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Original Research Article

COVID-19 in Rural Population: is Elevation of C-Reactive Protein Levels Reflecting Liver and Kidney Involvement

Kumari A[1], Singh SB[2], Mahajan S[3], Sharma V[4], Vohra P[5], Hasija S[6], Chatterji P[7], Singh N[8], Chawla H[9]

[1]Assistant Professor, Department of Biochemistry, SHKM GMC, Nalhar, Nuh, Mewat, Haryana

[2]Professor and Head, Department of Biochemistry, SHKM GMC, Nalhar, Nuh, Mewat, Haryana

[3]Associate Professor, Department of Biochemistry, SHKM GMC, Nalhar, Nuh, Mewat, Haryana

[4]Demonstrator, Department of Biochemistry, SHKM GMC, Nalhar, Nuh, Mewat, Haryana

[5]Associate Professor, Department of Biochemistry, SHKM GMC, Nalhar, Nuh, Mewat, Haryana

[6]Associate Professor, Dept. of Pathology, SHKM GMC, Nalhar, Nuh, Mewat, Haryana

7Assistant Professor, Dept. of Chest and TB, SHKM GMC, Nalhar, Nuh, Mewat, Haryana

[8]Ex-Demonstrator, Dept. of Biochemistry, SHKM GMC, Nalhar, Nuh, Mewat, Haryana

9Ex-Demonstrator, Dept. of Biochemistry, SHKM GMC, Nalhar, Nuh, Mewat, Haryana, Telangana

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Corresponding author: Dr. Asha Kumari
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Abstract

C-Reactive Protein (CRP) is one of the vital markers to assess COVID-19 severity. This study was planned to analyse the CRP levels of COVID-19 patients admitted in SHKM GMC, Nalhar, Nuh, Mewat, Haryana. 63 Covid-19 positive patients were included in the study. Data of CRP, blood Urea, Serum Creatinine, SGOT, SGPT, ALP and Bilirubin levels were collected retrospectively. Mean CRP level was 7.71 mg/dl with Standard Deviation (SD) 9.91 mg/dl. (Normal value <0.5mg/dl) Minimum and maximum CRP levels were 0.014 to 41.37 mg/dl. Percentage of subjects having CRP above normal level were 77.78%. There was no correlation of CRP with age, gender, liver function tests (SGOT, SGPT, ALP, S. Bilirubin) and kidney function tests (B. Urea, S. Creatinine). CRP levels were found to be significantly increased in COVID-19 patients before liver and kidney involvement. These results are different from many studies which were conducted in other populations.

Keywords: COVID-19, CRP, Blood Urea, Serum Creatinine, SGOT, SGPT, ALP and Bilirubin levels.

Introduction

Coronavirus disease 2019 (COVID-19) rooted from coronavirus, also known as "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2) in late 2019 from Wuhan, China[1]. Being an extremely infectious disease, it shook the whole world in few months like a blitzkrieg resulting in declaration of COVID-19 a pandemic on March 11, 2020, by WHO. By 12 August 2020, confirmed cases of COVID-19 rose to 20,120,919, including 736,766 deaths, as per WHO report[2].

Corona viruses possess four important structural proteins: the spike surface glycoprotein, small envelope protein, matrix protein, and nucleocapsid protein[3,4]. The corona name is given due to the resemblance of surface due to spike protein. The spike protein plays an important role by binding to host receptors through the receptor binding domains of Angiotensin-converting enzyme2 (ACE2)[5]. This protein is abundantly present in respiratory system, lymph nodes, spleen, liver, thymus, GI tract, bone marrow, kidney, and brain of humans[6].

The mild clinical features of COVID-19 included fever, dry cough, dyspnea, muscle pain, confusion, headache, sore throat, rhinorrhea, chest pain, diarrhoea, nausea, and vomiting[7]. On dangerous side of spectrum, however clinicians found interstitial pneumonia, respiratory failure, acute respiratory distress syndrome (ARDS) and sepsis[8]. Immune system, hematologic system and vascular system were intricately involved in pathophysiology of COVID-19.

C-Reactive Protein (CRP)- a proven indicator of inflammation, has been used as a surrogate marker to assess the severity of COVID-19 along with ferritin and IL-6 [9-11]. As exaggerated inflammatory response was implicated in death of patients, CRP was found to correlate with involvement of many organs. Indian population is different in the infection exposure, immune makeup, genetic variation, environment, diet and healthcare from other countries. As the number of patients continues to increase, Indian studies are required to assess the data of patient for development of better strategy for management of patients. This study was planned on COVID-19 patients admitted in SHKM GMC, Nalhar, Nuh, Mewat, Haryana which is the most backward district of India with the following aims and objectives:

1. Analysis of Biochemical parameters (CRP, B. Urea, S. Creatinine, S. Bilirubin, SGOT, SGPT, S. Alkaline Phosphatase), in COVID-19 positive patients

2. Assessment of any Correlation of CRP with age, sex and other biochemical parameters mentioned above.

Materials and Method

This observational study was conducted in the Department of Biochemistry, SHKM GMC, Nuh, Mewat, Haryana, India in July 2020. Ethical approval was obtained from the institutional ethical committee for the study. Retrospective biochemistry reports of 63 Covid-19 positive patients were included for the data. Data of CRP, blood Urea, Serum Creatinine, SGOT, SGPT, ALP and Bilirubin levels were collected.

CRP analysis method: Serum CRP was analysed by Particle enhanced immunoturbidimetric assay on Roche cobas c systems. Human CRP agglutinates with latex particles coated with monoclonal anti-CRP antibodies. The precipitate was determined turbidimetrically. Normal value: <0.5 mg/dl

Statistics

Mean, SD, median and Interquartile range were calculated for continuous data using python computer language. Percentages and frequency were calculated for nominal data. Correlation coefficient was calculated to analyse the relation between two parameters. P value <0.05 was taken as significant.

Results and Observations

Mean age of 63 cases was 30.63 years with Standard deviation of 15.54 years. Minimum and maximum age were 2 weeks 5days to 67 years respectively. 57.14 % patients were below 30 years, 22.22% were between 31-40 years and 20.63 % were older than 41 years.

Mean CRP level was 7.71 mg/dl with Standard Deviation (SD) 9.91 mg/dl.(Normal value <0.5mg/dl) Minimum and maximum CRP levels were 0.014 to 41.37 mg/dl. Median and Interquartile range (IQR) of CRP levels were 4. 39 and 7.93 mg/dl respectively. Percentage of subjects having CRP above normal level were 77.78%. Out of these 27.78% had CRP above 0.5 mg/dl and below 5 mg/dl. 50% had levels higher than 5 mg/dl.

Patients included 16 (25.39%) were males and 47 (74.61 %) females. Mean CRP concentrations in males was 8.30 mg/dl with SD 13.48 and median 3.33 mg/dl with IQR 6.48. Range of CRP in males was 0.014 to 41.37.

Female Mean CRP level was 7.04 mg/dl (SD 8.52 mg/dl) with median 3.88 mg/dl and IQR 8.18. Range of CRP in females was between 0.03 to 33.3. No statistical difference was noticed (p 0.66) between males and female CRP levels.

Mean (SD) for Blood Urea level was 28.50 (14.95 mg/dl), S. Creatinine was 0.66 (0.24)mg/dl, S.SGOT was 81.35 IU/L (122.63), SGPT was 59.93 (101.83) IU/L, S.ALP 171 was(104.22) IU/L and S.Bil was 1.006 (2.05 mg/dl).

Correlation coefficient of CRP with age, SGOT, SGPT, ALP, B.Urea, S.Creatinine, S.Bil was 0.192, -0.21, -0.11, 0.13, -0.01, -0.05, -0.01.

Discussion

This retrospective observational study was conducted in Mewat, Haryana which is the most backward district of India. Mean age of patients was 30.63 years. Our results demonstrated a significant elevation of CRP in these COVID-19 patients. There was no male-female difference in CRP levels. Kidney function tests were normal in patients. Liver function tests were mildly elevated. No correlation was found between CRP and Age, Kidney function tests and liver function tests.

These results give a very important indication that CRP is elevating in even young patients with normal liver and kidney patients. CRP levels rises before other routinely done parameters.

Serum C-reactive protein has been shown by previous studies to alter significantly in critically ill COVID-19 patients[12]. This acute phase protein is synthesised in liver and is used as early marker of infection and inflammation[13]. Normal concentration of CRP in blood is less than 10 mg/L and it increases rapidly within 6 to 8 hours, reaching the peak in 48 hours from onset of disease[14]. Half-life of CRP is about 19 hours[15]. Fall in concentration indicates end of inflammatory stage and healing and hence regarded as monitor of disease severity[14].

CRP attaches with the phosphatidylcholine which is expressed more on the membrane of damaged cells.[16] This activates the classical complement pathway of immune system. Phagocytic activity of immune cells is enhanced by this process[14].

Another study reported results similar to our study that severely ill patients had increased CRP levels with normal liver and kidney function tests[17]. In one research by Sahu et al, higher CRP was recorded in patients who expired due to COVID-19 than survivors[18].

CRP levels have been linked with induction of acute renal damage and severity of cardiac injury[19,20]. It is suggested that for handling viruses, immunity responds vigorously by synthesising CRP and other immune molecules[21]. Cytokines storm which is reported in some COVID-19 patients is well known to cause organ

dysfunction. CRP production is affected by genes and so different populations may respond differently to the infection[22].

Patients in our study had mild elevation in liver enzymes. Liver dysfunction suggested by increase in AST, ALT and GGT levels is evidenced to be common in many other studies[23,24,7,26-29]. In a study of 417 patients, 76.3% had deranged liver markers and 21.5% developed liver injury during hospital stay[29]. Mechanisms explaining liver damage in COVID-19 patients are immune mediated injury, direct cytotoxic effect of virus, drug induced and anoxia lead hypoxic hepatitis[30,31].

Kidney function tests like Blood Urea and S. Creatinine were in normal range in our study. Prevalence of Acute kidney injury in COVID-19 patients is noted to be between 0.5 and 19.1%[23,24,7,26-29,32]. Patients with high baseline serum creatinine are more likely to undergo ICU admission and mechanical ventilation[32]. Kidney markers analysis is warranted to detect kidney deterioration at early stages. Mechanisms behind kidney damage are similar to liver injury.

Conclusion

In this study conducted in rural population of Mewat, Haryana, India, CRP levels were found to be significantly increased in COVID-19 patients even with normal liver and kidney function parameters. Lower derangements in liver and kidney functions indicated lower risk of failure of these organs in COVID-19 in contrast with previous studies. CRP elevation was independent of gender and age. Hence liver and kidney involvement in COVID-19 varies with population and region.

Limitations of the study

CRP concentrations were not analysed with symptoms, hospital stay, disease severity and mortality which can add to the significance of CRP elevation. Duration of seroconversion can also be added in further studies. Pathological parameters like, D-Dimer, ESR and Neutrophil-Lymphocyte ration (NLR) may be compared with CRP.

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Informed consent

Informed consent was obtained from all individuals included in this study.

Ethical approval

Research involving human subjects complied with all relevant national regulations, institutional policies and has been approved by the authors' Institutional Ethical Committee

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