

Association of biochemical indices and severity of COVID-19

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Abstract

Introduction: COVID-19 is caused by SARS-CoV-2, was identified in China in Wuhan city. Since then, the novel coronavirus started to be compared to influenza. The inflammatory biomarkers are associated with severity of COVID-19 patients. Hence the **aims** of the study was to evaluate the association between COVID-19 and inflammatory biomarkers such as IL-6, CRP, ferritin & LDH. **Materials and Methods:** For this retrospective study we have included 433 confirmed covid -19 patients admitted in Muzaffarnagar Medical College & Associated Hospital, Muzaffarnagar. After Covid-19 pandemic this hospital changed to covid hospital and all the investigation including biochemical biomarkers were done in the central biochemistry lab of Muzaffarnagar Medical College itself. **Results:** We analyzed the biochemical biomarkers on covid-19 patients admitted in non-ICU, ICU & patients who are on intubation. In our study we found a significant association between severity of covid-19 and the biochemical indices. **Conclusion:** In this study we found elevated serum levels of CRP, LDH, IL-6, and ferritin in covid-19 patients. The increases in these biomarkers were more in the patient who are on intubation.

Key Words: Covid-19, Biomarkers, IL-6, Ferritin, CRP

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Introduction

In 2019 December end, a novel corona virus, responsible for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in Wuhan, China[1]. Its rapid spread and progression and lack of specific therapeutic strategy resulted in an epidemic [2]. It is highly infectious and even asymptomatic patients may also become the carrier for this virus [3]. In February 2020, World Health Organization announced that the disease caused by SARS-CoV-2 was coronavirus disease 2019 (COVID-19). The COVID-19 patients have clinical manifestations, like pharyngalgia, fever, cough, fatigue, anorexia, headache, diarrhea, nausea or vomiting, dyspnea [4], even acute respiratory distress syndrome (ARDS) and the infected severe patients and had to be admitted to the intensive care unit. The Covid- 19 infected patients who have other chronic disease like Diabetes, Hypertension have higher mortality rate. Most of the Covid -19 patients were mild in the early days; some patients progressed rapidly to acute respiratory failure, metabolic acidosis, septic shock, ARDS or death. Early identification of risk factors for critical patients could facilitate appropriate supportive care and thus reduce the mortality [5]. A researcher in their study confirmed that COVID-19 have altered neutrophil count, lymphocyte count, and other biochemical biomarkers like CRP, D-dimer etc [6]. Increased inflammation-related indicators were found

in patients with COVID-19, including erythrocyte sedimentation rate (ESR), interleukin-6 and C-reactive protein (CRP) [7]. In addition to the incidence and transmission of covid-19, the clinical characteristics and fatality rate of the patients, especially severely ill patients, have been a concern. There are many studies which have been reported the clinical manifestations and blood biochemical markers of covid-19 patients [8-10]. However, the study on relationship between disease severities and clinical and biochemical features in patients with COVID-19 are limited. Hence the aim of our study was to evaluate the association between severity of disease and biochemical markers like CRP, IL-6 etc.

Materials and method

The present study was carried out in the Department of Biochemistry and associated Laboratory, Muzaffarnagar Medical College and Hospital Muzaffarnagar from August 2020 to December 2020. After corona epidemic, earlier the associated Hospital converted into Covid -19 Hospital for asymptomatic patients. Later on, level-2 and Level-3 patients of Muzaffarnagar region were admitted in this Hospital. The blood sample were drawn by the trained doctor and nurses under complete precaution and guideline given ICMR. Than sample were sent to the central biochemistry laboratory for further investigation. After taking proper protection including facemask, PPEkit, gloves, the sample were run and the readings were noted.

Inclusion Criteria: We included all the diagnosed symptomatic Covid -19 patients. The test for covid -19 (RT-PCR) were done at district hospital Muzaffarnagar, and then all the covid-19 positive patients were shifted to the Muzaffarnagar Medical College and Associated Hospital.

Parameters Measured:

Following parameters were measures on Covid-19 serum.

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Ferritin, quantitative CRP and IL-6 were measured by fully automatic chemistry analyzer (Access-2) and LDH were measured by AU 480 analyzer.

Statistical Analysis: Data analysis was performed by using SPSS version-20. Sample size and the need for reliable markers for disease severity, the continuous variables were transformed into categorical variables.

Results

In our study we have enrolled 433 confirmed covid-19 patients. All the patients were \geq 18 years of age. Out of 433 patients, 255 patients were male and 178 were female. In the studied subjects, the prevalence of HTN, diabetes, CKD, COPD and Cardiac Disease were

38%, 30%, 15%. 17% & 28% respectively (Table-1). Distribution of patients in non-ICU, ICU and Intubation on the basis of severity were depicted in table no-1.

In the present study the mean value of IL-6, Ferritin, CRP & LDH were found to be increased in covid patients and the increase in these parameters were more in the patients who are on intubation. (Table-2).

Table -3 represent the mean and SD of biochemical indices in non-ICU, ICU and intubation patients. Out of 433 subjects, 335 patients were from non-ICU ward, 58 patients from ICU ward and 40 patients were on intubation.

Table 1: Comorbidities in Covid patients.

Characteristic		No. Of Subject	Non-ICU Admitted Patients	ICU Admitted Patients	Intubation Patients
Sex	Male (59%)	255	200	30	25
	Female (41%)	178	135	28	15
Hypertension (38%)		165	110	35	20
Diabetes (30%)		130	97	18	15
Cardiac Disease (28%)		121	88	13	20
COPD (17%)		74	28	10	25
Chronic Kidney Disease(15%)		65	25	23	17

Table 2: Biochemical Indices of studied subjects (N=433)

Parameters	Mean \pm SD
IL-6 (<1.8 pg/ml)	11.74 \pm 4.10
Ferritin (10 to 250 ng/ml)	494.11 \pm 251.04
CRP (<5.0 mg/ml)	122.21 \pm 57.72
LDH (140-270 IU/L)	558.84 \pm 272.10

Table 3: Biomarkers in Non-ICU, ICU admitted and in Intubation Patients

Parameters	Non-ICU Admitted Patients(335)	ICU Admitted Patients(58)	Intubation Patients(40)
IL-6 (<1.8 pg/ml)	10.36 \pm 3.59	13.74 \pm 2.56	17.51 \pm 3.16
Ferritin (10-250 ng/ml)	410.79 \pm 171.52	630.09 \pm 200.21	994.83 \pm 207.98
CRP (<5.0 mg/ml)	105.31 \pm 43.00	155.12 \pm 46.22	216.05 \pm 69.70
LDH (140-270 IU/L)	451.21 \pm 162.51	811.03 \pm 166.55	1094.55 \pm 254.64

Discussion

Corona virus is rapidly spreading worldwide increasing the health care burden. The disease ranging from asymptomatic to severe condition with development of acute respiratory failure makes it important to collect data from patient to determine the patient condition and to predict complications timely.[11] There is a significant increase in Inflammatory cytokines and biomarkers such as IL-2, IL-6, IL-7, granulocyte-colony stimulating factor, macrophage inflammatory protein 1- α tumor necrosis factor- α (TNF- α), CRP, ferritin, PCT, and D-dimer is elevated in hyperinflammation phase of covid-19 and this may lead to the severe manifestation of cytokine storm. Excessive hyperinflammation may cause cardiopulmonary collapse and multi-organ failure.[12, 13]. Estimation of biochemical parameters and biomarkers are the quantitative measurements that represent the pathophysiology of disease and help clinicians in recognizing the severity of disease. In our study, we have enrolled 433 covid patients and found the increased levels of CRP & IL-6 in all the Covid-19 patients admitted in the Covid hospital. The increase in these parameters were more in Intubation patient as compared to non-ICU and ICU patients suggesting the severity of intubation patients and formation of lung lesions in the early stage of covid-19. Our results are in accordance with the previously published study. [14-16] C-reactive protein (CRP) is a non-specific acute phase protein induced by IL-6 in the liver. It is used as a biomarker for infectious, inflammatory and several other conditions like cardiovascular disease. Increased CRP levels are directly associated with the level of inflammation and

severity of disease. Therefore, CRP is an important biomarker in diagnosis and assessing the severity of infectious diseases.[17] For the prediction of covid-19 progression, CRP can be used as sensitive and effective biomarkers. Many researchers in their study found significantly elevated levels of CRP and D-Dimer in COVID-19 patients. Elevated D-dimer was related with markers of inflammation, especially with CRP.[18-19] In our study we observed the elevated level of LDH in all the covid-19 patients. The increase in LDH level was more in the patient who are on intubation. LDH catalyze the conversion of Pyruvate to lactate by a NADH dependant reaction and is present in all the tissues in body. Decreased oxygenation may result alteration in the LDH levels and leading to upregulation of glycolysis and from multi-organ injury. Lactate leads to injury via the action of metalloproteinases and enhanced macrophage-mediated angiogenesis.[20] A researcher studied on COVID-19 patients and concluded that LDH can be a good predictor of lung injury and severe COVID-19 cases.[21] Elevated LDH has also been associated with worse outcomes in several studies.[22-24] We also found elevated levels of ferritin in covid patients. Ferritin associated with acute respiratory distress syndrome (ARDS), mortality and severe condition of covid-19. This may be due to the presence of (secondary hemophagocytic lymphohistiocytosis) sHLH in covid-19 patients. [25] Hyperinflammation characterized by cytokine storm may lead to the development of a condition, sHLH causing fatal multi-organ failure. [26] Hyperinflammation is most commonly triggered by viral infections,[27] which might lead to a hypothesis of SARS-CoV-2 inducing this hyperinflammatory

syndrome. A recent systematic review by Veronese et al in their review reported that 542 patients conflicting evidence in 4 studies and concluded that the routine use of cortico-steroid therapy in covid-19 is not recommended. Some findings suggested corticosteroids may reduce the mortality rate in COVID-19 patients aggravated with ARDS.

Hence these biomarkers can be used in understanding the COVID-19 and also help to prevent virus-induced acute inflammatory response complications such as acute hypoxemic respiratory failure and multi-organ dysfunction in affected patients. Immune system and lung infection are the pathological changes were reported in covid-19 subject; hence these laboratory parameters will be helpful in differentiating severely ill patients.

Conclusion

An elevated serum CRP, LDH, IL-6, and ferritin can be used as laboratory biomarkers for a poor outcome in COVID-19. Serum CRP may not only be used as a prognostic marker, but also to monitor disease improvement in COVID-19. All these laboratory parameters will be helpful to clinician in differentiating severely ill patients. Further studies to create prognostic model, along with these markers other prognostic factors can be use.

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