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A STUDY OF PROGNOSTIC ROLE OF NEUTROPHIL TO LYMPHOCYTE RATIO IN COVID-19 PATIENTS IN A TERTIARY CARE HOSPITAL

Dr Pratibha Meena Assistant Professor , Department Of Pathology.

Dr Shailendra Meena Assistant Professor, Department Of Community Medicine.

Prof. Dr. Gopal Krishna Sawke Professor and Head , Department Of Pathology.

ABSTRACT **INTRODUCTION** Coronavirus disease 2019 (COVID-19) is highly contagious, continues to spread rapidly and causes serious harm. Circulating biomarkers that can evaluate inflammation and immune status, and can be potentially useful in diagnosis and prognosis of COVID-19 patients. In present study , we assessed the potential of the neutrophil to lymphocyte ratio (NLR) as an indicator of severity severe versus nonsevere COVID-19 cases. **Methods:** It was a retrospective observational study .Age, gender, TLC, ANC, ALC and neutrophil-to-lymphocyte ratio (NLR) of 80 patients with laboratory confirmed COVID-19 were investigated and compared. Suitable statistics were applied to compare the data. **Results:** we analyzed 80 covid – 19 positive patients, which included 40 patients with COVID-19 and ICU admission and 40 patients with COVID-19 and admission in isolation ward or covid care centre. Maximum number of patients were male (68.8%). Mean age of study group was 52.12 year. Median TLC (Total Leukocyte Count)of study group was 8200, median ANC (Absolute Neutrophil Count) was 6479, median ALC (Absolute Lymphocyte Count) was 1282 and Median NLR (Neutrophil to Lymphocyte ratio) was 4.45. We found statistically significant association between age and severity of Covid-19 disease, gender was not significantly associated with the severity of the Covid -19 disease. TLC, ANC, ALC and NLR was found to be significantly associated with the severity of the Covid-19 disease. **Conclusions:** Elevated age and NLR can be considered independent biomarkers for indicating poor clinical outcomes in patients with COVID -19.

KEYWORDS

***Corresponding Author Dr Pratibha Meena** Assistant Professor , Department Of Pathology.

INTRODUCTION

In December 2019, there were many cases of pneumonia of unknown etiology reported in Wuhan, Hubei province, China 1 . The disease had similarities to severe acute respiratory syndrome coronavirus (SARSCoV) and has been named as the 2019-novel coronavirus disease (COVID-19) by the World Health Organization (WHO). As COVID-19 spreads rapidly and causes serious harm , it is important to continuously improve its clinical diagnosis and treatment research 2 . This is a highly contagious virus, mainly transmitted through respiratory droplets and close contact. The SARS-CoV-2 infection causes wide range of clinical symptoms, including asymptomatic, nonsevere, and severe forms, which can rapidly lead to death 3 . Studies have found that patients with severe pneumonia had a lower lymphocyte count and a lower percentage of helper T cells, as well as slow lymphocyte recovery, and lower number of lymphocytes during treatment. This may be related to virus-mediated immune paralysis 4 . It has been found in many studies that the neutrophil to lymphocyte ratio (NLR) has a good predictive value on disease severity and predicts mortality in patients with COVID-19 infection 5. The neutrophil-to-lymphocyte ratio (NLR) is also an indicator of the systematic inflammatory Response 6 . Higher values of NLR have been associated with more severe forms of illness with the worst prognosis 7. A high incidence of lymphopenia in COVID- 19 patients has been reported by Cao and his colleagues 8. Thus, it is important to consider whether NLR might be a potential predictor for critical illness of COVID-19 9. To test this hypothesis, we included NLR along with epidemiological history, comorbidity, and other laboratory tests for analysis.

MATERIAL AND METHODS

The present paper was a retrospective and observational study conducted at Atal Bihari Vajpayee Government Medical College And Hospital, a Tertiary care hospital, from Vidisha District in the state of Madhya Pradesh, a first-line hospital in the battle against COVID-19.

Study Design

Retrospective observational study

Study Population

The study included 80 patients with confirmed SARS-COV 2 infection consecutively hospitalized between October 2020 to December 2020. COVID-19 diagnosis was confirmed using reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay to test nasal and pharyngeal swab specimens according to WHO guidelines. The patients were either asymptomatic or had a severe or non severe form of the disease.

Inclusion criteria

Consisted of all hospitalized patients over 18 years old with confirmed COVID-19 infection.

Exclusion criteria

Patients with confirmed COVID- 19 and with other comorbidities such as cancer, hematological diseases, severe cardiac disease (NYHA III and IV cardiac failure, recent myocardial infarction -last three months, unstable arrhythmia), liver disease, systemic diseases, and pulmonary fibrosis.

Non-severe patients
Met following conditions:
(1) Epidemiology history
(2) Fever or other respiratory symptoms
(3) covid care centre or isolation ward admission
(4) Positive result of RT-PCR for SARS-CoV-2 RNA.

Severe patients

Additionally met at least one of the following conditions:
(1) Shortness of breath, RR ≥ 30 times/min,
(2) Oxygen saturation (Resting state) ≤ 93%,
(3)ICU admission.

Only the laboratory-confirmed cases were included in the study.

Data Collection

Demographic, clinical, laboratory, and treatment data were taken from the laboratory records . NLR ratio was calculated as the absolute count of neutrophils divided by the absolute count of lymphocytes. Blood

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examinations involved measuring complete blood cell count and differential Values . All laboratory tests were done in the hospital laboratory with standard procedures .

Statistical Analysis

It was performed using EPI info software . Median (25th percentiles;75th percentiles) was calculated for quantitative variables with a non-normal distribution; arithmetic means and standard deviation was calculated for quantitative variables with a normal distribution.

The comparison of two means was performed using a t-test for independent samples with equal or unequal variations depending on the Levene test result. Mann Whitney U test was applied for quantitative variables with non-normal distribution. Frequencies were compared with the Chi-square test.

RESULTS

In the present study, we analyzed 80 covid – 19 positive patients, which included 40 patients with severe COVID-19 and 40 patients with non severe COVID-19. Maximum number of patients were male (68.8%). Mean age of study group was 52.12 year. Median TLC of study group was 8200, median ANC was 6479, median ALC was 1282 and Median NLR was 4.45. We found statistically significant association between age and severity of Covid-19 disease, gender was not significantly associated with the severity of the Covid -19 disease. TLC, ANC, ALC and NLR was found to be significantly associated with the severity of the Covid-19 disease.

Table 1 : Demographic and baseline characteristics of Covid-19 patients

Characteristics		Non-severe (Mean ± SD)	Severe (Mean ± SD)	Test statistic	P
Age		47.82 ± 16.32	56.42 ± 14.87	2.46	0.01
Gender	Male	26	29	0.524	0.469
	Female	14	11		

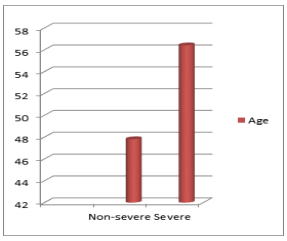
S. No	Characteristic		Value (N=80)
1	Age	Mean ± SD (Range)	52.12 ± 16.1 (18 - 85)
2	Gender	Male	68.8% (55)
		Female	31.3% (25)
3	Severity	Non severe	50% (40)
		Severe	50% (40)
4	Total leucocyte count	Median (IQR) (Range)	8200 (5225 -11550) (2000 -30300)
5	Absolute Neutrophil count	Median (IQR) (Range)	6479 (2226.7 - 9580) (0.6 - 49)
6	Absolute Lymphocyte count	Median (IQR) (Range)	1282 (864.9 - 1853) (353 - 4301)
7	Neutrophil to lymphocyte ratio	Median (IQR) (Range)	4.45 (2 – 8.8) (.6 - 49)

Table no 1 Shows demographic profile and baseline characteristics of Covid – 19 patients.There were total 80 patients , 40 in the non severe group and 40 in the severe group. Maximum number of patients were male (68.8%). Mean age of study group was 52.12 year. Median TLC of study group was 8200, median ANC was 6479, median ALC was 1282 and Median NLR was 4.45.

TABLE 2 Association of age and gender with the severity of Covid-19 disease

Table 2 shows association of age and gender with the severity of Covid-19 disease. Unpaired and Chi-square test was applied. Age was significantly associated with the severity of the Covid-19 disease (P=0.01).

Graph 1 shows association of age with the severity of Covid-19 disease. Age was significantly associated with the severity of the Covid-19 disease .



Graph 1 shows association of age with the severity of Covid-19 disease. Age was significantly associated with the severity of the Covid-19 disease .

The average age of the patients among non severe and severe cases was significantly higher in severe group as compared to the other group. Gender of the patients was not found to be significantly associated with the severity of the disease.

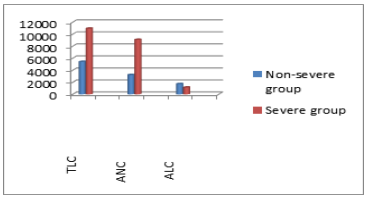
Table 3. Association between CBC values and Covid-19 disease severity

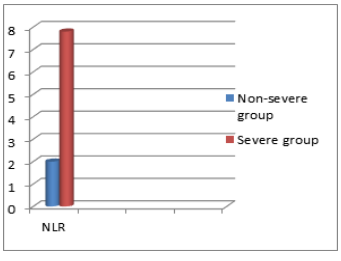
CBC values	Non-severe group (n=40)	Severe group (n=40)	P value
TLC Median (IQR) (Range)	5420(4225 - 7800) (16500)	10950 (8675 - 13250) (26100)	0.001
ANC Median (IQR) (Range)	3234.5 (2538.7 – 4734.7) (13676)	9095 (7210 - 11488) (24763)	0.001
ALC Median (IQR) (Range)	1723 (1723 - 2352) (1147)	1150 (729 - 1545) (2938)	0.014
NLR Median (IQR) (Range)	2.05 (1.42 – 3.42) (15.4)	7.85 (5.47 - 13) (46.2)	0.001

Table 3 shows association of CBC and NLR values wih the severity of Covid – 19 disease.

We found that TLC , ANC , and NLR was significantly associated with the severity of the Covid – 19 disease. The NLR of the two groups is also found to be significantly associated with the severity of the disease. Mann Whitney U test was applied as test of significance with the P Value of < 0.05 .

Graph 2 Shows association of CBC values wih the severity of Covid – 19 disease. We found that TLC and ANC was significantly associated with the severity of the Covid – 19 disease.





Graph 3 shows association of NLR values wih the severity of Covid – 19 disease. We found that NLR was significantly associated with the severity of the Covid – 19 disease.

In the present study we analyzed 80 covid – 19 positive patients, which included 40 patients with severe COVID-19 disease and 40 patients with non severe COVID-19 disease. Maximum number of

patients were male (68.8%). Mean age of study group was 52.12 years. Median TLC of study group was 8200, median ANC was 6479, median ALC was 1282 and Median NLR was

4.45. We found statistically significant association between age and severity of Covid-19 disease, gender was not significantly associated with the severity of the Covid -19 disease. In our study we found that values of TLC and NLR were higher in severe group compared to non severe group. The Patients with severe COVID-19 disease had significantly higher TLC (10950 vs 5420, p = 0.001). The Patients with severe COVID-19 disease had significantly higher NLR (7.85 vs 2.05, p = 0.001) as expected in the severe group as compare to non severe group.

CONCLUSIONS

We can say that for 1m3M20 grade of concrete consumption of fine aggregate is 775.96 kg. Here in specimen M-3 we replace fine aggregate by 24.62 kg of crumb rubber for 1m3M20 grades of concrete. So, we can say that up to 15% foundry sand utilized for economical and sustainable development of concrete.Uses of crumb rubberin concrete can reduce the harmfulness to the environment and produce a 'greener' concrete for construction. An innovative supplementary Construction Material is formed through this study.

DISCUSSION

COVID-19, is a highly infectious disease caused by SARS-CoV-2, which mainly targets the lungs and in severe cases may result in multiorgan injury and death 4 . SARS-CoV-2 binds to the alveolar ACE2 receptors and induces the release of inflammatory factors, which in turn activate the immune system, leading to a cytokine storm 10, 11. Thus, timely and accurate identification of severe COVID-19 cases after diagnosis is important for the immediate treatment of high-risk patients. Significantly lower lymphocyte and higher neutrophil counts have been observed in patients with severe COVID-19 compared to those with mild disease 12 . The present study aimed to compare the prognostic value of NLR for prediction of COVID-19 severity.

The present study included 80 patients admitted to hospital with positive RT-PCR tests for COVID-19. Most patients were non-smokers, not diabetic or hypertensive. In present study we observed highly significant positive relationships between COVID-19 severity and neutrophil levels, total leukocyte counts and NLR. We also observed a significant negative association between lymphocyte levels and COVID-19 severity.

The results of several previous studies agree with the data reported here, showing that severe COVID-19 (including fatal cases) was associated with higher neutrophil counts , lower lymphocyte counts and high NLR compared with non severe COVID-19 cases [4,5,7,9].

Similar results were obtained by Yang et al . They proposed that elevated NLR is an independent prognostic biomarker for COVID-19 patients 2. The findings of Sayed and co-workers agreed with our results and showed that NLR was of prognostic value in COVID- 19 patients and should thus be closely monitored [13].

The present study was conducted to compare the prognostic value of total leucocyte counts, neutrophil counts, and NLR in predicting COVID-19 severity.

CONCLUSION

The present study concludes that NLR is independent prognostic marker to differentiate severe versus non-severe disease in COVID-19 patients. Early recognition of the severe cases allows for early triaging and timely initiation of management. This marker is cost-effective and easily accessible in all laboratories. Future studies with larger sample size are needed to compare the trends of NLR with disease progression.

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