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Orignal Article

Evaluating COVID-19 Epidemiology, Clinical Outcomes and Neutrophil-To-Lymphocyte Ratio as a Prognosticator of Severity of the Disease

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ABSTRACT

Infectious Coronavirus disease 2019 (COVID-19) is the cause of the disease, which poses a significant public health threat worldwide. A poor prognosis is often associated with serious and life-threatening illnesses. In these circumstances, identifying potentially severe or critical cases soon and treating them promptly are vital. As a result of COVID-19, we can save medical resources, reduce mortality, and prevent the disease from progressing. **Objective:** To find out the public health perspective of COVID-19 and its associated clinical outcomes and to identify the neutrophil-to-lymphocyte ratio (NLR), a prognostic biomarker for the COVID-19 severity. **Methods:** A descriptive cross-sectional research was conducted in the Hematology section, Pathology Department of Lahore General Hospital/ Ameerudin Medical College Lahore. A total of 1000 patients were enrolled in the study for nine months. A RT-PCR test of a nasopharyngeal swab from COVID-19 patients was comprised in this research with their informed consent. An EDTA vial containing peripheral blood was taken and sent directly to the hospital lab. For every patient; a detailed history and clinical examination were performed. **Results:** In this study, the average age of participants was 40 years. In total, 68% (n=680) of the patients did not have any pre-morbid conditions, while 32% (n=320) did. Diabetes mellitus was a premorbid condition for 13.7% of patients (n=137), hypertension for 5% (n=50), ischemic heart disease for 5.7% (n=57), chronic respiratory infection for 2.3% (n= 23), chronic renal disease for 4.3% (n=43), chronic hepatic for 1.2% (n=12). Eight hundred and forty patients (84%, n=840) presented with NLR <3.13 and one hundred and sixty patients (16%, n=160) presented with NLR >3.13 along with lymphopenia. More than half of patients with NLR > 3.13 were anticipated to progress to serious illness. We prioritized patients based on the stratification of NLR according to their ages and guided their treatment decisions. **Conclusions:** In conclusion, NLR can be exploited as a predictor for ventilator support and protection. Patients with an NLR > 3.13 are at higher risk of mortality as well as requiring intensive care soon after receiving it.

INTRODUCTION

Infectious Coronavirus disease 2019 (COVID-19) is the cause of the disease, which poses a significant public health threat worldwide [1]. Patients suffering from COVID-19 show vastly divergent symptoms. The majority of COVID-19 infected individuals are asymptomatic. A significant proportion, still, exhibit mild symptoms, such as temperature, body pain, coughing, dyspnea, flu, etc. [2-4]. As a result, severe ARDS, pulmonary edema, or multiple organ dysfunction syndromes can result in a high mortality rate in some severe cases of severe pneumonia [4-6]. ARDS, septic shock, or even MODS may cause mild to moderate symptoms in patients that may progress

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suddenly [7]. A poor prognosis is often associated with serious and life-threatening illnesses. In these circumstances, identifying potentially severe or critical cases soon and treating them promptly are vital. As a result of COVID-19, we can save medical resources, reduce mortality, and prevent the disease from progressing [8]. A deregulated inflammation resulting in cytokine storms may worsen the outcomes of COVID-19 patients, as is the case with the Middle East respiratory syndrome (MERS) or severe acute respiratory syndrome (SARS) [9,10]. Researchers have demonstrated that the neutrophil-to-lymphocyte ratio (NLR) in peripheral blood plays a role in determining systemic inflammation. Furthermore, NLR has also been shown to be effective in predicting the course and outcome of a number of diseases, including solid tumors, chronic obstructive pulmonary disease (COPD), cardiovascular disease, and pancreatitis [11-14]. NLR is suggested to help distinguish mild/moderate COVID-19 infection patients from severe/critical groups in a recent study published in the Journal of Medical Internet Research. Additionally, multiple studies indicate that a high NLR corresponds to high COVID-19 mortality [15-18]. Neutrophil-lymphocyte ratio (NLR) is an easily obtainable biomarker that can be calculated from components of the differential white cell count (dividing neutrophil count by lymphocyte count). The purpose of our research was to evaluate the predictive value of NLR for disease severity and mortality among patients with COVID-19 and to provide a reliable, early indicator of critically ill patients.

METHODS

The study was designed as descriptive cross-sectional research that was carried out in Ameerudin Medical College Lahore, Pakistan. The study was conducted on a sequential group of infected individuals from February 1st, 2021, to December 31st, 2021. The sample was drawn using nonprobability, convenience sampling. Since there was no prevalence data for the illness at the time of the study, the sample size calculation was not applicable. Ethics and research committees at the hospital approved the research. The study included every patient admitted with a confirmed positive COVID-19 test for Reverse transcription-polymerase chain reaction (RTPCR) on a nasopharyngeal swab. An examination of demographic characteristics as well as epidemiological characteristics, such as possible exposure history, signs, symptoms, comorbidities, and drug history, was conducted. According to hospital protocol, laboratory tests were made, and radiological imaging was done. A certified radiologist reported all X-rays and CT scans. The NLR is derived from the ratio of neutrophils to lymphocytes. It was recommended that patients with NLR cut-offs of 3.8 be assessed upon admission and repeatedly thereafter. The WHO has established interim guidelines for defining the severity of cases. Asymptomatic (RT-PCR positive patients not showing signs or symptoms), mild (RT-PCR positive patients not showing any signs of hypoxia), moderate (RT-PCR positive patients not showing signs of severe hypoxia but with respiratory rate > 30 breaths/min or Spo2 > 90%) and critical (with ARDS or septic shock). Under the category of severe patients, we included severe as well as critical patients. IBM SPSS 25 software was used for the statistical analysis. In the case of continuous variables, like age and NLR, standard deviations were included along with the mean values. A number of categorical variables - such as disease severity categories, symptoms, and comorbidities - were analyzed for frequency and percentage. The statistical significance of categorical variables was calculated using Pearson's Chi-square test. A 95% confidence interval was assumed for categorical variables. The significance value was kept at less than 0.05.

RESULTS

The mean age was 40 years (Range- from 18 to 88 years) in a total of 1000 participants. A majority of the participants were males 880 (88%). The majority of the patients admitted (67%, or 670) were asymptomatic. In order of decreasing frequency, fever was the most common symptom (80%; n=800), cough was 60%; dyspnea was 40%; myalgia was 35%; sore throat was 21%; diarrhea and vomiting were 15%; headache was 7%; hemoptysis was 2% (Table 1).

Parameters	Status	Number	Percentages
Gender	Male	880	88%
	Female	120	12%
Location	Urban	700	70%
	Rural	300	30%
Travel History	Yes	280	28%
	No	720	72%
Fever	Yes	800	80%
	No	200	20%
Cough	Yes	600	60%
	No	400	40%
Flu	Yes	350	35%
	No	650	65%
Dyspnea	Yes	400	40%
	No	600	60%
Myalgia	Yes	350	35%
	No	650	65%
Sore Throat	Yes	210	21%
	No	790	79%
Diarrhea	Yes	150	15%
	No	850	85%
Headache	Yes	70	07%
	No	930	93%
Hemoptysis	Yes	20	2%
	No	980	98%
Loss of Taste	Yes	650	65%
	No	350	35%
Loss of Smell	Yes	465	46.5%
	No	545	54.5%

Table 1: Demographic details and Clinical outcomes of COVID-19

Sixty Eighty percent of patients (n=680) had no premorbid conditions, and thirty-two percent (n=320) had underlying chronic illnesses. There were 13.7% of cases reported to

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have diabetes mellitus (n=137), 5% of cases reported to have hypertension (n=50), 4.6% of cases reported to have ischemic heart disease (n=46), 2.3% of cases reported to have chronic respiratory disease (n= 23), 4.3% of cases reported to have chronic kidney disease, 1.2% of cases reported to have chronic liver disease (Table 2).

Pre-morbidities	Numbers	Percentages
No Pre-Morbidities	680	68%
Diabetes Mellitus	137	13.7%
Hypertension	50	5%
Chronic Respiratory Disease	23	2.3%
Chronic Renal Diseases	43	4.3%
Ischemic Heart Disease	45	4.6%
Hepatic Diseases	12	1.2%

Table 2: Pre-morbidities of the COVID-19 Infection

The severity of disease varied, with 68% (n=680) being asymptomatic, 17% (n=170) having mild disease, 5% (n=50) having moderate disease, and 11% (n=110) having severe disease. The total number of patients recovered at 97.8% (N=978) while 22 patients perished. On average, there were 1000 patients (range - 0.14 - 31.33). Table 3 presents a description of NLR and its variation across the four categories of severity. As can be seen, NLR showed a positive correlation between disease severity and NLR, going from 1.89 for asymptomatic patients to 2.18 for mild, 4.67 for moderate, and 9.71 for severe patients in our sample (Figure 1). Besides asymptomatic and mild categories, there is a statistically significant difference in NLR. Compared with patients who died from COVID-19, Table-3 shows the mean NLR for those who survived.

Parameters	Values
Hemoglobin	13.91 (g/dl)
Red Blood Cells (10^6/µl)	4.7
Total Leukocyte Count (10^3/µl)	8.42
Neutrophil (%)	68.1%
Lymphocyte	28.4%
Neutrophil To Lymphocyte Ratio	
Less than 3	84
Greater than 3	16
	840
	160

Table 3: Hematological Parameters, NLR, and COVID-19

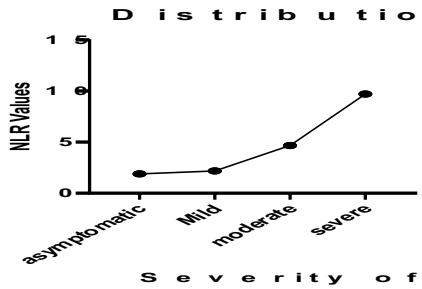

Figure 1: Distribution of NLR regarding status of severity of COVID-19

DISCUSSION

COVID-19 is an extremely contagious disease that continues to pose a serious threat to global health. As a result of its rapid spread, it has now reached its second peak in many countries [19]. Despite the fact that many of its patients suffer from mild illnesses, those who have more serious conditions are likely to suffer a very poor outcome. Very early in the pandemic, researchers observed that the NLR in severely ill patients was significantly higher than that in patients with milder diseases. Numerous methods have been proposed apropos the eliciting of neutrophils and lymphocytes to Coronavirus infection [19,20]. NLR has proven to be a reliable indicator of infection harshness in COVID-19. Immune cells trigger the immune system and produce reactive oxygen species which damage DNA within cells and expel the virus from the cells, afterward besieged by antibodies. A neutrophil can also produce many cytokines and effector molecules. However, systemic inflammation, in particular increased Interleukin 6, paradoxically reduces lymphocyte count and cellular immunity, though the viral infection itself elicits the immune retort primarily through lymphocytes. An elevated NLR is a consequence of both of these factors [20]. Consequently, a high-level NLR envisages inflammation rigorousness. COVID-19 develops at a variety of ages. It is known that COVID-19 has a preference for males which is in agreement with other studies of the disease [21]. Like other studies, this research comprises of majority of males [21]. Among the asymptomatic individuals in our study, most had a fever, respiratory symptoms, and myalgias, which are comparable to the symptoms described by the World Health Organization intervening supervision. In this article, the majority of patients were asymptomatic which was in line with WHO figures suggesting up to 80% of patients are asymptomatic. We have observed that NLR increases significantly as the severity of the disease increases, with the lowest NLR observed in mild and asymptomatic diseases. The results of our analysis are consistent with findings of a Cochrane critical appraisal of different research articles from China that showed neutrophil to lymphocyte ratio to be an independent

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prognosticator for differentiating severe from non-severe COVID-19 disease [22]. A study with 74 patients in Italy found NLR levels have a parallel relation between COVID-19 severity and neutrophil to lymphocyte ratio [23]. Moreover, there is a direct proportion between infection severity and neutrophil to lymphocyte ratio [24]. Studies in Pakistan have also found similar findings. Multiple research projects from China also predict the NLR as a surrogate prognosticator for the infection status assessment, then widely used pneumonia severity scoring criteria, particularly the CURB-65 Score (which assesses how good patients with community-acquired pneumonia do 30 days after their diagnosis) and the MuLBSTA Score (which provides an early indication of how a patient with viral pneumonia will fare). Furthermore, we ascertained that neutrophil to lymphocyte on divulgence was a steadfast prognosticator of the illness severity. As well, we examined differences between disease categories in mean NLR and found the greatest differences were between asymptomatic and severe patients. In this regard, our results of a correlation between mean neutrophil to lymphocyte ratio and severe illness were expected. According to our study, high NLRs are associated with mortality as well. In this study, 22 individuals died with a mean of 9.9 neutrophils to lymphocyte ratio, while the mean ratio for those recovering was 2.34. Both nationally and internationally, high NLRs are associated with death in patients with COVID-19. A research study conducted in China has found that elevated NLRs are independent risk factors in determining in-hospital morale [24]. Our study results concur with those mentioned above supporting the theory that neutrophil to lymphocyte ratio can be predicted as a surrogate biomarker to detect COVID-19 disease morbidity and mortality in an inexpensive, robust and readily available manner. This is a simple marker that can be used to determine whether patients are at risk of dying prematurely.

CONCLUSIONS

It is concluded that NLR can act as a predictive factor for disease severity and mortality in COVID-19 patients. Using NLR can help predict and stratify COVID-19 patients as per the severity and accurately predict their outcomes in a country with limited resources like ours.

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