A Study on C-reactive Protein and Liver Function Tests in Laboratory RT-PCR Positive Covid-19 Patients in a Tertiary Care Centre – A Retrospective Study

M. Muthu Uma Maheswari1, Velayutharaj A2, Saraswathi R3*, Prabhushankar S4, Shivakumar R5

1Final Year MD-Biochemistry PG, Trichy SRM Medical College Hospital & Research Centre, SRM Nagar, Irungulur, Tamilnadu-621105, India; 2Professor, Department of Biochemistry, Trichy SRM Medical College Hospital & Research Centre, SRM Nagar, Irungulur, Tamilnadu-621105, India; 3Associate Professor, Department of Microbiology, Trichy SRM Medical College Hospital & Research Centre, SRM Nagar, Irungulur, Tiruchirapalli, Tamilnadu-621105, India; 4Professor, Department of General Medicine, Trichy SRM Medical College Hospital & Research Centre, SRM Nagar, Irungulur, Tiruchirapalli, Tamilnadu-621105, India; 5Hon. Professor of Pharmacology, Trichy SRM Medical College Hospital & Research Centre, SRM Nagar, Irungulur, Tiruchirapalli, Tamilnadu-621105, India.

INTRODUCTION

COVID-19 pandemic has been one of the greatest challenges to the global healthcare system. People with Diabetes, Hypertension, coronary artery disease and the older population get affected more and the course of illness also severe.1,2 Although the respiratory system is the main target of SARS-CoV-2 infection; damages also may occur in other multiple organs. The liver is an important organ in the body and its exposure to viral infection might also be a concern for COVID-19 affected patients especially the cardiovascular system and liver.

ABSTRACT

Background: COVID-19 pandemic has been one of the greatest challenges to the global healthcare system. Although the respiratory system is the main target of SARS-CoV-2 infection; other organs, exposure to the viral infection might also be a concern for COVID-19 affected patients especially the cardiovascular system and liver.

Objective: To know the status of C-reactive protein (CRP) and Liver Function Tests (LFT) in Covid-19 positive patients before initiating any treatment in a tertiary care hospital.

Methods: Age and sex-matched 40 cases were taken for the study who were hospitalized and COVID-19 infection had been confirmed by real-time RT PCR for COVID-19. Patients with a previous history of liver illness, renal disorders, chronic inflammatory conditions, malignancy and autoimmune disorders were excluded from the study.

Results: Almost all the liver enzymes were higher than the normal levels as seen in aspartate transaminase (35%), alanine transaminase (22.5%), alkaline phosphatase (20%), and gamma-glutamyl transaminase (35%). And whenever the protein, especially albumin was low there was an increased value of CRP and correspondingly with increased total and direct bilirubin levels.

Conclusion: In our study liver function test was altered even before starting any treatment for SARS-CoV-2 indicates that LFT can be a tool to assess multiorgan involvement whenever the patient is going for complication or cytokine storm by doing serial measurements of liver function.

Key Words: C-reactive protein (CRP), Liver Function Tests (LFT), Severe acute respiratory symptom (SARS-CoV-2)
damage, especially of antibiotics, hepatotoxic antiviral drugs and steroids are given to the majority of the patients. The liver because of ACE2 expression in this site is prone to injury as a result of infection with SARS-CoV-2.

There were many studies have reported that laboratory investigations, results and clinical features suggestive of liver dysfunction in patients with COVID-19 infection. But in most of these studies, the pre-existing liver conditions have not been listed out and the pre-existing liver disease with COVID-19 has not been investigated thoroughly and underlying causes of liver injury in the severe liver disease, which are major limitations. However, it has been stated that decreased levels of albumin and Platelet count and increased levels of alanine aminotransferase (ALT) showed an association with higher mortality rates in COVID-19 patients.

It is still unknown that whether pre-existing liver diseases in severe patients, these laboratory tests are an indicator of liver failure caused by the SARS-CoV-2 itself or there is an over-reaction of the immune system which may cause progression and lead to hepatic injury. Our study is to know the status of C-Reactive Protein (CRP) and Liver Function Tests in Covid-19 laboratory positive patients before initiating any treatment in a tertiary care hospital.

**MATERIALS AND METHODS**

It was a retrospective observational study. After ethical clearance by our Institutional Review Board and Institutional Ethical Committee. Age and sex-matched 40 cases were taken for the study who were hospitalized and COVID-19 infection had been confirmed by TrueNat testing by real-time RT PCR for COVID-19. Patients with a previous history of liver illness, renal disorders, chronic inflammatory conditions, malignancy and autoimmune disorders were excluded from the study. The first blood sample was collected as a routine before starting treatment for the analysis of liver function and C-Reactive Protein along with other tests, was done in Cobas c-311 auto analyzer and the estimated values were recorded taken for the study.

**Statistical Analysis**

Data was entered into the MS Excel 2007 version and further analyzed using the SPSS version 20. For descriptive analyses, the categorical variables were analyzed by using percentages and the continuous variables by calculating mean ± Standard Deviation. Regression analysis was applied to numerical data. p<0.05 was considered as statistically significant.

**RESULTS**

In our study population >85% were more than 35 years with male predominance (>70%). Almost all the liver enzymes were higher than the normal levels as seen in aspartate transaminase (AST- 35%), alanine transaminase (ALT-22.5%), alkaline phosphatase (ALP-20%), and gamma-glutamyl transaminase (GGT-35%). And whenever the protein, especially Albumin was low there was an increased value of CRP showing the liver injury and also correspondingly with total and direct bilirubin levels (Tables 1-3).

**DISCUSSION**

COVID-19 infection predominantly causes pulmonary symptoms, but simultaneously affects other organs too, such as Cardiac, Renal and Liver. 14-53% of COVID-19 patients developed hepatic dysfunction, particularly those with severe COVID-19. In critically ill patients hepatic dysfunction was significantly higher and has been associated with poor outcome. Liver dysfunction can be assessed for liver cellular integrity (e.g. ALT and AST), synthetic function (e.g. albumin), or biliary canaliculi (e.g. ALP and GGT). Recent studies on SARS-CoV-2 clinical features have revealed that the liver enzyme abnormalities are common, but not as the prominent feature of this illness.

Many researchers reported that increased CRP is an observed clinical characteristic of most patients with COVID-19 infection. CRP levels were positively correlated with the severity of the disease according to the diameter of lung involvement. Through the recent pandemic of SARS-CoV-2, liver dysfunction in many varieties has been reported in many cases. Liver test abnormality at the admission time can be used as a predictor for the severity of the disease.

Hepatotoxicity is a common adverse event that could occur during clinical practice because of the systemic toxicity of drugs and chemicals. Drugs that are used for the treatment of COVID-19 patients, like antivirals, steroids, and antibiotics, potentially damage the liver, but still was not evident. CaiQetal observed in their study that an increase of liver enzymes could be due to drugs used for the treatment for Covid-19 patients, sepsis, and shock. However, for patients who were hospitalized, needed more attention for any drug-induced liver damage, hence our study was conducted in patients who got admitted and the first sample was sent for the analysis to assess the status of inflammation and liver insult before initiating any treatment after real-time RTPCR confirmation of COVID-19.

Incidence of liver damage in severe cases of COVID-19 with higher levels of total bilirubin ALT, AST, LDH, CRP, D-dimer and lower albumin indicating the severity of the disease is reported. Moreover, a study by Yang F, et al. on deceased cases of COVID-19 with liver abnormalities, it was reported that patients with severe complications enzymes like ALT, AST, and also Bilirubin, total and conjugated bilirubin, which is consistent with our study also the albumin levels.
were also reported lower as in our study.\textsuperscript{19} Hypoalbuminemia could be a result of inadequate nutritional intake and over-consumption during hospitalization\textsuperscript{20} but in our study, it is evident that even during admission there is lower albumin levels and albumin globulin ratio, which was statistically significant (p<0.001). It has been observed that in our study whenever there is an increase of 1 unit of conjugated bilirubin (direct) there was a 45.6 units rise of CRP indicating that the severity of illness and liver insult was even before starting any treatment likewise 1 unit increase of protein -5.8 unit decrease in CRP (down trending levels).

**CONCLUSION**

The liver because of ACE2 expression prone to cholangial tissue injury as a result of infection with SARS-CoV-2 and its mediators of inflammation. In our study liver function test was altered even before starting any treatment for SARS-CoV-2 indicates that LFT can be a tool to assess multiorgan involvement whenever the patient is going for complication or cytokine storm by doing serial measurements of liver function. We suggest from our observation that LFT may be performed along with the other markers to know the severity as well as the prognosis and for a better outcome of the patients.

**ACKNOWLEDGEMENT**

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references to this manuscript. The authors are also grateful to authors/editors/publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

**Conflict of Interest:** Nil

**Source of Funding:** Nil

**Limitations:** Small sample size and liver function test panel before covid infection not available to compare.

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Table 1: Frequency distribution of characteristics of the patients with COVID-19

| Indicators Variable | Frequency (N) | Percentage (%) |
|---------------------|---------------|----------------|
| **Age**             |               |                |
| <35 years           | 5             | 12.5           |
| >35 years           | 35            | 87.5           |
| **Sex**             |               |                |
| Male                | 29            | 72.5           |
| Female              | 11            | 27.5           |
| **Serum total bilirubin (mg/dl)** | | |
| Low (<0.3)          | 6             | 15             |
| Normal (0.3 to 1.3) | 33            | 82.5           |
| High (>1.3)         | 1             | 2.5            |
| **Serum Direct bilirubin (mg/dl)** | | |
| Low (<0.1)          | 7             | 17.5           |
| Normal (0.1 to 0.4) | 28            | 70             |
| High (>0.4)         | 5             | 12.5           |
| **Serum Indirect bilirubin (mg/dl)** | | |
| Low (<0.2)          | 12            | 30             |
| Normal (0.2 to 0.9) | 27            | 67.5           |
| High (>0.9)         | 1             | 2.5            |
| **Serum AST (U/L)** |               |                |
| Low (<12)           | 0             | 0%             |
| Normal (12 to 38)   | 26            | 65             |
| High (>38)          | 14            | 35             |
| **Serum ALT (U/L)** |               |                |
| Low (<7)            | 0             | 0%             |
| Normal (7 to 41)    | 31            | 77.5           |
| High (>41)          | 9             | 22.5           |
| **Serum ALP (U/L)** |               |                |
| Low (<33)           | 1             | 2.5            |
| Normal (33 to 96)   | 31            | 77.5           |
| High (>96)          | 8             | 20             |
| **Serum GGT (U/L)** |               |                |
| Low (<9)            | 0             | 0%             |
| Normal (9 to 58)    | 26            | 65             |
| High (>58)          | 14            | 35             |

Table 2: Bilirubin and Protein with CRP (applying Regression analysis)

| Variable | CRP |
|----------|-----|
| 1 unit increase in TB | 4.6 units increase in CRP |
| 1 unit increase in DB | 45.6 units increase in CRP |
| 1 unit increase in IB | -5.6 units decrease in CRP |
| 1 unit increase in PROTEIN | -5.8 units decrease in CRP |

Table 3: CRP with Albumin, globulin, AG ratio and AST (Applying Regression analysis)

| Variable | Regression Co-efficient value | 95% Confidence intervals | ’p’ Value |
|----------|-------------------------------|--------------------------|-----------|
|          | Regression Co-efficient value | 95% Confidence intervals | ’p’ Value |
| CRP      |                               |                          |           |
| ALBUMIN  | -116.3                        | -175.4                   | -57.1     | *<0.001 |
| GLOBULIN | 53.8                          | 4.6                      | 103.1     | *0.033  |
| AG       | -282.8                        | -405.8                   | -159.9    | *<0.001 |
| AST      | -0.2                          | -0.8                     | 0.5       | 0.620   |

(*p<0.05 is Statistically Significant)