rd day whereas those age more than 50 years with a NLR > 3.13 associated with outcomes like death and complications like shock and life threatening respiratory failure.

DISCUSSION

COVID-19 pandemic started in December 2019, with the first case reported in the city of China, Wuhan. This pandemic has exhausted the major resources of developed countries leading to financial crisis and the health system became crippled unfortunately. COVID-19 varies in symptoms from asymptomatic infection to fever, flu, cough, shortness

of breath, myalgias, seizures, encephalitis and respiratory failure. However, idiopathic immune mediated thrombocytopenic purpura, psychosis, anxiety and depression have been reported [10]. This zoonotic disease has a relatively small incubation period, that lasts from 2 to 12 days and disease course usually lasts for 28 days either leading to complete recovery, residual lung damage, circulatory collapse or death in about 5% of the cases [11,12]. SARS-CoV-2 infection leads to catastrophic changes at the cellular level with an increased cytokine production. However various studies have shown that certain parameters are disturbed in cellular injury because of bacterial infections like pneumonia, even gram-negative sepsis. There is a release of certain cytokines and inflammatory markers as well, certain hold a prognostic value as well like CRP levels, serum LDH, procalcitonin. Neutrophil and lymphocyte ratio have been disturbed in certain disorders [13,14].

Neutrophil to lymphocyte ratio predicts for severity and development in disorders like malignancies and metabolic disorder [15] and due to bacterial infections predominantly but for viral diseases the data is insufficient. It has been hypothesized that COVID-19 may act on T- cell lymphocytes leading to depletion. In our study, we observed that the presence of high neutrophil to lymphocyte ratio in patients with COVID-19 is a predictor to the need of mechanical ventilation. Our results are in accordance with the study of Cao et al., in which they reported that the Non-survivors and ICU patients presented with lymphopenia [16]. Another study in China showed that high NLR >3.13 along with high cytokine response can be an indicator of the worsening clinical condition of COVID-19 patient [17]. NLR cut off value of 3.13 has a sensitivity of 0.875 and specificity of 0.717 [4]. NLR <3.13 had a favorable outcome with a greater survival. The current data is empiric. Complete blood count is relatively easy, cheap and results are reproducible within 5 minutes. The risk stratification of NLR according to age improves patient management. Patients with age less than 50 years with a NLR < 3.13 are less likely to develop critical disease and they can be managed at home with isolation precautions and counselling about warning signs. Patients with NLR>3.13 with age more than 50 years need a close monitoring. So, when there are clusters of cases, it's a need of the time to anticipate the possible complications. NLR of more than 3.13 is associated with death as an outcome.

CONCLUSION

Our study shows clinical usefulness of a simple, relatively cost-effective test, complete blood count in that a neutrophil to lymphocyte ratio of more than 3.13 in COVID-19 patients on hospital admission provides a means of quick evaluation, as NLR more than 3.13 has been associated with respiratory complications with urgent need of mechanical ventilation within 48 hours of admission. With the help of these biochemical markers we can prioritize treatment guides and stratify patients for early invasive management.

AUTHORS CONTRIBUTION

Abida Pervaiz: Manuscript writing, data collection and supervised research.

Usman Pasha: Perform statistical analysis & data analysis.

Sadia Bashir: Design of research work & review manuscript.

Rabia Arshad: Perform statistical analysis & data analysis.

Muhammad Waseem: Manuscript writing, critical data analysis.

Omar Qasim: Data collection & data record.

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