

Analysis of Interleukin 6 and other Biochemical parameters in severity of Covid-19 patients: A retrospective observational study.

Sudama Rathore, Neha Rani Verma, Robby Kumar

Department of Biochemistry, Pt. JNM Medical College, Raipur, India.

Abstract

Background and aim: Biochemical parameters in Covid 19 have not been studied extensively. The main aim of this study was to establish a correlation between various biochemical markers with their role in the prognosis of Covid infected patients along with their diagnostic importance in severity and early detection of severity to overcome the mortality in intuitional patients.

Material and methods: This study was conducted at Pt.J.N.M. Medical College, Raipur and associated B.R.A.M. Hospital, Raipur a dedicated Covid hospital during the current epidemic. The samples available were divided into two groups namely mild and severe according to their hospital admission and duration.

Results: In our study it was found that Interleukin-6 and Ferritin was significantly ($p < 0.05$) raised in sever Covid patients when compared with mild and moderately affected patients. The other biochemical parameters were also influenced by Covid-19 as Covid affects various systems in human body.

Conclusion: By this study we want to establish the role of various markers for early detection of and prevention of severity in known cases of Covid-19. The investigation of effective laboratory biomarkers as a role in classifying the patients based on their risk is important for prognosis and treatment of disease.

Keywords: Covid, Interleukin-6, Ferritin, Biomarkers

Introduction

The corona virus disease 2019 (COVID-19) pandemic, declared by WHO, is a complex disease involving the whole body and affecting the biochemical parameters. The complexity of the severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is centred on the unpredictable clinical course of the disease that can rapidly develop, causing severe and deadly complications. The investigation of effective laboratory biomarkers as a role in classifying the patients based on their risk is important for prognosis and treatment of disease^[1].

Clinical Biochemistry provides a clear picture of, and contributes to manage most of the medical conditions including the novel corona virus disease 2019 (COVID-19). Although the relatively recent emergence does not allow to draw definitive conclusions as new studies and findings are kept on adding making diagnostics easier^[2].

SARS CoV2 is manifested from the clinical symptoms and pulmonary computed tomography (CT) findings, a large number of COVID-19 confirmed patients showed laboratory fluctuations including complete blood count (CBC) variables, cardiac and coagulation parameters, renal and liver function tests, electrolyte imbalance and inflammation-related factors^[2,3].

It has been found that combinations of some laboratory tests have been used to show the hyperinflammation state which contribute to cytokine storm which can be a factor along with Interleukin 6 and Ferritin for prognosis and outcome of disease^[4-6].

Among the CBC parameters of COVID-19 confirmed cases, decreased lymphocytes and normal or increased monocytes along with low albumin, high CRP, high LDH, lymphopenia and high ESR with increase in bilirubin, cytokines and leukocytes have been reported^[1,2].

Disturbed metabolic patterns have been found to be

Address for Correspondence:

Dr. Robby Kumar

Assistant professor, Department of Biochemistry
Pt. JNM Medical College, Raipur, India.

E-mail: kumarrobby1983@gmail.com

correlated with the progress of COVID from mild to severe cases which leads to all abnormalities in the disease^[7,8].

Materials and Method

This study was conducted in Department of Biochemistry, Pt. J.N.M. Medical College, Raipur and associated Dr. Bhim Rao Ambedkar Memorial Hospital a dedicated Covid center.

A total of 60 Samples were estimated for different biochemical parameters. All Covid 19 patients sample above 18 years of age were included in the study. Lipemic and Haemolysed samples were excluded from the study

The blood samples were brought to department in vacutainers, where it was centrifuged and processed

according to proper guidelines laid by departmental protocol committee for Covid-19 blood sample processing (based on WHO guidelines). Basic biochemistry parameters like Urea, Creatinine, Total Bilirubin, Direct Bilirubin, AST, ALT, Albumin and Total Protein were performed in fully automated biochemistry analyzer lab650. Parameters like Interleukin-6 and Ferritin were estimated in cobas e411. Results were analysed by student t test by SPSS software version 20. Ethical approval taken from institutional ethical committee (No/MC/Ethics/2021/29 Raipur, dated 15/02/2021).

Results

This study was retrospective observational study, so the data available in the laboratory was analysed and following results were obtained.

Table 1. Data showing inflammatory markers in Covid-19

S.no	Parameters	Mild (mean)	Severe (mean)	Normal Range
1.	INTERLEUKIN 6 (pg/ml)	518.94± 177.6	1409.74± 267.5	0-9
2.	Ferritin (ng/ml)	420 ± 65	646.36± 90.3	20-400

We have assayed Interleukin 6 and Ferritin in our lab and found following results (Table 1):- Interleukin 6 is significantly ($p < 0.05$) increased in severe samples (1409 ± 267.5) when compared with samples of mild

symptomatic patients (518.9 ± 177.6)

Both INTERLEUKIN 6 and Ferritin were increased in both mild and severe cases (normal range of INTERLEUKIN 6 – 0-9 pg/ml; Ferritin -20-400 ng/ml).

Table 2. Data showing routine biochemical parameters in Covid-19

S.no	Parameters	Mild	Severe	Normal Range
1.	Urea (mg/dL)	30 ± 10.57	60.75 ± 9.16	10-40
2.	Creatinine (mg/dL)	0.75 ± 0.2	2.2 ± 1.0	0.5-1.0
3.	Total Bilirubin (mg/dL)	0.58 ± 0.26	0.85 ± 0.46	0.3-1.2
4.	Direct Bilirubin(mg/dL)	0.21 ± 0.11	0.57 ± 0.39	0.2-0.4
5.	AST (IU/L)	41 ± 10	419 ± 112	10-45
6.	ALT (IU/L)	55 ± 16	409 ± 109	10-45
7.	Albumin (g/dL)	3.63 ± 0.71	2.7 ± 0.37	2.5-4.5
8.	Total Protein (g/dL)	6.08 ± 0.55	6.3 ± 0.24	6-8

The other biochemical parameters (Table. 2) most prevalent laboratory findings were increased renal markers viz urea and creatinine in severe cases of Covid-19 (urea 60.75 ± 9.16 ; creatinine 2.2 ± 1.0) with respect to mild cases (urea 30.02 ± 10.57 ; creatinine 0.75 ± 0.2)

There were also significant increase in SGOT (419 ± 112) and SGPT (409 ± 109) in severe cases but near normal SGOT (41 ± 10) and SGPT (55 ± 16)

A slight increase was also seen in Bilirubin when compared. (Severe cases Total Bilirubin 0.85 ± 0.46 , Direct Bilirubin 0.57 ± 0.39 ; mild cases Total bilirubin 0.58 ± 0.26 , direct bilirubin 0.21 ± 0.11)

The electrolytes were normal in both mild and severe

cases. A slight decrease was seen in Albumin (Mild 3.63 ± 0.71 ; severe 2.7 ± 0.37) but slight increase was found in Total proteins.

Discussion

The severity of Covid-19 is manifested in the form of changes in biochemical parameters, most important parameter which changes are Interleukin-6 and Ferritin. Few most important biochemical parameters for prognosis and severity of Covid-19 are D-Dimer, NT-proBNP, CRP, Serum Ferritin, procalcitonin and Interleukin 6.

Interleukin 6 is increased due to inflammation which is the hallmark of severe COVID-19 manifested as the hyperinflammatory host response due to the "cytokine

storm". Interleukin 6 an inflammatory cytokine signals through the JAK-STAT pathway. This cytokine storm is defined as an uncontrolled systemic inflammatory response due to the release of large amounts of pro-inflammatory chemicals as cytokines, resulting due to the viral infection of SARS-CoV-2 which induces host immunity^[7].

Inflammation is known to induce hepcidin expression. Hepcidin causes internalization and degradation of ferroportin, which is responsible for increase in Ferritin^[9,10]. Interleukin 6 is specifically useful in predicting prognosis of Covid-19 patients; other inflammatory markers like WBC, hsCRP, PCT, ESR and IL-10 are associated with increased severity of Covid-19. Current evidences shows that a positive correlation has been found between increased Interleukin 6 level and the risk of mortality, thus making Interleukin 6 an indicator of poor prognosis^[11].

Electrolyte imbalance such as hyponatremia, hypokalemia, and hypocalcemia has been associated with severity of the disease^[12,13] even though in our study it was not significant. Electrolyte imbalance is mainly due to the fact that virus infects host by binding with angiotensin converting enzyme 2 (ACE2) receptors. Due to the presence of ACE2 receptors in kidneys and gut water and electrolyte disturbance is caused^[13].

The mechanism involved in the increase in urea and creatinine levels in severe case of Covid-19 infection is due to the fact that angiotensin-converting enzyme 2 (ACE2) is the primary cellular receptor of SARS-CoV-2 and highly expressed in renal epithelial cells, thus the viral infection directly lead to an interaction of SARS-CoV-2 with its receptor in the kidney to reduce ACE2 expression, resulting in abnormal activation of the renin-angiotensin-aldosterone system, which in turn significantly increase the absorption of water by kidney tubules and enhances the resorption of urea, leading to elevated urea levels^[14,15].

The increase in urea and creatinine is not only a kidney dysfunction indicator but it can also reflect inflammatory status, catabolism, nitrogen equilibrium, and renal hypoperfusion from hypovolemia, sepsis, or reduced cardiac output, many of which have been reported to be closely associated with the poor outcomes in COVID-19 patients^[15].

The alteration of hepatocytes damage biomarkers, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin, and albumin, is a common laboratory finding in COVID-19 patients is due to hepatocytes and bile duct epithelial cells expression of ACE2 receptor^[9].

Thus, COVID-19-related liver dysfunction could be the result of secondary liver damage due to the administration of hepatotoxic drugs, systemic inflammatory response, respiratory distress syndrome-induced hypoxia, and Multiple organ failure. Increased levels of liver dysfunction biomarkers have been associated with severe COVID-19 and a worse prognosis^[16].

Conclusion

Covid-19 has affected the world like none before, the role of biochemistry in diagnosis and prognosis has given a ray of hope in managing the Covid-19 patients. The role of biochemical monitoring in the screening of COVID-19 cases has not been definitely established. Severely affected patients are characterised by cytokine release syndrome. Laboratory parameters such as INTERLEUKIN 6 and other markers of inflammation such as CRP, PCT, Ferritin, LDH, FDP and D-dimer can be used in monitoring severity of disease in COVID-19 patients. Targeting INTERLEUKIN 6 may be useful in treating the cytokine storm in severely affected individuals. Other biochemical parameters can serve as to establish a proper way to predict the severity of Covid-19.

Limitations:

1. Even though we tried to cover all routine aspects of Covid-19 few special investigations are need for better understanding of disease and its outcome.
2. Less sample size.

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