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Original Research Article

COVID-19's Effect on Hepatic Functions

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Abstract

Background: COVID-19 infection is a recent pandemic that has occurred in three years with varying severity and impact around the world. It has an impact on the respiratory tract. It also affects multiple systems, including the hepatobiliary, as a result of systemic inflammation associated with the respiratory tract. It is being studied how much it affects the liver, what the outcome is, and whether there is any correlation between disease severity and hepatic involvement. The link between COVID infection and hepatic involvement was investigated in this retrospective study. We also looked into the relationship between disease severity markers and hepatic involvement.

Aim and Objectives: To investigate the impact of COVID-19 infection on hepatic function.

Material and Methods: This is a retrospective study conducted at Bharti Vidyapeeth Medical College in Pune, Maharashtra, India, a tertiary care centre. Data were collected from Covid-19 patients admitted between October 2021 and March 2022 were screened for abnormal liver function. An increase in hepatic parameters (AST, ALT), or total bilirubin that exceeds two times the upper limit of normal. D-dimer, CRP, and ferritin levels were used to determine disease severity. Data on abnormal liver function and disease severity parameters were gathered and analyzed.

Results: We discovered 54 (4.08 percent) patients with deranged liver function in the form of raised hepatic parameters (SGOT and/or SGPT) two times the upper limit of average value after reviewing the records of 1123 patients. Males outnumbered females (46:8). Around two-thirds of the patients were over the age of forty. SGOT and SGPT are affected more frequently than other liver function test parameters. The higher the inflammatory marker levels is the more severe the hepatic involvement. All patients recovered, and no one died as a result of liver failure. The hospital stay was also proportionately longer in patients with more severely impaired liver function.

Conclusion: COVID infection frequently affects the liver. Hepatocellular damage ranging from mild to moderate is expected. In patients without a history of liver disease, there is no overall influence on outcomes.

Keywords: COVID-19, Hepatic, Liver.

Introduction

In China's Wuhan province, a pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or novel coronavirus disease (COVID-19)

began in December 2019 and expanded over the world by April 2020. In 2020, it had an impact on 187 countries. It had an effect on the world for the next two years [1]. Aside from respiratory tract involvement, other organ injuries have been reported, including acute kidney injury, liver damage, cerebrovascular stroke, and gastroenteritis [2]. The severity and death rate in the third wave caused by the omicron variant were significantly lower than in the first and second waves. In comparison to previous waves, the third wave had significantly lower mortality and morbidity, as well as better overall results [3].

Studies conducted in more severe waves revealed up to 10-35 percent hepatic involvement. Early studies in 2019 had higher haptic participation than studies in 2020. Because the third wave was shorter in duration, less severe, and required fewer admissions, there may have been fewer hepatic involvements [4,5].

Hepatic involvement may occur before admission due to infection, but the drug-induced liver injury should be considered because multiple hepatotoxic drugs, such as acetaminophen, lopinavir/ritonavir, and remdesivir were used [6].

Material and Methods

Study design

This is a retrospective study conducted at Bharti Vidyapeeth Medical College in Pune, Maharashtra, India, a tertiary care centre. Data from COVID-19 patients admitted between October 2021 and March 2022 were screened for abnormal liver function. Abnormal liver function is defined as an increase in AST, ALT, or total bilirubin that exceeds two times the upper limit of normal. D-dimer, CRP, and ferritin levels are used to determine disease severity. Data on abnormal liver function and disease severity parameters were gathered and analyzed. We looked at the relationship between severity and hepatic involvement, as well as the overall effect on outcome.

Results

On evaluation of five months,1123 COVID patients data from third wave, we have received 54 (4.08%) cases with abnormal LFT. Males were 46 and females were 9 out of them. Affected age group was between 24-85 years. Two third patients were above 40 years. Co-morbidity seen in 23 patients, commonly diabetes and hypertension. Rare co-morbidities were cerebrovascular accident, bronchial asthma, hypothyroidism and ischemic heart disease. In few patients there were more than one co-morbidities. Except of one, patients had hepatitis B positive status none had history of chronic liver disease. HRCT (n=8) score was 10-21,and it hepatic injury was more with higher HRCT score ($p < 0.05$). Other inflammatory markers were also significantly increased-dimer (137-7893, 1,926.15 ± 1,101.2 mcg/dl), CRP (3.2-583.45,88.6 ±27.2 mg/dl) and ferritin (7.6-6671.37, 1,893.6 ± 1,272.4 mcg/L). SGOT (n=54) and SGPT (n=53) was increased in all patients. Total bilirubin (n=6), direct bilirubin (n=25), indirect bilirubin (n=9) and alkaline phosphatase (n=15) affected in less number of patients and less severely. All patients were recovered from COVID 19 infection and discharged. One had liver failure or liver related mortality. Only 17 patients received remdesivir, there was no hepatic function difference in the form of enzyme elevation (SGOT mean 211.12 vs. 246.65U/L, p=0.27, SGPT mean 241.95 vs. 244.76U/L, p=0.4) between remdesivir receivers and non recovers group of patients ($p <0.4$) (Table 1)Total bilirubin raised in 6 patients (mean 3.74 ± 1.9, range 4.5-7.05 mg/dl). Direct bilirubin raised in 25 patients (mean 0.58 ± 0.1, range 0.32-2.17 mg/dl). SGOT affected in 54 patents (mean 235.46±52.3, range 94-969 U/L). SGPT affected in 53 patients (mean 246.41 ± 40.2, range 86-544U/L). Alkaline phosphatase elevated in

15 patients (mean 418.2 ± 54.60, range 263-508 IU/L).(Table 2).

Direct bilirubin, total bilirubin and alkaline phosphatase increased less than five times of upper limits i.e. 4.7, 3.61 and 3.91 respectively. Highest change was seen in SGPT raised 24.22 times, followed by SGOT raised 13.6 times.

Inflammatory markers like D-dimer, ferritin and C-reactive protien were increased in all patients. Inflammatory marker levels, SGOT and SGPT levels were also high ($p<0.005$). Highest d-dimer was 7893 mcg/ml,mean 1678.8261 ± 615.2. Hospital stay was much higher with high SGOT and SGPT patients. These patients also having high inflammatory markers. Hospital stay was between 2-17 days, (mean 5.22 days, mode-2days). (Table 3).

Table 1: Basic demographic data

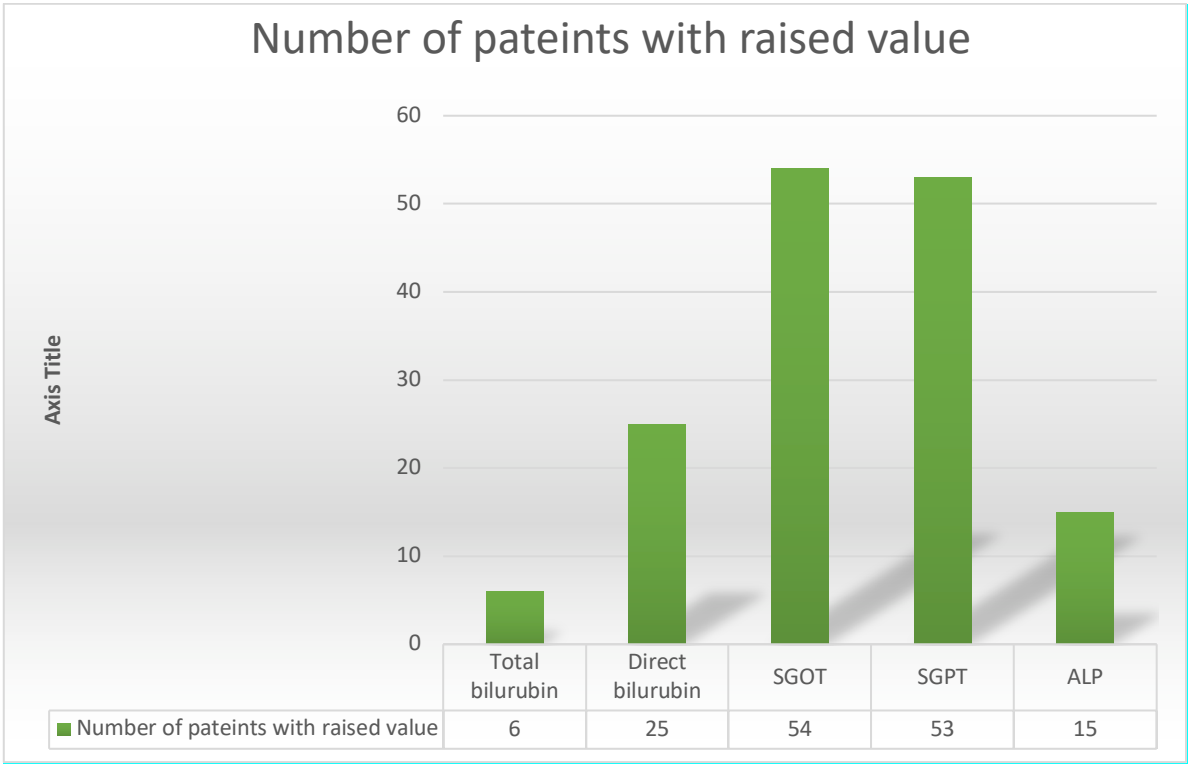
Category	Range	Mean
Age	24-85 Years	47.5 ±3.09 years
Sex	Male 46; Females -8	
Comorbidity	23 DM-14 HTN-13 Other – (IHD,BA,CVA,Hypothyroidism)	
Admission	1-17 days	4.18 ±1.09 dasy
Underlying CLD	2	
HRCT score (n=8)	Oct-21	13 ±2.8
Haemoglobin	2.9-16.9gm%	13.187 ±0.619
Total count /L	2200-33300	7,527.7±1,310.6
Platelets /L	13000-437000	227,685.1 ±26,707.7
HbsAg	N=1 positive	
Anti HCV Positive	Nil	
HIV Positive	Nil	
Received Inj. Remdesivir	17 patients	
D dimer (mcg/ml)	137-7893	1,926.15±1,101.2
Ferritin (mcg/L)	7.6-6671.37	1,893.6 ±1,272.4
CRP (mg/L)	3.2-583.45	88.6 ±27.2
Total bilirubin (mg/dl)	0.2-7.05	1.02±0.34
Direct bilirybin (mg/dl)	0.1-2.13	0.36±0.08
Indirect bilirubin (mg/dl)	0.1-6.09	0.6783 ±0.302
Albumin (gm/dl)	2.2-4.9	3.70 ±0.15
SGOT (U/L)	94-969	235.30 ±53.36
SGPT (U/L)	86-625	246.41 ±40.23
ALP (IU/L)	28-608	229.07 ±36.60
Outcome	All recovered from COVID 19 infection and discharged	

TB, Total bilirubin; DB, Direct bilirubin; SGOT, serum glutamic-oxaloacetic transaminase ; SGPT, Serum Glutamic Pyruvic Transaminase; ALP, Alkaline phosphatase; CRP, c-reactive protein

Table 2: Liver function test result

TB mg/dl			DB mg/dl			SGPT U/L				SGOT U/L			ALP IU/L	
No. of patients with raised TB	Mean	Range	No. of patients with raised DB	Mean	Range	No. of patients with raised SGPT	Mean	Range	No. of patients with raised SGOT	Mean	Range	No. of patients with raised ALP	Mean	Range
6	3.74±1.9	4.5-7.05	25	0.58±0.1	0.32-2.17	54	235.46±52.3	94-969	53	246.41±40.23	86-544	15	418.2 ±54.60	263-508

TB, Total bilirubin; DB, Direct bilirubin; SGOT, serum glutamic-oxaloacetic transaminase ; SGPT, Serum Glutamic Pyruvic Transaminase; ALP, Alkaline phosphatase



Graph 1: Deranged Liver function test

Table 3: Comparison between SGOT,SGPT and Inflammatory marker

	D-DIMER mcg/ml, (n=46)			FERRITIN mcg/L, (n=46)			CRP mg/L (n=46)			Hospital stay (days)		
	Mean	Range	P value	Mean	Range	P value	Mean	Range	P value	Mean	Range	P value
SGOT U/L, (n=54,mean 235.46±52.3)	1,678.826 1 ±615.2	154-7893	P<0.05	1,333.7±3 90.1	29.81-6671.37	<0.05	101.3±29. 71	10.29-583.45	<0.05	4.22±1.10	1-17	<0.05
SGPT U/L (n=53,mean 246.41±40.23)	1,678.826 1 ±615.2	154-7893	P<0.05	1,333.7 ±390.1	29.81-6671.37	<0.05	101.3 ±29.71	10.29-583.45	<0.05	4.22±1.10	1-17	<0.05

SGOT, serum glutamic-oxaloacetic transaminase ; SGPT, Serum Glutamic Pyruvic Transaminase ;CRP, c-reactive protein.

Discussion

India experienced the third wave between January 2022 and April 2022. The third wave's severity was far lower than the previous two waves. Just 1% of people experienced severe symptoms, while 42% reported symptoms of moderate severity [7]. Several studies have found that severe COVID-19 cases are more likely to have severe liver damage than mild cases [2]. Male patients were more likely than female patients to suffer from liver function impairment [8]. Hepatic involvement varies depending on the area and the period of the investigation. Hepatic damage was present in 25% of the individuals. Alanine transaminase and aspartate transaminase levels were also high in 21% and 24% of the participants, respectively. As they are from a milder disease period, our patients have up to 4% hepatic invent. Males affected more than females. In deranged LFT, ALT was elevated in all 54 (100%) patients and AST was elevated in 53 (98.14%) patients. Total bilirubin, direct bilirubin and alkaline phosphatase affected less frequently (<50% cases). In study by Guan et al. have conducted in first wave (2020) found elevated levels of ALT in 19·8% of patients with non-severe disease and 28·1% [2]. So there is correlation between severity of COVID -19 disease and hepatic involvement. According to preliminary research, ACE2 receptor expression was higher in cholangiocytes [10]. This suggests that SARS-CoV-2 may directly bind to ACE2-positive cholangiocytes and disrupt liver function. Nonetheless, pathological analysis of liver tissue from a COVID-19 patient revealed that no viral inclusions were found in the liver [11-12]. The liver impairment could be due to drug hepatotoxicity, which could explain the wide variation observed across the different cohorts. Furthermore, immune-mediated inflammation, such as cytokine storm and pneumonia-associated hypoxia, may contribute to liver injury or even lead to liver failure in critically ill COVID-19 patients. In our study, the overall disease severity and duration of admission were much lower. Indicates a link between disease severity and, most likely, drugs taken during illness. Shenzhen et al. have showed patients with abnormal liver function were older, had a higher proportion of cough as the first symptom, a higher BMI, a higher proportion of males and had more underlying liver diseases. In our analysis, there was no correlation between age and liver involvement (p=

0.1, age >40 and 40 years) [13]. The degree of lung lesions on CT was found to be a predictor of liver dysfunction ($p<0.05$). Severe lung lesions were more likely to cause liver dysfunction [14]. Hepatic involvement was linked with ferritin, IL-6 D-dimer, CRP, procalcitonin, CK, and high sensitivity troponin levels CT scan was commonly done in our patients as they had milder disease. We also discovered a strong link between inflammatory markers and hepatic involvement. D-dimer, CRP, and ferritin levels are correlated with AST and ALT levels ($p<0.05$). A systematic review and meta-analysis revealed that an increase in liver biochemistry during the first visit or illness was an important indicator of disease severity. Low serum albumin levels indicate a serious disease. COVID-19 outcome was determined by the severity of elevated liver enzyme [15]. Incidence of liver injury was as high as 58–78% in the death cases of COVID-19 indicates liver involvement was sign of severe disease.

The treatment for impaired liver function is to regularly monitor LFT as well as rule out viral, autoimmune, and drug-induced liver injury. Patients taking remdesivir or tocilizumab should be carefully monitored [16].

In mild cases of COVID-19, liver damage is often transient and returns to normal without any special treatment. However, when severe liver damage occurs, patients are usually given liver protective drugs [17].

The hospital stay in our study was brief. The majority of the patients had less severe disease. Twenty-one patients had NAFLD risk factors and one had hepatitis B. There was no history of chronic liver disease in any of these patients. The mean length of stay in the hospital was 4.22 ± 1.10 days (1-17 days). All of our patients were given COVID -19 and UDCA 300mg bd until their LFTs returned to normal. There was no mortality and all patients recovered well.

Considering their immunocompromised status, severe COVID-19 patients with pre-existing chronic liver disease require more intensive surveillance or individually tailored therapeutic approaches, particularly in older patients.Further research should focus on the causes of liver injury in COVID-19, as well as the impact of pre-existing liver-related comorbidities on COVID-19 treatment and outcome.

Conclusion

In conclusion, elevated liver enzymes are usually mild in COVID-19 disease and usually resolve without treatment. It correlated with disease severity. Rule out other causes for deranged LFT and monitor for drug induced liver injury.

References

1. Ghoda A, Ghoda M. Liver Injury in COVID-19 Infection: A Systematic Review. Cureus. 2020 Jul 31;12(7): e9487.
2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 2020; 382(18):1708-1720.
3. Accessed on 30th Mar 2023. https://www.cdc.gov/ Updated Mar. 29, 2022
4. Xie H, Zhao J, Lian N, Lin S, Xie Q, Zhuo H. Clinical characteristics of non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: A retrospective study. Liver Int 2020;40(6):1321-1326.
5. Zhang Y, Zheng L, Liu L, Zhao M, Xiao J, Zhao Q. Liver impairment in COVID-19 patients: A retrospective analysis of 115 cases from a single centre in Wuhan city, China. Liver Int 2020; 40(9):2095-2103.
6. Bertolini A, van de Peppel IP, Bodewes FAJA, Moshage H, Fantin A, Farinati F, et al. Abnormal liver

function tests in patients with covid-19: relevance and potential pathogenesis. Hepatology 2020; 72(5):1864-1872.
7. Jayadevan R, Shenoy R, Anithadevi TS. COVID-19 third wave experience in India, a survey of 5971 adults. BMJ Yale 2022. https://doi.org/10.1101/2022.04.26.22274273
8. Xie H, Zhao J, Lian N, Lin S, Xie Q, Zhuo H. Clinical characteristics of non-ICU hospitalized patients with coronavirus disease 2019 and liver injury: a retrospective study. Liver Int 2020;40(6):1321-1326.
9. Kullar R, Patel AP, Saab S. Hepatic injury in patients with COVID-19. J Clin Gastroenterol 2020; 54(10): 841-849.
10. Chai X, Hu L, Zhang Y, Han W, Lu Z, Ke A, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. bioRxiv 2020. https://doi.org/10.1101/2020.02.03.93176.
11. Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020; 8(4):420-422.
12. Cai Q, Huang D, Yu H, Zhu Z, Xia Z, Su Y, et al. COVID-19: Abnormal liver function tests. J Hepatol 2020;73(3):566-574.
13. Zhang Y, Zheng L, Liu L, Zhao M, Xiao J, Zhao Q. Liver impairment in COVID-19 patients: a retrospective analysis of 115 cases from a single centre in Wuhan city, China. Liver Int 2020;40(9):2095-2103.
14. Phipps MM, Barraza LH, LaSota ED, Sobieszczyk ME, Pereira MR, Zheng EX, et al. Acute liver injury in COVID-19: Prevalence and association with clinical outcomes in a large U.S. Cohort. Hepatology 2020;72(3):807-817.
15. Kulkarni AV, Kumar P, Tevethia HV, Premkumar M, Arab JP, Candia R, et al. Systematic review with meta-analysis: liver manifestations and outcomes in COVID-19. Alim Pharmacol Therap 2020;52(4):584-599.
16. Fix OK, Hameed B, Fontana RJ, Kwok RM. Clinical best practice advice for hepatology and liver transplant providers during the COVID-19 pandemic: AASLD Expert Panel Consensus Statement. Hepatology 2020;72(1):287-304.
17. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol 2020; 5(5):428-430.