

Original Article

The Role of Haematological and Biochemical Parameters for Diagnosis and Management of COVID-19 Patients

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Introduction : COVID-19 Pandemic has affected the Healthcare System adversely. It should be diagnosed early to prevent mortality and morbidity. Thus various Haematological and Biochemical markers can be used specially in developing countries where clinicians have limited access to Molecular Diagnostic Technique.

Aim and objectives : The study aims to observe the role of haematological and biochemical parameters in diagnosing as well as predicting the prognosis along the course of the disease.

Material and methods : Retrospective study performed in Department of Pathology from April, 2021 to May, 2021 on 200 COVID-19 positive patients. The tests were conducted using the Haematological and Biochemistry Auto analysers.

Results : Out of 200 Reverse Transcription Polymerase Chain Reaction (RT-PCR) positive COVID-19 patients analysis of Haematological Parameters showed Leucocytosis, Neutrophilia, Lymphopenia and Eosinopenia. Neutrophil Lymphocyte Ratio, Platelet Lymphocyte Ratio and Systemic Inflammatory Index were also found to be elevated in comparison to the control cases. Statistically significant difference was observed in Total Leucocyte Count, Absolute Neutrophil Count, Absolute Lymphocyte Count, Kidney Function Tests (KFT) and Liver Function Tests (LFT) between severe and non severe cases. Biochemical parameters were found to be more elevated in severe cases. C-Reactive Protein (CRP) levels >50 mg/dl and Lactate Dehydrogenase (LDH) levels >1000U/L were found only in severe cases.

Conclusion : Haematological and Biochemical Markers being easily available and reliable can be utilised as useful prognosticator for early prediction of disease. Elevated Neutrophil Lymphocyte Ratio, Platelet Lymphocyte Ratio and Systemic Inflammatory Index can be useful in diagnosing COVID-19 especially when clinical suspicion is present despite negative Polymerase Chain Reaction (PCR) reports.

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Key words : COVID 19, Haematological parameters, Biochemical parameters.

The World is facing a Public Health crisis with the emergence and spread of a new Type of Coronavirus (Severe Acute Respiratory Syndrome Coronavirus 2; SARS-CoV-2)¹. Coronavirus Disease was first reported in Wuhan City, Hubei, China, in December, 2019. It was termed as Coronavirus Disease 2019 (COVID-19) by the World Health Organization (WHO) in February, 2020². The disease spread Globally and hence was declared as a Pandemic on 11th March, 2020³.

SARS-CoV-2 belongs to the Coronavirus family being part of genus β coronavirus, which has Genetic Homology similar to Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome-related Coronavirus (MERS-CoV)⁴. SARS-CoV-2 is enveloped, Ribonucleic Acid (RNA) virus which

Editor's Comment :

- Leucocytosis and Neutrophilia in Covid 19 patients indicate severe disease and patient needs hospitalisation.
- High CRP (>50 mg/dl) and/or high LDH (>1000U/L) in COVID-19 patients show that there is Severe Lung Damage and patient needs ICU care.
- Elevated Neutrophil Lymphocyte ratio (>3), Platelet lymphocyte ratio (>130) and Systemic Inflammatory Index (>7.0) are useful in diagnosis of COVID-19 in clinical suspicion even when RTPCR test for COVID-19 is negative.

Calculation of NLR, PLR, SII:

- ◆ Neutrophil Lymphocyte ratio is calculated by Absolute Neutrophil Count/absolute Lymphocyte Count,
- ◆ Platelet Lymphocyte Ratio is calculated by Platelet count in lakhs/cmm $\times 100$ / Absolute Lymphocyte Count,
- ◆ Systemic Inflammatory Index is calculated by multiplying Neutrophil Lymphocyte Ratio and Platelet Count in lakhs/cmm

has led to the COVID-19 Pandemic. The main routes of transmission of the virus are through Respiratory Droplets and Contact Transmission. The virus enters the body through Pulmonary Epithelial Cells via ACE2 receptors, leading to Pneumonia, followed by Systemic Inflammatory phase which can advance to respiratory failure or even Multi-organ Dysfunction⁵. The patient

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can be asymptomatic or can have symptoms like Fever, Cough, Headache, Body Ache, Increased Sputum Production, Dyspnoea, Haemoptysis, Diarrhoea, Acute Respiratory Distress Syndrome, Cardiac Failure or any Secondary infection⁶.

COVID-19 Pandemic has affected the Health Care System Adversely with an increase in severe cases which require intensive care, leading to a huge economic burden on our inadequate Healthcare facilities⁷. To control the pandemic, diagnostic tools help in detecting cases early and accurately. Various molecular techniques have been developed but in developing Countries the Healthcare Professionals have limited access. The most commonly used Molecular Technique is the Real-time Reverse Transcriptase-PCR but it has the limitations like long turnaround time, limited availability, expensive equipment, need for trained staff and chances of false-negative results⁸. Thus, tests for early diagnosis should be developed to rapidly detect the cases and identify severity of diseases to reduce mortality and prevent the spread of this pandemic⁹.

This study aims to observe the role of various Haematological and Biochemical Biomarkers in COVID-19 patients and also assess the role of these markers in the severity of the disease. This will help the Clinicians to Group the Patients and predict the prognosis and mortality, thereby help in better management of the patients.

MATERIALS AND METHODS

The retrospective study comprises of 200 patients hospitalised due to COVID-19 from April, 2021 to May, 2021 at Acharyashree Bhikshu Government Hospital (Government of NCT of Delhi) Delhi. These patients were tested positive by RT-PCR test or Rapid Test as per ICMR Criteria. The data of the patient including Age, Sex, Clinical Condition as well as any associated comorbidity was collected from the Medical Records Department. The Haematological and Biochemical Parameters were assessed during the time of admission. Clinical features were used as a tool to classify the patients into severe and Non-severe categories. Whole Blood Ethylenediamine Tetraacetic Acid (EDTA) samples sent at the time of admission were run on Automated Haematological Analyser SYSMEX XN-1000. Biochemical Parameters were assessed using Biochemistry

Auto Analyser Erba Mannheim XL 640. Statistical significance was calculated based on 't' test using Microsoft excel.

RESULTS

Demographic Data :

A total of 200 COVID-19 positive cases were included in the study. The mean age of the patients

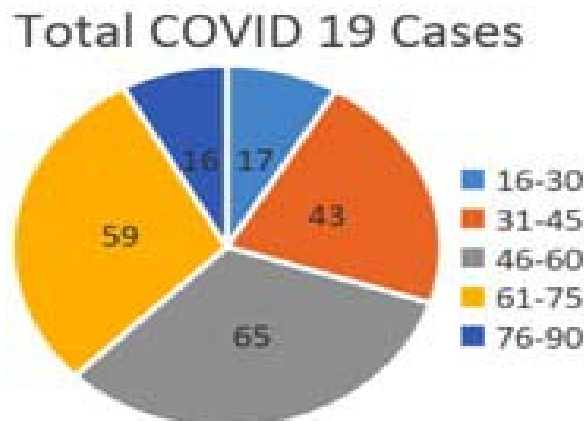


Fig 1 — Age Range of COVID-19 patients (in years)

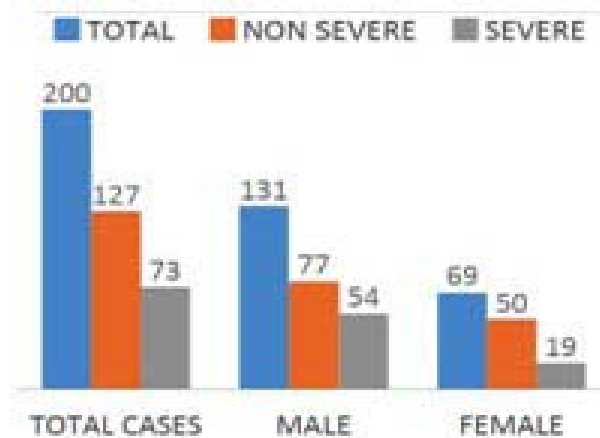


Fig 2 — Gender Profile of COVID-19 patients

Table 1 — Laboratory Parameters of Patient with COVID-19 (N = 200)

Laboratory Data	Normal Range	Mean ± SD	Median (IQR)
Total Leucocyte Count (X 10 ⁹ /L)	4.0-11.0	12.26±5.46	12.13 (8.22-15.80)
Absolute Neutrophil Count (X 10 ⁹ /L)	2.0-8.0	10.75±5.07	10.35 (6.96-14.06)
Absolute Lymphocyte Count (X 10 ⁹ /L)	1.0-5.0	0.92±0.59	0.79 (0.53-1.18)
Platelet count (X 10 ⁹ /L)	150-450	150±54	151 (119-177)
LDH (U/L)	250-400	1300.95±637.82	1063.5 (868.75-1597)
CRP (mg/L)	0-5	117.33±98.01	96.6 (32.65-170)
Urea (mg/dl)	5-20	51.35±36.12	45.5 (29-62)
Creatinine (mg/dl)	0.7-1.2	0.96±0.87	0.8 (0.6-1.1)
Bilirubin (mg/dl)	<1.2	0.64±0.46	0.5 (0.40-0.80)
SGOT (U/L)	8-40	66.5±52.86	49 (35-75.25)
SGPT (U/L)	5-35	59.79±55.14	45 (28-71)

were 54.45±15.51 years with 32.5% of the patients belonging to the age range 46-60 years (Fig 1). The severity of the disease increases as age increases. Of all the cases, 131 (65.5%) were male and 69 (34.5%) were female (Fig 2).

Analysis of Haematological profile in these patients showed Leucocytosis, Neutrophilia, Lymphopenia, Eosinopenia and normal to reduced Platelet Count. Comparative analysis of Severe to Non-severe group showed statistically significant difference in White Cell Count (<0.00001) and Absolute Neutrophil Count (ANC) (<0.00001). 71.2% of all the severe cases showed Thrombocytopenia while most of the patients of the Non-severe group had Platelet Count in the normal range.

The reference range for novel Hematological parameters were determined using the control subjects, Neutrophil Lymphocyte Ratio (NLR) (Reference range: 1.75-2.93), PLR (Reference range: 90-130) and Systemic Inflammatory Index (SII) (Reference range: 3.6-6.6). It was observed that these parameters were significantly higher in COVID-19 cases and also Statistically Significant difference was observed between Severe and Non-severe group (p value< 0.0001) (Figs 3-5).

Biochemical Parameters like Kidney Function Tests (KFT) and Liver Function tests (LFT) were found to be abnormal in most of the COVID 19 cases especially as the severity of the disease increases. C Reactive Protein (CRP) was found to be raised in all the cases and it was noted that patient with CRP> 50mg/dl had severe disease (Fig 6). At the time of admission, LDH levels correlated with the condition of the patient which could help Clinicians to stratify the cases based on severity of the disease. It was noted that 90% of the severe cases had LDH levels >1000U/L (Fig 7). Thus, LDH and CRP can be used as early parameters for ICU admission.

Correlation analysis showed a significant direct relation between LDH and WBC count (r = 0.4328, p < 0.0001), Neutrophil Count (r = 0.46, p < 0.0001), CRP (r = 0.59, p < 0.0001), NLR (r=0.34, p<0.001) and Age (r=0.27, p <0.001). CRP values correlated with WBC count (r = 0.37, p<0.0001), Neutrophils Count (r = 0.41, p < 0.0001) and showed a slight inverse correlation with Lymphocyte Count (r = -0.19, p < 0.05)(Tables 1-3).

Table 2 — Comparison of Laboratory parameters among severe and non severe COVID-19 patients

	Cut Off	Total (%)	Severe (%)	Non-severe(%)
Leucocytosis	>11 X10 ⁹ /L	57.5	76.7	46.4
Neutrophilia	>8 X10 ⁹ /L	70	84.9	61.42
Thrombocytopenia	<150 X10 ⁹ /L	49.5	71.2	37
High NLR	>3	94.5	100	91.33
Very High NLR	>15	46	82.2	25.19
PLR	>130	76.5	86.31	71.87
Very High PLR	>200	44	58.9	33.85
SII	>7	85	98.7	77.2
Very High SII	>20	50.5	76.7	35.4
Very High CRP	>50 MG/DL	69.5	100	51.9
Very High LDH	>1000 IU/L	60.5	90	43.3
Urea	>45 Mg/Dl	50	64.38	41.73
Creatinine	>1.4 MG/DL	9.8	13.69	7.08
SGOT	>35IU/L	73	91.78	62.2
SGPT	>35IU/L	63	75.34	55.9

Table 3 — Statistical significance of haematological and biochemical parameters

Parameters	Mean Value in Severe Covid Cases	Mean Value in Non Severe Covid Cases	t' stat	p-Value	Statistical Significance
Total Leucocyte Count	15507.12	10396.97	6.387025	<.00001	Significant
Absolute Neutrophil Count	13.76863	8.948976	6.50959	<.00001	Significant
NLR	26.49364	11.76006	6.127058	<.00001	Significant
PLR	272.4009	194.3462	2.438808	<0.01	Significant
SII	31.43937	17.70679	5.236452	<.00001	Significant
CRP	214.7027	56.82441	14.82839	<.00001	Significant
LDH	1876.315	970.2835	10.78435	<.00001	Significant
Urea	64.80822	43.52126	3.62125	<.00001	Significant
Creatinine	1.219178	0.815748	2.594602	0.011	Significant
SGOT	105.411	44	7.461603	<.00001	Significant
SGPT	84.84932	44.7874	4.184927	<.00001	Significant

DISCUSSION

SARS-CoV-2 has spread Globally with most of the patients having mild to moderate disease while few suffering from life threatening severe disease¹⁰. The

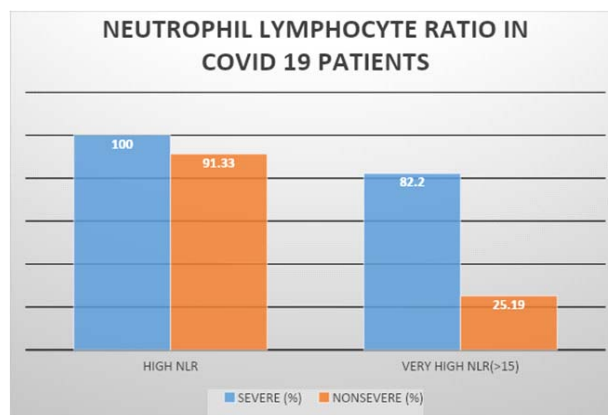


Fig 3 — Neutrophil Lymphocyte Ratio among severe and non severe COVID-19 patients

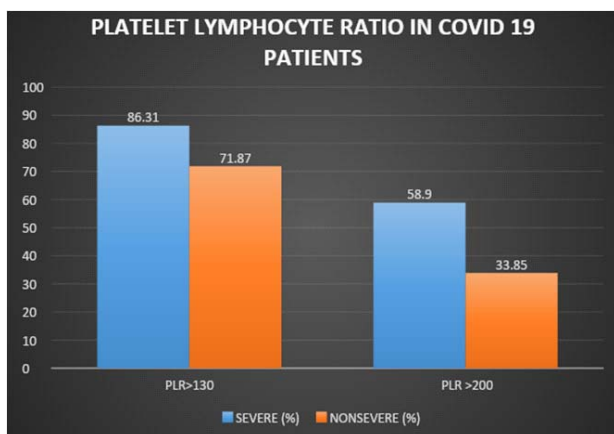


Fig 4 — Platelet Lymphocyte Ratio among severe and non severe COVID-19 patients

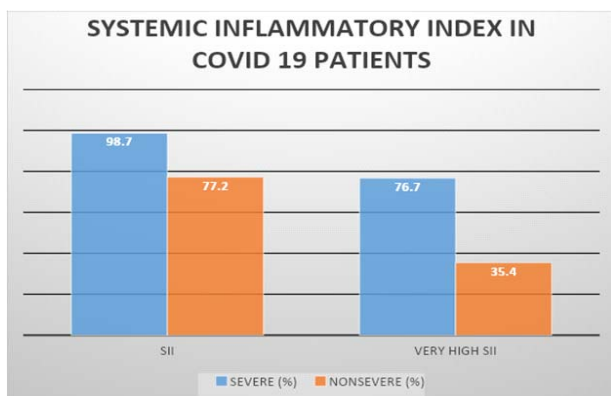


Fig 5 — Systemic Inflammatory Index (SII) among severe and non severe COVID-19 patients

present study will help to analyse the accuracy of Haematological, Inflammatory and Biochemical Parameters for diagnosing the patients with COVID-19 and thus help during the unavailability of PCR test or false negative PCR test. Thus, we summarised a comparative analysis of laboratory parameters among cases having non-severe disease and cases needing immediate hospital admissions which will be useful in the clinical settings to support clinical management which will lead to improvement in the Survival Rate.

The study showed that the most common age range for patients suffering from COVID is between 46-60 years. It also observed that as age increases severity of the disease increases which is in accordance with the studies done by Shen *et al*¹¹ and Qin *et al*¹². This can be explained with the fact that as age increases it leads to Biological Ageing, Impaired Immune Function and decreased Lung capacity¹³. We also observed that majority of our patients were male and severity of the disease was also seen more in male cases. Similar observations were done by Li *et al*¹⁴ and Guan *et al*¹⁵.

Thus, it can be considered that COVID-19 is more frequently seen in males and in middle-aged patients.

In the study, TLC and Neutrophil Counts were increased while Lymphocyte Count was reduced. This was seen more frequently in severe cases which is also supported by studies done by Singh *et al*¹⁶ and Sheng *et al*¹¹. In COVID-19, Cytotoxic Lymphocytes which help in control of viral infection get exhausted this correlates with progression of disease. After one to two weeks, there is ‘Cytokine Storm’ and Lymphopenia becomes prominent due to Atrophic Lymphoid Organs. Thus, Lymphopenia is considered to be the most important prognostic markers in COVID-19 cases¹⁷. NLR, PLR and SII were found to be significantly increased in COVID-19 patients as compared to the control cases in the present study. Our findings show that Thrombocytopenia is associated with severely diseased individuals similar to many previous studies Hypercoagulability state in COVID-19 disease is accompanied with microthrombi formation along with consumption of Platelet which leads to Thrombocytopenia¹⁸. Therefore, Thrombocytopenia could be used as a useful indicator

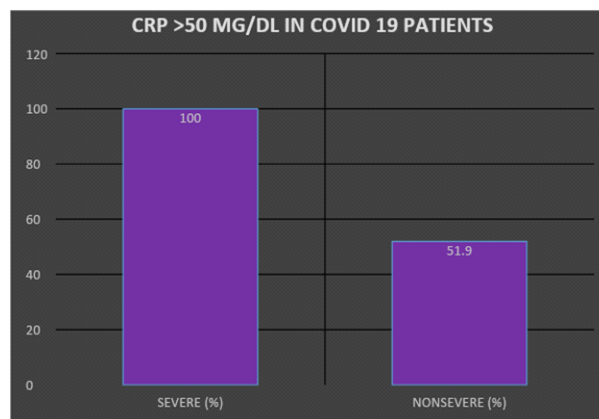


Fig 6 — CRP>50mg/dl among severe and non severe COVID-19 patients

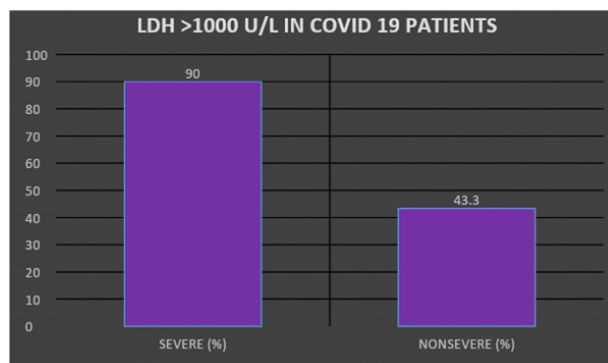


Fig 7 — LDH>1000 U/L among severe and non severe COVID-19 patients

for disease stratification.

Biochemical parameters help in assessing disease severity. LDH, an enzyme used in production of energy by converting Lactate to Pyruvate, is present in almost all body tissues being a General Indicator of Tissue damage and considered as marker of inflammation¹⁹. CRP is considered as a reliable marker of Acute Inflammation. LDH and CRP thus can be markers of Lung damage and reflect respiratory distress due to Abnormal Inflammation Status. Thus the levels of both these parameters is markedly increased as the severity of disease increases which is seen in most of the previous studies¹⁵.

Thus, evaluation of laboratory parameters at the time of admission and along the course of the disease can assist Clinicians in working out an Effective Treatment Protocol and promptly providing Intensive Care to Severe Patients.

CONCLUSION

The study concluded that Leucocytosis, Neutrophilia, Lymphopenia and Eosinopenia along with elevated LDH, CRP, higher Liver enzymes and abnormal KFT is seen in patients with severe COVID-19 disease. Hematological, Biochemical and Inflammatory Markers, being easily available and reliable Markers, can be utilized as useful prognosticator for early prediction of disease. Thus, appropriate management can be planned for patients at an early stage. The Abnormal Hematological Parameters can serve as markers for diagnostic and prognostic importance in determining the course, outcome and severity of COVID-19 infection. Thus, mortality and morbidity can be lowered in Critical Patients and those having comorbidities. We suggest that, elevated NLR, PLR and SII can be useful in diagnosis of COVID-19 along with other relevant tests, especially when clinical suspicion is present despite negative RT-PCR Reports.

Limitations : Main limitation of this study is small sample size.

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Conflict of Interest : None.

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