Review Article

Contribution of Laboratory Findings in Assessing the Severity of Covid-19 Infection: In A Tertiary Care Hospital

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Abstract

Background: In December 2019 first case of Coronavirus disease (COVID-19) was reported in China and then has spread across the world. With the use of biomarkers categorising patients becomes easier and can help clinicians in identifying patients with higher risk of disease progression and initiating effective management in time and thereby reducing the mortality due to COVID-19. **Methods**: The Data was collected retrospectively from medical records of 126 hospitalized patients diagnosed with COVID-19 from a tertiary care hospital between August and September 2020. Laboratory parameters on admission in patients who required intensive care unit (ICU) support and those who did not require ICU support were compared. **Results:** The patients who required ICU care (n = 47) were older (median, 55 vs. 49 years), with more underlying comorbidities (42.5% vs. 17.7%). ICU patients had higher leucocytes, neutrophils, Neutrophil to Lymphocyte Ratio (NLR), urea, creatinine, lactate dehydrogenase (LDH), and D-dimer but lower lymphocyte count when compared with non-ICU patients ($p < 0.05$). **Conclusions:** Elevated D-dimer and NLR appear to be independent biomarkers for severe COVID-19 infection. These laboratory parameters may help the clinicians to determine the patients who have a higher risk of disease progression and thus initiate effective treatment in time.

Key Words: COVID-19, Laboratory parameters, D-dimer, NLR.

Introduction

COVID-19 pneumonia was first reported in Wuhan, China, in December, 2019, followed by an outbreak across other parts of China and then has spread to the whole world. On 11th March 2020 COVID-19 was declared as a pandemic by the World Health Organization (WHO)[1,2].

In India the first COVID-19 case was confirmed on 30th January and the first death due to COVID-19 infection occurred in Kalaburagi district of Karnataka on 11th March 2020[3,4].

Most patients only develop mild to moderate symptoms, but a small subset develops a critical illness. Sepsis, acute respiratory distress syndrome (ARDS), thromboembolic complications, disseminated intravascular coagulopathy (DIC) and multi-organ failure (MOF) are all life-threatening complications of this new disease[5,6]. Because of the difficulty to control the dissemination of COVID-19 and the severity of its complications, there is an urgent need to develop the most possible effective care. Stratification of risk seems essential to optimize the resource allocation during this pandemic[7].

With the use of biomarkers categorising patients into mild, moderate or severe becomes easier and can help clinicians in identifying patients with higher risk of disease progression and initiating effective management in time and thereby reducing the mortality due to COVID-19[8-10].

Many published studies concentrated on symptoms and epidemiology and mortality rates of the disease but the articles that discuss laboratory parameters specific for COVID 19 infections is limited[21]. In addition, the correlation between specific laboratory diagnosis and disease severity deserves attention[11-13]. This study was conducted to compare the levels of laboratory parameters between patients needing treatment in an intensive care unit (ICU) and those not needing ICU care and to predict the role of laboratory findings in assessing the severity of covid-19 infection.

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Materials and methods

This retrospective observational study includes all the COVID-19 patients admitted to ESIC Medical College and Hospital, Gulbarga from 18th August to 18th September 2020 after taking approval from the Institutional Ethics Committee (No. ESICMC/GLB/IEC/03/2021). The criteria of WHO interim guidance was used[19]. Clinical and laboratory data were extracted from inpatient department files from medical records department (MRD) and laboratory records.

All the laboratory parameters of the patients which were performed within 24hours of admission were noted, so as to assess the severity of the patients when they first presented to the hospital. Data on the following laboratory parameters was collected: complete blood count (CBC), Urea, Creatinine, Total protein, Albumin, Aspartate aminotransferase (AST), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), Total bilirubin, Direct bilirubin, C- Reactive Protein (CRP), D-dimer, Lactate Dehydrogenase (LDH), Serum Ferritin, Prothrombin time (PT)and International Normalized Ratio (INR). Patients needing treatment in an intensive care unit (ICU) (ICU group) and those not requiring ICU support (non-ICU group) were compared with respect to clinical data and routine blood test results.

Statistical Analysis

Epi info 7.0 software was used to perform the statistical analyses. Descriptive analysis was expressed as mean and Standard Deviations or as medians. Laboratory parameters were compared between the two groups by using the Student's t test and the Mann-Whitney U test. Chi square test or the Fisher's exact test was used for categorical variables. Binary logistic regression analysis was done to identify the independent prognostic factors for the disease severity. The odds ratio was calculated for significantly associated variables. A p value of < 0.05 was considered as statistically significant.

Results

126 patients were included in the study, the median age of patients was 50 years (min–max, 20–78), and 87 patients (69%) were males. Thirty-seven patients (29.36%) had comorbidities. Diabetes and Hypertension were the most common pre-existing conditions. Among

these patients, 79 (62.7%) were isolated in clinical wards and 47 (37.3%) required ICU admission. When compared with the non-ICU group (n = 79), patients who received ICU care (n = 47) were significantly older [median age 55 years (min–max, 29–78) vs 49 years (min–max, 20–75); p < 0.03]. In addition, patients in the ICU group had more number of underlying comorbidities [20 (42.5%) vs 17 (17.7%); p < 0.003].

All the routine parameters were recorded on admission day for all patients and then compared between groups. There were many significant differences. The ICU group had higher total leucocyte count, neutrophil count, Neutrophil to Lymphocyte ratio (NLR), Monocyte to Lymphocyte ratio (MLR), Platelet to Lymphocytes ratio (PLR), D-dimer, CRP, ferritin, LDH, urea, creatinine, PT, INR levels, as well as lower lymphocytes (p < 0.05) (Table 1).

Table 1: Baseline blood-routine parameters of patients with COVID-19

Parameters	Normal range	Non-ICU group (79)	ICU group (47)	P Value
Leucocytes (x 10^9 per L)	4.0-11.0	6.09(2.7-8.8)	8.1(5.9-24.2)	**0.001**
Neutrophils (x 10^9 per L)	2.0-7.0	4.04 (1.7-16.28)	6.96(2.43-21.84)	**0.0002**
Lymphocytes (x 10^9 per L)	1.0-3.0	1.57(0.26-3.78)	1.07(0.18-3.72)	**0.008**
Monocytes (x 10^9 per L)	0.1-0.9	0.16(0.1-0.37)	0.15(0.1-0.47)	0.697
Eosinophil (x 10^9 per L)	0.02-0.55	0.18(0.03-0.78)	0.21(0.04-0.72)	0.303
Platelet (x 10^9 per L)	150-400	243(50-490)	252(60-494)	0.85
NLR		2.47(0.71-18.5)	5.72(1.07-32)	**0.0002**
MLR		0.05(0.01-0.08)	0.09(0.01-0.5)	**0.0002**
PLR		158.3(65.6-585.7)	232.4(68.2-1744.4)	**0.002**
C -reactive protein (mg/L)	<6	9.7(0.4-188)	32(0.5-221)	**0.004**
D-dimer (µg/ml)	<0.5	0.37 (0.1-4.7)	0.6(0.1-10)	**0.0001**
Ferritin (mg/ml)	20-220	219 (20-442)	338 (48-1000)	**0.043**
LDH (mg/dl)	<130	386(110-2581)	544(70-1916)	**0.0001**
Urea (mg/dl)	<50	29(11-77)	29(20-82)	**0.010**
Creatinine (mg/dl)	0.5-1.2	0.9 (0.6-1)	1(0.7-3.2)	**0.016**
Aspartate amino transferase (U/L)	10-50	35(13-75)	35(18-163)	0.820
Alanine amino transferase (U/L)	<40	30(17-73)	28(16-175)	0.08
Alkaline Phosphatase (U/L)	40-130	132.5(96-322)	129(99-365)	0.22
Total bilirubin (mg/dl)	<1.2	0.8(0.3-2.6)	0.7(0.3-2)	0.933
Direct bilirubin (mg/dl)	<0.2	0.2(0.1-0.8)	0.2(0.1-1.3)	0.6
Total protein (mg/dl)	6.6-8.7	6.8(5.4-7.5)	6.8(5.1-8.4)	0.56
Albumin (mg/dl)	3.5-5.2	3.9(3-5)	3.7(2.3-5.1)	0.188
Sodium (mEq/L)	136-145	141(128-151)	137.5(129-148)	**0.034**
Potassium (mEq/L)	3.5-5.1	4.1(2.9-5.8)	4.25(2.6-6.4)	0.77
Chloride (mEq/L)	97-114	102(84-115)	101(87-111)	0.24
Prothrombin time (sec)	10-14	15.65(11.3-18.6)	17.4(12.37-43.9)	**0.04**
INR	0.8-1.2	1.19(0.83-1.9)	1.35(0.9-3.25)	**0.01**

Data are median (minimum value – maximum value). P values comparing ICU patients and non-ICU patients. ICU = intensive care unit. P values indicate differences between ICU and non-ICU patients. P <0.05 was considered statistically significant. NLR= Neutrophil Lymphocyte Ratio, MLR=Monocyte Lymphocyte Ratio, PLR= Platelet Lymphocyte Ratio.

Discussion

A total of 126 patients were included in the study, of which 37.3% were admitted in ICU. Similar to Bastug et al, the patients in the ICU group were older and showed more comorbidities compared with those in the non-ICU group. In addition, gender was not found to be a determinative factor for critical illness.

SARS-CoV-2 causes some changes in routine blood parameters. As for admission laboratory parameters, increased total leucocytes, neutrophils, NLR, ferritin, D-dimer, creatinine, LDH levels and decreased lymphocyte count are distinguishing features of those requiring ICU admission. Increased levels of leucocytes was prominent in critically ill patients in the present study, and consistent with Bastug et al, Qin et al and Wang et al, who reported higher total leucocyte count in patients with severe COVID-19[20-22]. Regarding the platelet count, there was no significant difference between the ICU and Non- ICU group, which was in line with Wang et al[24]. But Liu et al and Yang et al reported lower platelet count in their study[25,26].

Decreased lymphocyte count along with an elevated Neutrophil to Lymphocyte Ratio has been reported as predictors for severe prognosis[27-30]. Although lymphocytes are expected to increase in viral infections, but in COVID-19 infection lymphocytes are depleted possibly because lymphocytes express angiotensin converting enzyme 2 (ACE 2) receptor, which virus uses to enter the host[23,31]. Lymphopenia was seen in our study, similar to other studies[20-22,29].

SARS CoV-2 induced cytokine storm results in neutrophilia. These activated neutrophils have a damaging effect on host[32]. In the meta-analysis by Zeng et al, increased neutrophil count were associated with severity of COVID-19, similar to Qin et al our findings also reveals that neutophilia can be a predictor of severe cases[23,21].

The virus triggered exaggarated inflammation increase the NLR, which promotes disease progression[30]. Various studies have shown the importance of NLR as a predictor for disease severity[23, 30, 33]. Our study also suggests that NLR, MLR and PLR may be used as predictive marker for identifying patients needing ICU care.

Viral infection induces a systemic inflammatory response and produces an imbalance between procoagulant and anticoagulant mechanisms leading to thrombotic complications[34]. A markedly elevated D-dimer was associated with poor prognosis in COVID-19 patients and it is consistent with our findings[20,24,35]. Binary logistic regression analysis for D-dimer showed (p = 0.002, OR:1.451; 95% CI: 1.094-1.924) and NLR was also found to be an independent prognostic factor for severe COVID-19 infection (p = 0.007).

In SARS-CoV2 infection there is an excessive inflammatory response and cytokine storm which not only cause damage to lungs but also to other organs like liver and kidney[36,37]. In the present study, although liver enzymes were elevated in most of the patients but there was no significant difference between the two groups.

Kidney is also affected in COVID-19 infection as ACE2 receptors of the virus are also expressed on renal tubule cells[38]. The creatinine

levels were significantly increased in the ICU group. In study done by Frontera et al Hyponatremia was associated with increased chances of ICU admission, longer duration of hospital stay and increased mortality rates and even in our study hyponatremia was seen in ICU group[39,40].

When compared with non-ICU admitted patients, the ICU admitted patients had various abnormal laboratory parameters as discussed above with few literature findings.

Conclusion

To conclude, our findings suggest that the elevated D-dimer and NLR appear to be independent biomarkers for severe COVID-19 infection. These laboratory parameters may help the clinicians to determine the patients who have a higher risk of disease progression and thus initiate effective treatment in time.

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Competing interests

None

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