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PREDICTIVE ROLE OF NLR, d-NLR, LMR AND PLR IN DISEASE SEVERITY OF COVID-19 PATIENTS

Medicine

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ABSTRACT

Introduction: On 31st March 2020 WHO declared coronavirus disease 2019 as global pandemic caused by SARS-COV-2019. Covid-19 virus elicits severe inflammatory reaction upon entering the body. This inflammation is also reflected in blood parameters like complete blood count, liver function test, renal function tests etc. By studying some of these parameters, we have tried to determine the severity of covid-19 infection.

Aims And Objectives: To review the blood parameters that are affected by virus triggered inflammation in covid-19 disease.

Materials And Methods: An observational cross-sectional study was conducted in a tertiary COVID-19 care hospital over a course of 4 months. Infection was diagnosed by RT-PCR method done on either nasopharyngeal or oropharyngeal swab. Patients were grouped into severe and non-severe category according to the interim guidelines for diagnosis and treatment issued by WHO. There were 50 severe and 100 non severe cases in total. T-test was applied for comparing continuous variables and ROC curve was applied to determine the cut off values of various parameters studied. P value <0.05 was recognized as statistically significant.

Results: The difference between mean value of NLR in severe group (11.72+8.57) and in non-severe group (2.57+1.53) was significant with the p value of <0.0001. The ROC curve shows AUC of 0.8835 and cut-off value of >3.5 with 80% sensitivity and 82% specificity. Similar results were found with d-NLR (7.59+5.71 vs 1.95+1.06) with p value <0.0001 with ROC-AUC of 0.8808 and cut-off of >2.65 with 80% sensitivity and 80% specificity. The findings of LMR were also significant with mean value of 4.22+3.75 in severe, 6.80+3.19 in non-severe, p value of <0.0001, ROC-AUC of 0.7663, cut-off of <4.65 (72% sensitivity and 75% specificity). The findings of PLR had mean value of 263.33+179.47 in severe, 128.46+73.70 in non-severe, p value of <0.0001, ROC-AUC is 0.7237, cut off of >47.50 (72% sensitivity and 72% specificity.

Conclusion: The values of NLR, d-NLR, LMR, and PLR varied significantly among severe and non-severe cases. Thus, they have a good predictive role in disease severity in covid-19 infection. These variables are easy to assess and may help in triage and better management.

KEYWORDS

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a newly emerged coronavirus, that was first recognized in Wuhan, Hubei province, China, in December 2019 (1). SARS-CoV-2 is a positive-sense single-stranded RNA virus that is highly contagious in humans (2). It is the successor to SARS-CoV-1, the strain that caused the 2002–2004 SARS outbreak (3). The proportion of persons who become infected with SARS-CoV-2 and are asymptomatic remains to be better understood. A recent meta-analysis reported an overall estimate of 31% of asymptomatic cases, from seven studies with predefined screened populations, prediction interval ranging between 26–37% (4). In those patients that do become symptomatic, most people with COVID-19 develop only mild (40%) or moderate (40%) disease, approximately 15% develop severe disease that requires oxygen support, and 5% have critical disease with complications such as respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multiorgan failure, including acute kidney injury and cardiac injury (5). Older age, smoking and underlying noncommunicable diseases (NCDs), such as diabetes, hypertension, cardiac disease, chronic lung disease and cancer, have been reported as risk factors for severe disease and death (6,7). Clinical manifestations of COVID-19 are generally milder in children compared with adults (8,9,10).

The WHO COVID-19 disease severity categorization is as follows: (11)

· Severe COVID-19: Defined by any of:
1. Oxygen saturation < 90% on room air,
2. Respiratory rate > 30 breaths/min in adults,
3. Signs of severe respiratory distress (accessory muscle use, inability to complete full sentences, and in children, very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger signs).

· Non-severe COVID-19: Defined as absence of any criteria for severe or critical COVID-19.

Severe inflammatory response contributes to weak adaptive immune response, thereby resulting in immune response imbalance. Circulating biomarkers that can represent inflammation and immune status are potential predictors for the prognosis of COVID-19 patients (12). Peripheral white blood cell (WBC) count, neutrophil-to-lymphocyte ratio (NLR), derived NLR ratio (d-NLR, neutrophil count divided by the result of WBC count minus neutrophil count), platelet-to-lymphocyte ratio (PLR) and lymphocyte-to-monocyte ratio (LMR) are indicators of the systemic inflammatory response (13). Therefore, we aimed to study these parameters in cases of coronavirus pneumonia to predict severity of infection.

MATERIALS AND METHOD

Study Area:
New Medical College Hospital, the only dedicated Government tertiary care Covid-19 hospital in Hadoti region.

Study Design: Observational cross-sectional study.

Study Period: April 2020 to August 2020 (4 months).

Inclusion Criteria:
All established patients of COVID19 admitted in the COVID care Unit of GMC, Kota. (Diagnosed by RT-PCR; done on either nasopharyngeal or oropharyngeal throat swab).

Exclusion Criteria:
All patients who were a known case of tumor-related diseases, autoimmune diseases, and tuberculosis, chronic kidney disease and chronic liver disease.

Study plan:
Since admission in COVID care unit, each patient was monitored by a multispecialty team. Temporal assessment of the patient's profile was ensured by regular monitoring of vitals, daily assessment of the patients clinically, by serial blood biochemistry, ABG and imaging. We reviewed medical records of these patients for:

1. Detailed History (regarding symptomatology, past medical history)
2. Clinical Examination
3. Complete Laboratory work up –
· Complete blood count
· Plasma glucose level
· Renal function tests
· Liver function tests
· LDH, CRP, ECG, serial Chest X-Ray, HRCT-chest

Statistical Analysis:
Continuous variables were expressed as the appropriate means and standard deviations. Categorical variables were summarized as the counts and percentages in each category. Patients were grouped into severe and non-severe COVID-19 according to the interim guidelines of WHO for diagnosis and treatment of COVID-19. T-test was applied to compare continuous variable and ROC curve applied to establish cut off values for Age, WBC, NLR, d-NLR, LMR, and PLR. $P < 0.05$ was recognized as statistically significant.

RESULTS

Table 1:Distribution of various parameters in both groups.

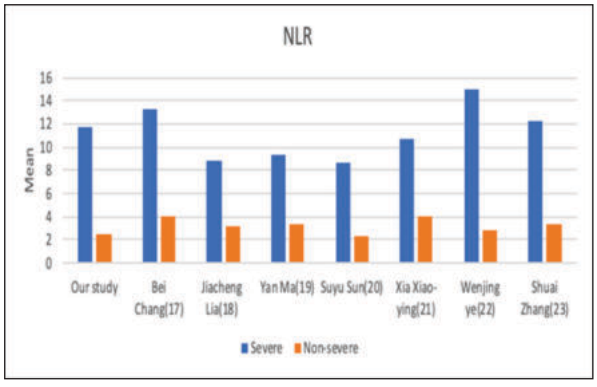
Parameter	Severe	Non severe	P value
Age	57.66+14.54	37.09+15.41	<0.0001
WBC	11.055+5.86	6.21+2.37	<0.0001
NLR	11.72+8.57	2.57+1.53	<0.0001
d-NLR	7.59+5.71	1.95+1.06	<0.0001
LMR	4.22+3.75	6.80+3.19	<0.0001
PLR	263.33+179.47	128.46+73.70	<0.0001

In our study the applicable thresholds for NLR, d-NLR, LMR and PLR were observed using the ROC curve.

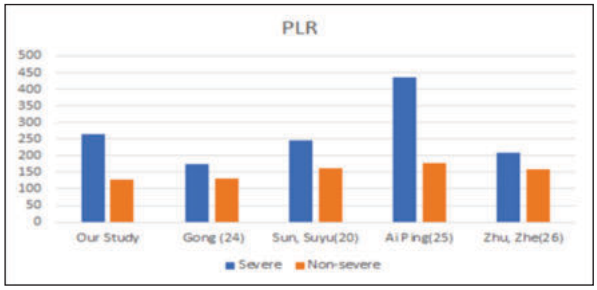
	NLR	d-NLR	LMR	PLR	AGE	WBC
AUC	0.8835	0.8808	0.7663	0.7237	0.8289	0.7793
Std. Error	0.0343	0.0328	0.4496	0.05135	0.3455	0.0442 7
95% CI	0.8162 to 0.9508	0.8164 to 0.9452	0.6782 to 0.8544	0.6231 to 0.8243	0.7612 to 0.8966	0.6925 to 0.8661
P value	<0.000 1	<0.0001	<0.0001	<0.0001	<0.000 1	<0.000 1
Cut Off	>3.55	>2.65	<4.65	>157.3	>47.50	>6.825
Sensitivity	80%	80%	72%	68%	72%	72%
Specificity	82%	80%	75%	74%	73%	72%

DISCUSSION

The mean value of NLR in the non-severe group was 2.57±1.53 cells/ul whereas the severe group had NLR of 11.72±8.57 cells/ul which was significantly different with a p-value of <0.0001. This was consistent with the more severe inflammatory response in severe category patients as human immune response triggered by viral infection mainly relies on lymphocytes (14) and systemic inflammation significantly depresses cellular immunity, which in turn significantly decreases CD4+ T lymphocytes and increases CD8+ suppressor T lymphocytes (15). Thus, infection with SARS-COV-19 causes lymphopenia which results in neutrophilia and raised NLR. NLR is a very useful indicator of acute inflammation and is also applicable in tumour-related diseases, autoimmune diseases, bacterial infectious pneumonia, and tuberculosis (16). The mean value of NLR in our study was very similar to other studies as indicated in the graph below.



The similar results were found with PLR as the mean value was 128.46+73.70 cells/ul in non-severe group and 263.33+179.47 cells/ul which was significant with p-value of <0.0001. Following infection with SARS-COV-19 causes lymphopenia, which in turn results in raised PLR. The mean value of NLR in our study was very similar to other studies as indicated in the graph below.



CONCLUSION:

We concluded that age, NLR, d-NLR, LMR and PLR vary significantly among severe vs non-severe patients so they may be used to assess the severity of the cases and predict prognosis at admission. These variables are easy to assess and may help in triage and better management.

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LIMITATIONS: The data were obtained from a single clinical research centre and not from multiple clinical research centres.

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