ORIGINAL ARTICLE

Biochemical Markers in Patients with Mild and Severe COVID-19 Infection

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Abstract

Background: The 2019 novel coronavirus disease (COVID-19) is the greatest public health problem to date as number of COVID-19 patients are dramatically increasing worldwide. Clinical criteria are susceptible to subjective and objective factors, which may lead to an extended time for diagnosing and the possibility of misdiagnosing severe COVID-19. Therefore, it makes sense to find a potential biomarker that could effectively diagnose severe COVID-19. ***Objective:*** To study biochemical markers in mild and severe patients of covid-19 infection. ***Material and Methods:*** This observational study was conducted in the Department of Biochemistry, Seth G S Medical College and KEM Hospital, a tertiary care hospital of Mumbai. Our study included COVID-19 positive patients diagnosed for COVID-19 based on the results of RT-PCR conducted at our centre. Patients were categorized into 2 groups mild (n-50) and severe (n-50) on the basis of severity of clinical presentation, each between 18-80 yrs. of age. Biochemical parameters were compared between these two groups and various biochemical parameters were evaluated using independent-samples t-test. ***Results:*** The biochemical markers were compared in group-1 and group-2. Group-2 patients had significantly higher levels of serum LDH (p=0.0001), CRP (p=0.0001), BUN (p= 0.007), serum creatinine (p=0.0001), serum AST (p=0.02) and serum ALT (p=0.02). ***Conclusion:*** The biomarkers studied in the present research work, if considered together provide a brief overview on most frequent laboratory abnormalities encountered in patients with COVID-2019 infection which might be useful in indicating progression from mild to severe disease.

Key Words

COVID-19, Biochemical markers, LDH, BUN, Creatinine, ALT, AST, CRP

Introduction

The 2019 novel coronavirus disease (COVID-19) is the greatest public health problem to the date as number of COVID-19 patients are dramatically increasing worldwide. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the cause of coronavirus disease 2019 (Covid-19), emerged in China in late 2019 from a zoonotic source (1). Coronavirus (COVID-19) is an enveloped RNA virus that is diversely found in humans and wildlife. There are six species have been found to cause disease in humans and are known to infect the neurological, respiratory, enteric, and hepatic systems. SARS-CoV-2 is highly contagious and has resulted in a rapid pandemic of COVID-19 (2). Clinical spectrum of COVID-19 ranges from asymptomatic patients to septic shock and multiorgan dysfunction. The disease can be classified into mild, moderate and severe on the basis of severity of clinical presentation (3,4).

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Patients with mild illness may present with uncomplicated upper respiratory tract infection and may have mild symptoms such as fever, cough, sore throat, nasal congestion, malaise, headache without evidence of breathlessness or hypoxia (normal saturation). Around 80% cases are mild in severity. Patients with moderate illness presents with pneumonia and no signs of severe disease. Patients with severe disease present with severe pneumonia, acute respiratory distress syndrome (ARDS), sepsis, or septic shock and clinical presentations include the presence of severe dyspnea, tachypnea (respiratory rate > 30/minute), respiratory distress, SpO2 d" 90% (5). However, these clinical criteria are susceptible to subjective and objective factors, which may lead to an extended time for diagnosing and the possibility of misdiagnosing severe COVID-19. Therefore, it makes sense to find a potential biomarker that could effectively diagnose severe COVID-19. Furthermore, acute respiratory distress syndrome could lead to death in some severe COVID-19 patients, and this is often accompanied by heart failure, liver failure, and kidney failure (6,7).

In this study, we investigated 6 serum biochemical markers Aspartate transaminase (AST), Alanine Transaminase (ALT), Lactate dehydrogenase (LDH), C-reactive protein (CRP), Blood urea nitrogen (BUN) and creatinine. These Vital biochemical markers will give evidence for assessing disease severity. Therefore, the aim of this article is to provide a brief overview on the most frequent laboratory abnormalities encountered in patients with COVID-2019 infection. This might be useful in indicating progression from mild to severe disease and reducing mortality and shortening the hospitalization period.

Material and Methods

This observational study was conducted in the Department of Biochemistry, Seth G S Medical College and KEM Hospital, a tertiary care hospital of Mumbai. The posteriori (retrospective) strategy was used for data collection. The study used data of patients who were presented with symptoms of COVID-19 to our centre. Our study included COVID-19 positive patients diagnosed for COVID-19 based on the results of RT-PCR conducted at our centre. The exclusion and inclusion criteria were based on WHO guidelines. Patients were categorized into 2 groups mild (n 50) and severe (n 50) on the basis of severity of clinical presentation, each between 18-80 yrs. of age. Biochemical parameters were compared between these two groups using independent-samples t-test. The study was approved by the Ethics Committee of Seth G S Medical College & KEM Hospital, Mumbai.

We reviewed retrospectively the clinical, radiological and laboratory findings from patients admitted under medicine department. The clinical data summarized was conveniently collected between 1st April to 30th June 2020. Total 100 patient's data was used for analysis. Information about age, gender and values of biochemical parameters were noted and used for data analysis.

The values of biochemical parameters of COVID-19 patients were collected from Central Clinical Biochemistry Laboratory of Seth G S Medical College and KEM Hospital, Mumbai. Biochemical parameters included Sr. ALT, Sr. AST, BUN, Sr. Creatinine, CRP and LDH. The tests were conducted on fully automatic Clinical Biochemistry analyser- AU-680 (ERBA Diagnostics, Mannheim). All the tests were performed using ERBA diagnostic reagents.

Statistical analysis was performed by using Graph Pad Prism software. Quantitative variables were expressed as the mean and SD and were normally distributed. Group wise comparison of various biochemical parameters was done using indipendent-samples t-test. A p value of <0.05 was considered statistically significant.

Results

Total 100 COVID-19 positive patient's data was used for analysis. Study subjects were categorized into 2 groups, mild (n 50) and severe (n 50) on the basis of severity of clinical presentation as per WHO guidelines.

Table 1 presents the comparison of demographic

Table 1: Baseline Demographic Characteristics of Study Population

Characteristics	Group- 1 (Mild Cases) (n=50)	Group- 2 (Severe Cases) (n=50)	*p* value
Gender: Males N (%)	27 (54%)	23 (46%)	0.57 (NS)
Age (years) (Mean ± SD)	36 ± 10.2	55 ± 16.4	0.0001***

***p < 0.001; NS: Not Significant

Table 2: Comparison of Biochemical Markers in Study Population

Characteristics	Group- 1 Mild Cases (n=50) (Mean ± SD)	Group- 2 Severe Cases (n=50) (Mean ± SD)	*p* value
Serum LDH (IU/L)	923 ± 281	1427 ± 693.7	<0.0001***
Serum CRP (mg/dl)	94.3 ± 83.7	218 ± 153	<0.0001***
Blood Urea Nitrogen (BUN) (mg/dl)	32 ± 13.3	46.5 ± 35	<0.007**
Serum Creatinine (mg/dl)	5.7 ± 3.2	13.2 ± 4.9	<0.0001***
Serum AST (IU/L)	54 ± 26.2	73 ± 51.1	<0.02*
Serum ALT (IU/L)	41 ± 18.2	52.8 ± 30.6	<0.02*

*P < 0.05; **P < 0.01; ***P < 0.001

characteristic in both the groups. In mild cases, 54 % were male while in severe cases, 58% were male. Severe cases had significantly higher age compared to mild cases (p <0.0001). No significant difference was observed with regard to gender in both the groups.

Table 2 depicts the comparison of biochemical markers in group-1 and group-2. Group-2 patients had significantly higher levels of serum LDH (p=0.0001), CRP (P=0.0001), BUN (p=0.007), serum creatinine (p=0.0001), serum AST (p=0.02) and serum ALT (p=0.02).

Discussion

Even though clinical characteristics of COVID-19 have been broadly defined, an outline of the most representative laboratory abnormalities found in patients with COVID-2019 infection is still lacking. The clinical presentation-based criteria are susceptible to subjective and objective factors, which may lead to an extended time for diagnosing and the possibility of misdiagnosing severe COVID-19. Hence the present study is aimed to find potential biomarkers that could effectively assess disease severity.

In our study it was observed that the mean age (49.29 years) of group-2 was higher compared to group-1 which indicates that age is associated with severity of the disease. Mean serum LDH of group-2 was significantly higher compared to group-1. LDH is a major player in glucose metabolism which is present in tissues throughout the body and catalyzes pyruvate to lactate conversion. It is released from cells upon damage of their cytoplasmic membrane. Potential clinical and biological significance of elevated LDH are associated with pulmonary injury as well as widespread organ damage and severe course of the disease (8).

In the present study the mean CRP of group-2 was significantly higher compared to group-1. CRP levels are correlated with the level of inflammation, and its concentration level is not affected by factors such as age, sex, and physical condition. It is an important index for the early diagnosis and assessment of severe pulmonary infectious diseases. Viral infection is responsible for extensive immune reactions in the host; cytokine and chemokine production. Interleukins produced by activated leukocytes are responsible for B lymphocyte differentiation and acute phase proteins production elevated. Inflammatory organ injury may occur in severe Covid-19, hence levels of CRP correlate directly with disease severity and progression (9).

In the present study the mean BUN and serum creatinine of group-2 were significantly higher compared to group-1. SARS-CoV-2 can directly infect the renal tubular epithelium and podocytes through an ACE2-dependent pathway and cause mitochondrial dysfunction, acute tubular necrosis, the formation of protein reabsorption vacuoles, collapsing glomerulopathy, and protein leakage in Bowman's capsule. Another potential mechanism of acute kidney injury involves SARS-CoV-2-related immune response dysregulation, as indicated by observed lymphopenia and cytokine release syndrome (cytokine storm) (10). It suggests that the glomerulus could be one of the target organs for the coronavirus in severe patients and may be related to the high expression of ACE2 in glomerular cells (11).

In the present study the mean AST and ALT of group-2 were significantly higher compared to group-1. Liver damage in patients with corona virus infections might be directly caused by the viral infection of liver cells. Patients with severe COVID-19 appear to have more frequent signs of liver dysfunction than those with milder disease. Approximately 2-10% of patients with COVID-19 present

with diarrhea, and SARS-CoV-2 RNA has been detected in stool and blood samples. This evidence implicates the possibility of viral exposure in the liver. SARS-CoV-2 bind to the angiotensin-converting enzyme 2 (ACE2) receptor to enter the target cells, where the virus replicates and subsequently infects other cells in the upper respiratory tract and lung tissue. It is also likely that any immune mediated inflammation may lead to liver damage in critically ill COVID-19 patients (12).

Limitations - The relatively small number of participants in the survey may not fully reflect the overall situation. So, further studies are necessary to execute a large number of data surveys in multiple regions by multi-centre cooperation.

Conclusion

The biomarkers studied in the present research work, if considered together provide a brief overview on the most frequent laboratory abnormalities encountered in patients with COVID-2019 infection. This might be useful in indicating progression from mild to severe disease and ultimately it may helpful in reducing mortality and shorten in the hospitalization period.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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