Evaluation of Hematological and Biochemistry parameters in COVID-19 Disease

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Abstract

The coronavirus disease (COVID-19) pandemic has resulted in a massive health crisis across the world. This rapid viral spread has created the need to detect significant predictors that will provide assistance to stratify the risk and help in better clinical management. This study aimed to analyze the hematological and biochemical parameters in 200 patients diagnosed to have COVID-19 admitted in MGM Hospital, C. B. D. Belapur.

The median age was 52.6 years and 65.5% were male. Out of the 200 patients, 128 had mild to moderate disease whereas 72 had severe form of the disease and were admitted in the ICU. Advanced age and existence of comorbidities in these patients were noted as risk factors for progression to severe disease.

The presence of deviations in hematological and biochemical parameters that were strongly associated with progression to severe disease are white blood cell count (WBC), Neutrophil: Lymphocyte ratio (NLR), Interleukin - 6, C-reactive protein (CRP), D-dimers, lactate dehydrogenase (LDH) and serum ferritin during both admission and hospitalization.

On the basis of the above findings, we observed that close monitoring of these parameters will help to identify affected individuals in the initial phase and discontinue disease progression to an advanced stage

Introduction

Coronavirus disease (COVID-19) is a highly infectious disease caused by novel coronavirus which requires isolation of the infected patients. Coronavirus is an enveloped virus comprising a positive-sense single-stranded RNA genome. The virus has remarkably large RNA genomes of approximately 30 kilobases along with a helical symmetry. [1] The name of the virus originates from the Greek word (κορώνα, meaning crown) as the virus envelope appears to be crowned with viral spike proteins. It can be transmitted by droplets, aerosols, contact and feco-oral route of infection. More than 261.44 million cases of infection have been reported all around the world and approximately 5.21 million deaths have occurred as on December 1, 2021.[5]

A majority of those who acquire SARS-CoV-2 appear to experience mild to moderate respiratory illness or could even be asymptomatic and recover without requiring drug therapy. However, older people and patients with other comorbidities such as cardiovascular disease, diabetes, chronic respiratory disease and cancer are more prone to serious form of illness and can develop severe pneumonia, multi-organ failure (MOF), acute respiratory distress syndrome (ARDS), multi-organ failure (MOF) and death. [2, 11, 12] As a result of advanced age and higher incidence of other comorbidities such as hypertension and diabetes, patients having end-stage renal disease (ESRD) are extremely vulnerable to severe disease outcome. [22]

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COVID-19 infection is diagnosed by direct detection of SARS-CoV-2 nucleic acids in nasopharangeal and throat swab samples with the help of a polymerase chain reaction (PCR). [6]

The clinical symptoms are very similar to any other viral infection and as a result the diagnosis of COVID-19 depends on virus nucleic acid detection which is affected by virus levels in patients and also errors that could occur during the process of sample collection. Many false-negative results have also been witnessed.

Patients who test positive present with common symptoms such as fever, cough, myalgia, fatigue, expectoration and dyspnoea. Minor symptoms include headache or dizziness, diarrhoea, nausea and vomiting. [3]

With a daily rise in the number of patients acquiring the coronavirus disease and as the pandemic rages on, it is imperative to identify significant laboratory parameters that predict the clinical course of the disease towards severe forms.

Materials and Methods:

A prospective study was carried out on 200 patients admitted in MGM CBD Belapur Hospital, Navi Mumbai, India over a period of 6 months. Institutional Ethics committee approval was obtained. The patients who tested positive for COVID-19 through reverse transcriptase-polymerase chain reaction (RTPCR) of nasal and pharyngeal swabs by RT-PCR were included in the study. Patients who tested negative for COVID-19 were excluded from the study. In this study, for both Non-ICU and ICU patients, three blood samples were collected at an interval of 3 days from the time of admission to the time of discharge or demise for assessing the haematological and biochemical parameters compared for statistical analysis. Clinical details of the COVID positive cases were recorded.

Blood samples were collected in ethylenediamine tetraacetic acid and plain vacutainers from each patient after informed consent. Complete blood count was performed on a 3-part haematological analyzer, i.e., Sysmex XN 330. Blood biochemistry parameters were assessed using automated biochemistry analyzers, C-reactive protein (CRP) using celltac chemi, D-dimer on I Chroma 2, fine care, Serum Ferritin as well as Interleukin-6 using Fine Care and lactate dehydrogenase (LDH) was done on Ditron. Total bilirubin, SGOT (Serum glutamic-oxaloacetic transaminase), SGPT (Serum glutamic pyruvic transaminase) and serum creatinine were assessed on P500 Ditron and values were noted.

The Statistical analysis was completed by means of SPSS 21 software. The test of significance was established at the level of significance of 0.01 or 0.05. For correlating the mean and standard deviation (SD), an independent t-test was utilized.

Results:

Out of the 200 COVID-19 patients, 128 cases (64%) were admitted in the wards (Non-ICU group) and 72 cases (36%) in the ICU. The common clinical presentation in the patients from the non-ICU group presented with fever, sore throat, head ache, cough and generalized weakness. On the other hand, patients admitted in the ICU reported with more severe symptoms, such as, dyspnoea, respiratory distress, multiorgan failure and shock. A significant number of these patients also required mechanical ventilation. There was a significant difference in the age between the two groups (P<0.001). Out of the total 200 patients, 131 were male (65.5%) and 69 were female (34.5%).

Table 1: Haematological and biochemical parameters in COVID - 19 patients

Parameters	NON- ICU		ICU		P value	Test significance
	Mean	SD	Mean	SD		
Age (years)	34.16	11.21	56.8	18.86	< 0.001	Significant
Hb (g/ dL)	12.33	1.37	11.42	2.71	0.24	Not significant
WBC (/cumm)	7039.6	2561.48	14740.85	6022.79	< 0.001	Significant
Platelet (lakh/cumm)	3.04	1.34	2.12	1.80	0.61	Not significant
NLR	1.89	1.58	15.73	11.62	< 0.001	Significant
PLR	129.59	49.83	184.46	151.43	0.54	Not significant
Total bilirubin (mg/dL)	1.45	0.56	2.12	1.68	0.37	Not significant
SGOT (U/L)	23.9	6.27	32.31	14.92	0.36	Not significant
SGPT(U/L)	18.62	11.68	25.83	18.67	0.18	Not significant
Serum Creatinine (mg/dL)	0.91	0.48	1.73	1.42	0.57	Not significant
Interleukin – 6 (pg/mL)	7.43	4.59	65.74	47.75	< 0.001	Significant
CRP (mg/L)	24.31	9.53	171.7	114.39	< 0.001	Significant
D-dimer (µg/mL)	2.1	2.3	5.48	2.75	< 0.001	Significant
LDH (U/L)	182.35	67.2	438.13	118.74	< 0.001	Significant
Serum Ferritin (ng/mL)	168.61	59.34	334.41	301.27	< 0.001	Significant

In the present study, we observed that age was a significant factor in detecting COVID -19 disease progression to a severe form (p value < 0.001) and the median age was 52.6 years. 131 patients admitted, that is, 65.5% of the cases were male and 34.5 % (69 cases) were female.

The haemoglobin values did not show significant difference between the patients admitted in wards and the ICU, though few of the patients had lower haemoglobin values in the ICU.

The total leukocyte count and Neutrophil: Lymphocyte Ratio (NLR) showed marked significance with a p value of less than 0.001. There was no significant difference noted in the platelet count and the Platelet: Lymphocyte ratio with p value of 0.61 and 0.54 respectively, in the present study.

The study did not demonstrate significant difference in values of total bilirubin (p value = 0.37), SGOT (p value = 0.36) and SGPT (p value = 0.18) as can be seen in the table. No significant difference was noted

on comparing the serum creatinine values of the ICU and Non – ICU group.

Our study indicated extremely significant correlation in CRP, D-dimer, LDH, serum ferritin and interleukin-6 between the covid patients of ICU group and non- ICU group (p value < 0.001). Markedly raised values were reported in the critical patients.

Discussion

Biomarkers help in early detection of severe category of patients and framing the hospital admission criteria. Numerous laboratory parameters play a crucial role in reflecting disease progression and predicting more severe complications such as disseminated intravascular coagulation (DIC), acute respiratory distress syndrome (ARDS), and multiple organ failure (MOF). [21] It has been noticed since the onset of the coronavirus disease outbreak that patients with severe disease had a significantly

increased white blood cell (WBC) count with lymphopenia compared to patients who presented with mild symptoms. [4] A high number of the lymphopenic patients also had few reactive lymphocytes, of which a subset appeared lymphoplasmacytoid. Critical ICU patients tend to develop neutrophilia during hospitalization. As the patients begin to recover the values of WBC and NLR ratio improve over time. [5]

Biomarkers of inflammation, cardiac and muscle injury, liver and kidney were also seen to be raised in those patients who were progressing towards critical illness. Elevated levels of Interleukins 6 (IL-6) and serum ferritin were also documented in patients who presented with severe symptoms. [4] There is a risk of injury to the hepatic tissue during cytokine storm or as a result of various drugs given during therapy. [23] Therefore, levels of ALT, AST and bilirubin should be determined while treating the patients with any of the hepatotoxic drugs.

During the early phase of the disease the white blood cell counts are usually normal. With evolving infection, the virus begins to affect the tissues with high levels of Angiotensin Converting Enzyme (ACE2), i.e. the lungs, heart and gastrointestinal tract.

Approximately 7 to 14 days after onset of infection, there is a surge in the clinical symptoms with a marked systemic elevation of inflammatory mediators and cytokines, which may even be characterized as a "cytokine storm". [7, 15] It is only at this time that the peripheral blood smear shows significant lymphopenia. The cytokine storm evolves through various pathways, like the NF- κB, JAK/STAT and the macrophage activation pathway, causing release of interleukin-6 (IL-6) and TNF-alpha. [8]

Elevation in Interleukin-6 values correlated with disease severity, bilateral interstitial lung disease. [9, 10] Higher risk of Acute Respiratory Distress Syndrome, ICU support and death have also been associated with Increased levels of LDH. [16] Raised D-dimer levels (>1μg/mL) and DIC may be common in patients with a severe form of the disease. [17]

A study by Mardani et al. showed that patients with positive RT-PCR had significantly higher neutrophil count (p = 0.0001), lower white blood cell (WBC) count (p = 0.0001) and C-reactive protein (CRP) (p = 0.04), lactate dehydrogenase (LDH) (p = 0.0001), aspartate aminotransferase (AST) (p = 0.001) and alanine aminotransferase (ALT) (p = 0.0001) helpful in predicting course of disease in cases with positive for COVID-19.[18]

In a study conducted by Saha S K et al. in a tertiary care hospital at Dhaka, highly significant correlation was found between critical and non-critical groups in parameters such as haemoglobin, TLC, platelet count, Serum Creatinine and D-Dimer test which presented p values of <0.001. However, significant correlation was found with respect to NLR, CRP and LDH test results with p values calculated as <0.05. [13]

Fan et al. analysed the haematological indices of COVID-19 infected patients between the intensive care unit (ICU) and Non-ICU patients and concluded that lymphopenia and raised lactate dehydrogenase (LDH) were associated with higher rate of ICU admissions. Patients who were transferred to the ICU had a lower lymphocyte count and haemoglobin, and higher peak Neutrophil Count and peak LDH levels compared to patients who did not require critical care. [14]

In a retrospective study during the first two months of the epidemic in China, 260 out of 560 patients (46.4%) with laboratory confirmed COVID-19 infection had elevated D-dimer (≥0.5 mg/L), whereas the elevation was more pronounced among severe cases (59.6% versus 43.2% for non-severe ones). [19] D-dimer dynamics can reflect the severity and their increased levels are associated with adverse outcomes among patients with community-acquired pneumonia.

A case study of the 30 hospitalized patients with confirmed COVID-19 in Huizhou Municipal Central Hospital by Qu R, Ling Y, Zhang YH, et al. suggested that the patients with significantly elevated platelets during treatment had longer average hospitalization days. The higher PLR of patients during treatment had longer period of hospitalization. It is presumed that the number of platelets and their dynamic changes during cytokine storm and the treatment course may correlate with the severity and prognosis of the disease. [20]

Conclusion:

On evaluating the haematological and biochemical laboratory parameters, we found that the biomarkers are extremely significant in predicting severity of the clinical course in patients tested positive for COVID-19. SARS-CoV-2 disease has noticeable manifestations from the hematopoietic system varying with age and presence of co-morbidities. We observed that neutrophilic leucocytosis, lymphopenia, increased NLR, CRP, D-dimer, LDH, IL – 6 and serum ferritin are of paramount importance as biomarkers. The escalation in the levels of these parameters in critically-ill ICU patients is noteworthy as compared to the non-ICU group. Vigilant assessment of laboratory indices during the entire course of the disease can assist clinicians in formulating a tailored approach in management and promptly provide intensive care to those who are in urgent need. These biomarkers will also prove beneficial in assessing response to the treatment provided, predicting the disease outcome and to decide the criteria for hospital discharge.

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