

Original Research Article

A clinical profile of liver function tests in COVID-19 patients at tertiary care centre from north India

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Received: 16 August 2021

Revised: 21 August 2021

Accepted: 23 August 2021

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ABSTRACT

Background: The coronavirus is a large group of virus, which spread rapidly as an epidemic in china and was named initially as 2019 novel corona virus and subsequently named as Coronavirus disease 2019 (COVID-19) by World Health Organization (WHO). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to a dramatic loss of human life globally and manifests a variety of clinical symptoms varying from fever, cough, headache, myalgias, nausea, vomiting to more severe pneumonia, ARDS, septic shock and multiorgan failure. SARS-CoV-2, primarily affect respiratory system but COVID-19 patients also have varying levels of liver injuries or liver dysfunction. This retrospective study was designed to analyze the clinical features, liver function and duration of hospital stay with confirmed cases of covid-19 in a tertiary care centre.

Methods: We conducted a cross-sectional study in the Isolation ward, Level -2 Covid Hospital, Government Medical College, Kannauj, Uttar Pradesh (India), from April to June 2021. A detailed history and examination was carried out as per the pre-designed proforma. The liver function test included alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and total bilirubin. Patients were considered with abnormal LFTs when any value of these tests was higher than upper limit of normal.

Results: One hundred and ten patients with covid-19 were enrolled during the study period. There were 74 males (67.2%) and 36 (32.7%) females. The mean age of study population was 49.07±12.05 years. In present study, the mean value of serum bilirubin, SGPT, SGOT and ALP were 0.85±0.47 mg/dl, 74.6±66.9 IU/l, 48.45±36.86 IU/l and 229.25±69.79 IU/l, respectively. In present study, the abnormal liver function was seen in 67.2 % cases with COVID-19 patients. The mean duration of hospital stay among normal LFT and abnormal LFT patients group were 13.33±2.12 and 17.10±2.07 days, respectively.

Conclusions: The present study highlighted that abnormal liver function was observed in 67.2% cases with COVID-19 patients. Further research should focus on the cause of liver injury in covid 19 and on treatment and outcome.

Keywords: Severe acute respiratory syndrome coronavirus, Liver injuries, Alanine transaminase, Aspartate aminotransferase, Alkaline phosphatase, Bilirubin

INTRODUCTION

Severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2), has been emerged from Wuhan, China in

December 2019 and spread rapidly across the world and was later declared as a global pandemic by the World Health Organization (WHO) in March 2020. This pandemic also created major turmoil globally and has

resulted in millions of deaths and also responsible for collapsed economy and devastated social life.

SARS-CoV-2 is an enveloped, single-stranded RNA (26–32 kb) virus and has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins.¹ It belongs to the genus Betacoronavirus of the family Coronaviridae and the subgroups of the family are alpha (α), beta (β), gamma (γ) and delta (δ) coronaviruses.²

The initial step during SARS-CoV-2 infection is the binding of S to the angiotensin-converting enzyme 2, or ACE2 receptor, inducing uptake of virus particles by endocytosis and fusion between host and viral membranes.^{3,4} This receptor present in epithelial cells and tissues of the lungs, heart, blood vessels, kidneys, liver and gastrointestinal tract.⁵

The virus is typically rapidly spread from one person to another via respiratory droplets produced during coughing and sneezing. It is considered most contagious when people are symptomatic.⁶ The median incubation period is 5.1 days (range 2-14 days). As per the current evidence, the period of infectivity starts 2 days prior to onset of symptoms and lasts up to 8 days.⁷

Most patients with COVID-19 predominantly have a respiratory tract infection associated with fever, cough, sneezing and shortness of breath. However, in small percentage of cases, it can lead to ARDS, severe sepsis and multiorgan failure, including acute kidney injury and cardiac injury.⁸ Autopsy carried out in China and European countries showed endothelial damage of pulmonary vasculature, microvascular thrombosis and hemorrhage that ultimately results into vasculopathy, pulmonary intravascular coagulopathy, hypocoagulability and refractory ARDS.⁹

Although COVID-19 primarily affects the Lungs, but about 60% patients also have varying levels of liver injuries or liver dysfunction in various studies.¹⁰⁻¹²

Abnormal levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin were reported in 11%-56.3%, 15.0%-86.8%, and 2.7%-30.6% of patients with COVID-19, respectively.¹³⁻¹⁵

The potential mechanisms of pathogenesis may be broad spectrum, ranging from direct cytotoxicity from viral infection to indirect involvement of the inflammatory cytokine storm, hypoxic changes caused by respiratory failure, endotheliitis, and drug-induced liver injury.¹⁶

ACE2 is highly expressed in the lung (type II alveolar cells), intestine, and gall bladder, but it seems to be almost absent in the liver. ACE2 expression patterns is also seen in the central hepatic vein and portal vein endothelial cells.¹⁷ The expression level of ACE2 in the bile duct

epithelium is comparable to that in alveolar epithelial cells, being almost 20-times higher than that in hepatocytes.¹⁸

In this study we prospectively investigated the abnormal liver function in COVID-19 patients from single level -2 isolation centre at Kannauj, UP with aim to provide a reference for clinical management of the patients.

METHODS

We conducted a cross-sectional study in the Isolation ward, Level -2 COVID Hospital Government Medical College, Kannauj, Uttar Pradesh (India), from April to June 2021. During this period about 500 patients were admitted and treated at this centre. The medical record of 110 patients were collected and analyzed for final analysis.

Inclusion criteria

All the RT-PCR confirmed covid-19 cases aged more than 12 years were included in the study.

Exclusion criteria

Chronic liver disease. Hepatitis B. Hepatitis C.

Lab investigations

A detailed history and examination was carried out for every patient, as per the pre-designed proforma. All patients were evaluated for Complete Blood Count (CBC), fasting blood sugar level, kidney function test and liver function test and Chest imaging. The liver function test i.e. alanine aminotransferase (ALT, 9-40 U/l by Ultra spectrophotometry), aspartate aminotransferase (AST, 13-40 U/l by ultraviolet spectrophotometry), alkaline phosphatase (ALP, 38-126 U/l by PNPP AMP buffer method), and total bilirubin (TB, 0.2-1.3 mg/dl by Azobilirubine) were routinely measured. We defined abnormal liver damage as any parameter more than the upper limit of normal value. Others investigation like, chest x-ray, kidney function tests, ECG, random blood glucose, hepatitis B surface antigen (HBsAg), anti-hepatitis C antibodies test (Anti-HCV), HIV testing, urine routine and microscopy were also done.

Ethical approval

The study was approved by Ethics Committee of the Institution, GMC Kannauj, India.

Statistical analysis

Categorical variables were described as frequency and percentages, and continuous variables as mean and SD. Means for continuous variables were compared using independent group t tests when the data were normally distributed. Comparison of categorical variables was done using the χ^2 (chi square) test or the Fisher exact test.

RESULTS

In present study, a total of 110 patients with COVID -19 were admitted and analyzed during the study period.

Table 1: Clinical profile of COVID-19 patients (n=110).

Name of parameter	Observed value
Mean age (in years)	49.07±12.05
Males (in years)	47.65±12.6
Females (in years)	52±10.36
Sex	
Male	
Female	
Symptoms	
Fever	66 %
Weakness	58 %
Cough	43.6 %
Breathlessness	31 %
Diarrhea	5%
Mean haemoglobin	11.8±1.80 g/dl
Mean total leucocyte count	13055.51±5657.42 cu/mm ³
Mean polymorph %	80.73±12.93
Mean lymphocyte %	16.74±11.8
Mean serum creatinine	1.05±0.74
Mean blood urea	32.8±15.29 mg/dl
Mean serum bilirubin	0.85±0.47 mg/dl
Mean SGPT	74.6±66.9 IU/l
Mean SGOT	48.45±36.86 IU/l
Mean ALP	229.25±69.79 IU/l
Pt with normal LFT function	32.7%
Pt with abnormal LFT function	67.2%
Mean duration of hospital stay	15.8±2.7 days

There were 74 males and 36 females. The mean age of males and females patients were 47.65±12.6 years and 52±10.36 years respectively. The male patients presented at an earlier age as compared to female patients. In covid-19 patients, 66% presented with fever and 58% patients had weakness and 43.6% had cough. Breathlessness was observed in 31% cases and diarrhea in 5% cases. 15% of patients had no symptoms. The mean durations of hospital stay among the cases was 15.8±2.7 days.

The mean Haemoglobin levels in cases with COVID-19 were 11.8 g/dl±1.80. The mean total Leukocyte Count was 13055.51±5657.42 cu/mm³. The mean Polymorph percentage was 80.73±12.93. The mean Lymphocyte percentage was 16.74±11.8. The mean Eosinophil percentage was 2.5. In present study, the mean Serum creatinine level was 1.05±0.74 mg/dl. The mean Blood Urea level, among the patients was 32.8±15.29 mg/dl. The liver function test revealed a mean total bilirubin of 0.85±0.47 mg/dl, SGOT mean value was 48.45±36.86 IU/l

and for SGPT it was found to be 74.6±66.9 IU/l and ALP was 229.25±69.79 IU/l.

Table 2: Comparison of normal LFT and abnormal LFT group among COVID-19 patients.

Parameter	Normal LFT group (N=36)	Abnormal LFT group (N=74)	P value
Mean serum bilirubin	0.68±0.21 mg/ dl	0.94±0.54 mg/dl	0.006
Mean SGPT	32.8±7.5 IU/l	94.93±73.32 IU/l	0.0001
Mean SGOP	27.11±6.62 IU/l	58.83±40.91 IU/l	0.001
Mean ALP	189.33±40.19	248.66±73.01	0.84
Mean duration of hospital stay	13.33±2.12	17.10±2.07 days	0.002

In present study, abnormal liver function test were observed in 67.2% cases, while 32.7% had normal liver functions. In present study, the deranged parameters of total bilirubin, SGOT, SGPT and SAP were seen in 15.4%, 35.4%, 51.8% and 27% cases, respectively.

The mean values of serum bilirubin in abnormal and normal LFT group were 0.94 mg/dl and 0.68 mg/dl respectively. The mean value of SGOT in abnormal and normal LFT group was 58.83 and 27.11 IU/l respectively. The mean value of SGPT in abnormal and normal LFT group was 94.93 and 32.8 IU/l respectively. The mean values of ALP in abnormal and normal LFT group were 248.66 and 189.33 IU/l respectively. The mean durations of hospital stay among abnormal and normal LFT group were 17.10 days and 13.33 days, respectively.

Management

In present study, patients were managed as per the COVID-19 protocol guideline issued by ministry of health and family welfare, GOI (MOHFW).

DISCUSSION

COVID pandemic followed in expeditious boost in total number of cases in our country leading to enormous burden on health care delivery system both government and private.

After the binding of SARS-CoV-2 to the host protein, the two-step sequential protease cleavage occurred to activate the spike protein.¹⁹⁻²¹ The characteristics unique to SARS-CoV-2 among coronaviruses is the existence of furin cleavage site ("RPPA" sequence) at S1/S2 site. The S1/S2 site was also subjected to cleavage by other proteases such

as transmembrane protease serine 2 (TMPRSS2) and cathepsin L, the ubiquitous expression of furin likely makes this virus very pathogenic.^{21,22}

Patients with severe diseases showed lymphopenia, reduction in peripheral blood T cells, increased plasma concentrations (IL)-6, IL-10, tumor necrosis factor (TNF)- α , LDH, Serum ferritin, CRP, D-dimer, fibrinogen level and APTT also.^{11,23} In severe cases, there is alteration of coagulation cascade and have been observed in lungs and other vital organs also and risk of pulmonary embolism on higher side.²⁴

In present study, COVID-19 infection was more observed in males than female's population.

A study had been done in India and they reported that slight male preponderance was noted with male:female ratio of 1.4:1, for COVID infection.²⁵ Another study done in India among covid-19 patients and they reported the percentage of male and females were 60.9 and 39% respectively.²⁶ Another study done in India among 152 COVID-19 patients and in which the number of male and female populations were 58.5% and 41.4% respectively.²⁷

Another study done in Portugal among COVID-19 patients and in their study the number of male and female populations were 50.5% and 49.5% respectively.²⁸

In present study, the mean age of males and females patients were 54.4 \pm 1.8 & 58.4 \pm 1.8 years respectively.

While the mean age of 49 years, 55.5 years and 56 years were noted by Huang et al, Chen et al and Wang et al respectively, in their study with patients with COVID-19 infection.^{11,29,30} Fan et al reported mean age of 50 years (36-44) among 148 patients with COVID-19 cases.³¹

In present study, the value of mean haemoglobin, total Leukocyte Count, Polymorph percentage and Lymphocyte percentage were 11.8 g/dl, 13055.51 cu/mm³, 80.73% and 16.7% respectively.

Rao et al had done a retrospective cohort study among 395 patients with COVID-19 patients. In their study, the mean Hb, total leucocyte count, polymorph % and lymphocyte % were 11.1 gm/dl, 14.63, 78.73% and 15.46% respectively.³² Another retrospective study was conducted in India among 226 patients with COVID-19. In this study, the mean total leucocyte count, polymorph % and NLR ratio were 14.28 \pm 9.09 cells/cumm³, 84.24 \pm 9.54% and NLR ratio 10.53 \pm 12.74, respectively.²⁵ Gupta et al had done a study among COVID-19 patients and in their study, the mean Hb, total leucocyte count were 14.4 g/dl and 5758/mm³ respectively. They further reported that only one patient had leukopenia with a count of 2900/mm³.³³ Saluza et al conducted a study with aimed to analyze radiological presentation, prognostic factors and complications among COVID-19 patients. They

highlighted that lymphopenia, thrombocytopenia and raised LDH were present in >35 % cases.³⁴

Increasing evidences support that patients with COVID-19 could develop liver injury mainly manifested as abnormal ALT or AST levels accompanied by slightly elevated bilirubin levels.^{30,35} The exact pathogenesis of liver injury in SARS-COV-2 infection remains unclear. Possible mechanism includes direct virus-induced cytopathic effects, exacerbation of preexisting liver disease, hypoxemia, drug induced, and overshooting inflammatory responses.¹³

In present study, the total bilirubin, SGOT and SGPT were 0.85 mg/dl, 48.43 IU/l and 74.7 IU/l respectively.

A study done from India and they reported that Out of 105 patients associated with COVID-19, 59.04% had abnormal Liver function tests at admission. The percentage of patients with elevated AST, ALT, ALP and total Bilirubin were 45.71%, 25.71%, 20% and 6.67% respectively.²⁶ Cai et al had done a study in China to know the clinical characteristics of COVID-19 in patients with abnormal liver tests. They further reported that of 417 patients with COVID-19, 318 (76.3%) had abnormal liver function and 21.5% had liver injury during hospitalization. Regarding the patterns of abnormal liver test results, 20.75% were hepatocyte type, 29.25% were cholestatic type, and 43.4% were mixed type.³⁶ Another study done in India and they reported that 58.5% patients had raised levels of liver enzymes at any time point during their hospitalisation. In these patients, the median values of AST, ALT and ALP were found to be 57.0 U/l, 64.65 U/l and 122.0 U/l respectively, as compared to 24.60 U/l, 24.80 U/l and 86.0 U/l, respectively, in patients with normal liver enzymes. Out of these 89 patients, abnormal liver enzyme levels up to 2 \times ULN were observed in 42 patients whereas 47 patients had abnormal liver enzyme levels higher than 2 \times ULN.²⁷ Another study done in China to know the changes of liver function tests (LFTs) and its clinical significance in 158 hospitalized patients with COVID-19. They further reported that of 158 patients with COVID-19, 67 (42.41%) patients had abnormal LFTs on admission and another 50 (31.65%) patients developed abnormal LFTs during hospitalization. Author further highlighted that in patients with abnormal LFTs, 30 (33.0%), 45 (49.5%), 8 (8.8%) and 4 (4.4%), patients had elevated ALT, AST, TB and ALP, respectively 37. Another study done in Portugal to describe clinical outcomes in 317 COVID-19 patients regarding the presence of abnormal liver tests and CLD. They further reported that about half of the patients (n=148/294, 50.3%) showed abnormal liver tests, and 122 (41.5%) patients showed elevated AST levels, from which the majority (75.4%) were mild elevations of 1-2 \times the upper limit of normal. AST levels were elevated in 117 (40.3%; median 46.0 U/l, IQR 39.0-67.0) and ALT levels in 46 (15.6%) patients (median 70.0 U/l, IQR 53.0-87.0). ALP was elevated in 33 (11.4%; median 167 U/l, IQR 145-231) and GGT in 72 (24.6%) patients (median 105

U/l, IQR 84.8–154). Total bilirubin was abnormal in only 14 (4.81%) of the patients.²⁸

In present study, the mean durations of hospital stay among the cases was 15.8 days. The mean durations of hospital stay among abnormal and normal LFT group were 17.10 days and 13.33 days, respectively.

A study done in India reported that Patients with normal LFTs (n=22) had mean hospital stay of 10 days (7-11days) as compared to patients with abnormal LFTs (n=27) who had prolonged mean hospital stay of 15 days (10-16 days).²⁶

Limitations

The present study has several limitations. Firstly, this study included patients from single centre, so these finding cannot be generalized. Similar types of more studies are needed to make justifications. Second, the present study reveals association of abnormal liver function among COVID-19 patients and not causation. Third, the present study included lesser number of patients.

CONCLUSION

Abnormal liver tests are more common in both non severe and severe cases with COVID-19. To know, the presence of liver injury, the liver enzymes like Serum bilirubin, SGPT and SGOT are most commonly used markers. However liver biopsy is strongly recommended for those with unexplained acute liver failure. In present study abnormal liver functions are more common in Male patients. These findings may help to elucidate the role of liver function tests on COVID-19 prognosis and provide a scope for improvement in the clinical treatment of patients during this COVID-19 pandemic.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Priyadarshi BP, Kumar A, Singh V, Varma SK, Yadav R, Pandey P. A clinical profile of liver function tests in COVID-19 patients at tertiary care centre from north India *Int J Res Med Sci* 2021;9:2633-8.