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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

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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 CVID-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)

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 CVID-19 affected patients. Up to now, there are a few pieces of evidence that the hepatic cells are exposed to SARS-CoV-2 in severe cases also it remains unclear that at what extent liver diseases are considerable risk factors of severity and mortality.

As it has been observed with a similar coronavirus, SARS, liver derangement is also an emerging concern with COVID-19. According to many studies with respiratory viral infection in the past, about 60% of patients had a liver impairment as was shown by liver biopsy.[3-5] Almost all the studies researchers noted that it might have been the result of drug-induced liver

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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.[6] 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.[2,7,8]

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 overreaction of the immune system which may cause progression and lead to hepatic injury.[1,9-11] 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 byTrueNat 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 version20. 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.).[12] 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.[13]

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.[13] 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.[14,15]

Hepatotoxicity is a common adverse event that could occur during clinical practice because of the systemic toxicity of drugs and chemicals.[16] 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.[17] CaiQetalobserved 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.[15] 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.[18] 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.[19] Hypoalbuminemia could be a result of inadequate nutritional intake and over-consumption during hospitalization[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.

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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 withAlbumin, globulin, AG ratio and AST (Applying Regression analysis)

Variable	Regression Co-efficient value	95% Confidence intervals		'p' Value
		Lower	Upper	
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)