Original Article

Liver function tests at admission as marker of severity and prognosis in COVID-19 patients – A retrospective analysis

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Abstract

Introduction: With evolving pandemic, a substantial proportion of patients are presenting with liver dysfunction as an extra-pulmonary manifestation of COVID-19 illness. We planned this study to evaluate the incidence of liver dysfunction in COVID-19 pneumonia and find an association between abnormal liver function and the severity of the disease. **Method:** We retrospectively analysed the hospital records of 344 patients with moderate to severe COVID-19 illness admitted to a Dedicated COVID Hospital in North India. **Results:** Out of 344 patients included in the study, 59.9% were males. The abnormal liver functions were present in 78.49% of patients at admission. Mean age of the patient with liver dysfunction was 53.41 ± 15.71 years. The incidence of elevated aspartate aminotransferase (AST), alanine aminotransferase (ALT), and hypoalbuminemia was 82.96%, 74.91%, and 69.7%, respectively, in patients with COVID-19 at admission. A positive correlation was found between the levels of AST, ALT and hypoalbuminemia with severity of disease. Mortality was 33% in patients with liver dysfunction in comparison to 18.9% in patients with normal liver functions. **Conclusion:** More than 75% of the patient had abnormal liver functions at admission, and mortality was also high in this group. Mortality can be effectively reduced if laboratory parameters such as elevated AST and ALT and hypoalbuminemia are closely monitored at admission and during hospital stay in patients with risk factors like male, age <55 years and HTN.

Keywords: COVID-19, liver function tests, markers, prognosis, severity

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), which is a positive-strand RNA virus.[1] Since the outbreak of COVID-2019 in Wuhan, China, in December 2019, the disease spread rapidly and was declared a pandemic by WHO on 11th March 2020. There are over 639 million confirmed cases of COVID-19, including around 6 million deaths till 1st December 2022 worldwide. India is the second country after the United States with the highest burden of cases, with over 44 million confirmed cases of COVID-19 and approximately 530 thousand deaths due to the SARS-CoV-2 infection.[2]

The common clinical manifestations of COVID-19 include fever, dry cough, myalgia, fatigue and shortness of breath. Headache, diarrhoea, nausea, vomiting and abdominal pain

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were less common. The SARS-CoV-2 virus enters the target cell after binding the spike glycoprotein present on the surface of the virus to the angiotensin-converting enzyme 2 (ACE2) receptors expressed on the surface of epithelial cells of the lower respiratory tract. This entry is facilitated by transmembrane serine protease 2 (TMRPSS2). Besides the lung, other organs such as heart, kidney, and liver are also infected by the virus. With the evolving pandemic, liver dysfunction has become a frequently reported extra-pulmonary manifestation of COVID-19 pneumonia.[1,3]

Nardo *et al.*[4] has defined liver injury as any liver damage occurring during disease course and treatment of COVID-19 patients with or without pre-existing liver damage. The exact pathological mechanism of SARS-CoV-2-related hepatic dysfunction is not known, but the purported mechanisms are thought to be the combination of direct virus-induced cytopathic effect, immune-mediated inflammatory response, microthrombotic endothelitis, and hypoxic/ischaemic injury.[3-5] Higher expression of ACE-2 receptors in cholangiocytes (59.7%) in comparison to hepatocytes (2.6%) may probably suggest the role of bile duct epithelium in liver injury.[6] However, the markers of bile duct injury or cholestasis (alkaline phosphatase; ALP, gamma-glutamyl transpeptidase; GGT and total bilirubin) are not significantly raised in the majority of studies. Cytokine storm is another mechanism attributable to abnormally elevated liver enzymes. This may result in excessive and uncontrolled production of early response inflammatory cytokines like interleukin-6 (IL-6), IL-10, IL-2 and interferon-gamma. The rise in inflammatory cytokines levels mirrors the magnitude of tissue and organ damage and death.[3,7]

The clinical spectrum of the disease varies from asymptomatic to life-threatening manifestations such as acute respiratory distress syndrome or multiorgan failure. Severe COVID-19 illness, male sex, older age, underlying liver disease, cough as initial symptom, and higher body mass index are commonly associated risk factors for developing liver dysfunction.[8] Abnormal liver functions have been reported in 14-53% of individuals with SARS-CoV-2 infection during hospitalisation, and this has been linked to severity as well as outcome of disease.[6] Most of the literature is reported from the western population, with very few studies on this topic from India. This is the first study of its kind with the largest sample size from the sub-Himalayan region. We planned this retrospective study to evaluate the incidence of abnormal liver function at admission and its clinical importance in assessing the severity of disease.

Study setting

Shri Lal Bahadur Shastri Govt. Medical College and Hospital, Mandi, is situated in the north-west of the Himalayas at an altitude of 880 metres. Our college was declared a Dedicated COVID Hospital (DCH) by the state government during the second wave of COVID-19. Moderate to severe COVID-19 patients from district Mandi and neighbouring districts were admitted at the DCH.

Study design

We conducted a retrospective study. Medical records of confirmed COVID-19 adult patients admitted to DCH Mandi from 21 April 2021 to 21 May 2021 were analysed after taking approval from Institutional Ethics Committee.

Study population

Adults aged 18 years and above were included in the study. Diagnosis of COVID-19 was based on positive rapid antigen test/reverse transcriptase polymerase chain reaction (RT-PCR) in oropharyngeal/nasopharyngeal swabs for SARS-CoV-2. Categorisation of severity was performed as per National COVID-19 Management Protocol version 3, 2020, issued by the Ministry of Health and Family Welfare, India. Severe COVID-19 pneumonia was defined as 'adult with clinical signs of pneumonia plus one of the following: respiratory rate >30 breaths/min, severe respiratory distress, SpO_2 <90% on room air'.[9]

Patients with insufficient medical records, with a history of underlying liver disease including liver cancer, cirrhosis, chronic hepatitis B, mild COVID-19 illness and pregnant females were excluded from the study.

Data collection

Hospital records of the patients admitted in the COVID ward and intensive care unit were collected and analysed for the pattern of abnormal liver function test (LFT) at admission. Demographic details including age, sex and place of residence, symptoms and their duration, duration of hospital stay, and comorbidities details were extracted from the medical records.

Normal reference range for normal LFTs was: (1) alanine aminotransferase (ALT)—2-41 U/L, (2) aspartate aminotransferase (AST)—2-40 U/L, (3) total bilirubin—0.1-1 mg/dl, (4) alkaline phosphatase (ALP)—40-129 U/L, and (5) albumin—3.4-5.0 g/dl. Abnormal liver functions were defined as any parameter more than the upper limit of normal value (ULN).

As there are no consensus guidelines to define liver injury in patients with COVID-19 illness, we classified the pattern of liver injury as hepatocellular, cholestatic or mixed in our study. The hepatocellular injury was defined as ALT and/or AST more than 3 × ULN; cholestatic injury as ALP or GGT 2 × ULN; and mixed liver injury as a combination of both ALT/AST elevated more than 3 × ULN and ALP/GGT twice ULN.[10]

Statistical analysis

Quantitative data was presented as mean ± standard deviation (SD) or mean and interquartile range, as appropriate. The normality of quantitative data was checked by Kolmogorov–Smirnov tests of normality. For normally distributed data, means were compared using an unpaired *t*-test, for skewed data or scores Mann–Whitney test were applied. For categorical variables, numbers and percentages were calculated. Pearson Chi-square method and Fisher's exact test were used to compare the

categorical variable. All calculations were performed using SPSS trial version 20 (Chicago, IL). A p value of <0.05 was considered to indicate statistical significance.

Results

Profile of study participants

Out of 344 patients included in the study, 206 (59.9%) were males and 138 (40.1%) were females, with male: female ratio of 1.5:1. The mean age of the study participants was 54.69 ± 16.05 years (mean ± SD). 133 (38.7%) patients were above the age of 60 years (p=0.004; not shown in table). The time from the onset of symptom to hospital admission was 4.34 ± 3.38 days. The mean (SD) duration of hospital stay was 9.74 ± 7.34 days. The most common symptom reported by the patients was dyspnoea (75.6%), followed by fever (54.1%) and cough (52.3%). Hypertension (28.5%), followed by diabetes mellitus (22.1%) and coronary artery disease (4.1%), were the most common comorbidities observed in the study participants. 78.49% of the patients with severe COVID-19 pneumonia had abnormal liver functions at the time of admission. A total of 241 (70.06%) were discharged, and 103 (29.94%) patients died during hospital stay [Table 1]. Out of 103 deaths, 89 patients (86.41%; p=.019) had abnormal liver function at presentation. All four patients requiring mechanical ventilation could not survive. Out of 47 patients put on noninvasive ventilation (high flow nasal cannula; HFNC and continuous positive airway pressure; CPAP), 10 (21.3%) patients survived (not shown in table).

Normal versus abnormal liver function tests

Out of 270 patients with abnormal LFTs, 50.74% had liver function results higher than 2 × ULN [Table 2]. The patients with abnormal liver functions were younger (53.41 ± 15.71 years) than those with normal liver function (59.38 ± 16.51 years). Mean ALT was higher in patients with age <55 years (112.04 ± 79.16 IU/L) in comparison to patients with age >55 years (101.26 ± 80.39 IU/L). A significant difference (p<0.022) in abnormal liver function was observed among the various age groups. Incidence of liver dysfunction was more in the 46-60 years age group (30.4%) followed by the 31-45 years age group (27.8%) and 61-75 years age group (26.7%). Derangement of liver function was significantly higher in males (64.1%, p=0.003) than in females (35.9%). The duration of hospital stay among patients with normal liver function was 10.04 ± 7.76 days and 9.39 ± 6.05 days among patients with abnormal LFTs. Shortness of breath was a common symptom among both groups. Hypertension (28.1%) was the most common comorbidity among the patients with abnormal liver functions, followed by diabetes mellitus (18.5%) and coronary artery disease (4.8%). AST levels are elevated in 224 (82.96%) patients with mean AST level of 86.03 ± 72.40 U/L in the abnormal liver function group. The difference in the distribution of AST at different levels between the two groups was statistically significant (p< 0.001). Two hundred and three (75.19%) of the study participants had elevated ALT levels at admission. Mean ALT level was 88.74 ± 76.96 U/L in the patients with abnormal liver function. The difference in distribution of ALT at different levels between the two groups was statistically significant (p<0.001). The mean total bilirubin was 0.61±0.0.49 mg/dl in patients with abnormal liver function (p=0.149). Serum alkaline phosphatase was elevated in 79 patients out of 270. The mean serum ALP was 122.36 ± 75.0 IU/L in the study participants with abnormal liver function. The difference in the distribution of

Table 1: Baseline characteristics of study population with normal and abnormal LFTs*

Variable	Total (*n*=344)	Normal LFT (*n*=74)	Abnormal LFT (*n*=270)
Age (years, SD)	54.69±16.05	59.38±16.51	53.41±15.71
Gender			
Male (*n*, %)	206 (59.9%)	33 (44.6%)	173 (64.1%)
Female (*n*, %)	138 (40.1%)	41 (55.4%)	97 (35.9%)
Symptoms duration before admission	4.34±3.38	4.51±3.72	4.30±3.29
Duration of hospital stay (days)	9.74±7.34	10.04±7.76	9.39±6.05
Fever (*n*, %)	186 (54.1%)	43 (58.1%)	143 (53.0%)
Cough (*n*, %)	180 (52.3%)	36 (48.6%)	144 (53.3%)
Shortness of breath (*n*, %)	260 (75.6%)	53 (71.6%)	207 (76.7%)
Myalgias (*n*, %)	21 (6.1%)	6 (8.1%)	15 (5.6%)
Gastrointestinal symptoms (*n*, %)	12 (3.49%)	4 (5.4%)	8 (3.0%)
Comorbidities			
DM† (*n*, %)	76 (22.1%)	26 (35.1%)	50 (18.5%)
HTN‡ (*n*, %)	98 (28.5%)	22 (29.7%)	76 (28.1%)
CAD§ (*n*, %)	14 (4.1%)	1 (1.4%)	13 (4.8%)
CKD‖ (n, %)	9 (2.6%)	2 (2.7%)	7 (2.6%)
Hypothyroidism (*n*, %)	10 (2.9%)	2 (2.7%)	8 (3.0%)
Serum Total Bilirubin	0.577±0.449	0.46±0.28	0.61±0.0.49
Aspartate aminotransferase (AST)	73.677±68.402	28.61±6.72	86.03±72.40
Alanine aminotransferase (ALT)	74.701±73.142	24.57±8.23	88.74±76.96
Alkaline phosphatase (ALP)	114.439±68.984	85.53±23.56	122.36±75.0
Serum albumin	3.422±0.502	3.43±0.63	3.42±0.47

*LFT: liver function tests, †DM: Diabetes mellitus, ‡HTN: Hypertension, §CAD: coronary artery disease, ‖CKD: chronic kidney disease

Table 2: Comparison of liver function tests at admission in patients (normal versus abnormal liver function)

Variable	Normal LFT (*n*=74)	Abnormal LFT (*n*=270)	*P*
Age (years)			
<30	1 (1.4%)	17 (6.3%)	0.022
31-45	17 (253%)	75 (27.8%)	
46-60	21 (28.4%)	82 (30.4%)	
61-75	19 (25.7%)	72 (26.7%)	
>75	16 (21.6%)	24 (8.9%)	
Sex			
Male (*n*, %)	33 (44.6%)	173 (64.1%)	0.003
Female (*n*, %)	41 (55.4%)	97 (35.9%)	
Aspartate aminotransferase (U/L)			
<40	74 (100%)	46 (17%)	<.001
1-2 ULN*	0 (0.0%)	129 (47.8%)	
2-3 ULN	0 (0.0%)	46 (17.0%)	
>3 ULN	0 (0.0%)	49 (18.1%)	
Alanine aminotransferase (U/L)			
<40	74 (100%)	67 (24.8%)	<.001
1-2 ULN	0 (0.0%)	102 (37.8%)	
2-3 ULN	0 (0.0%)	48 (17.8%)	
>3 ULN	0 (0.0%)	53 (19.6%)	
Total serum bilirubin (mg/l)			
<1	74 (100%)	247 (3.3%)	0.149
1-2	0 (0.0%)	17 (6.3%)	
2-3	0 (0.0%)	4 (1.5%)	
>3	0 (0.0%)	1 (0.4%)	
Alkaline phosphatase (U/L)			
<135	73 (98.6%)	191 (70.7%)	<.001
1-2 ULN	1 (1.4%)	66 (24.4%)	
2-3 ULN	0 (0.0%)	10 (3.7%)	
>3 ULN	0 (0.0%)	3 (1.1%)	
Serum albumin (g/L)			
<3.5	46 (62.2%)	143 (53%)	0.188
>3.5	28 (37.8%)	127 (47.0%)	
Outcome			
Discharge	60 (81.1%)	181 (67.0%)	0.022
Death	14 (18.9%)	89 (33%)	

*ULN: Upper limit of normal

ALP levels at different levels between the two study groups was significant (p<0.001). However, the mean serum albumin was decreased in both groups, but this decrease was not statistically significant (p=.188). In-hospital deaths due to severe COVID-19 were significantly higher in patients with abnormal liver function (33%, p=0.022) compared to patients with normal liver functions (18.9%). [Tables 1 and 2]

Thirty per cent of the patients with abnormal liver functions had liver injury in our study. The most common pattern of injury was hepatocellular (83.95%), followed by mixed (8.64%) and cholestatic (7.41%), respectively. Mortality was higher in patients with hepatocellular liver injury (48.53%) compared to mixed (28.57%) and cholestatic pattern (16.67%).

Analysis of liver function test results in survivors and non-survivors at time of admission

The mean age of nonsurvivor group was higher than survivors (58.56 ± 14.75 years vs. 53.04 ± 16.33 years). 143 (59.34%) male patients and 98 (40.67%) female patients with COVID-19 illness survived. Out of 103 deaths, 63 (61.17%) were males, and 40 (38.83%) were females. The duration of hospital stay among survivors was 10.5 ± 7.7 days and 7.97 ± 6.08 days among nonsurvivors. Shortness of breath was the most common symptom among survivors (74.3%) and nonsurvivors (78.4%) [Table 3]. Elevated AST levels were observed in 224 out of 344 patients at admission. Mean AST levels were 66.39 ± 58.62 U/L and 90.72 ± 85.04 U/L in the survived and non-survived groups, respectively. The difference in the distribution of AST at different levels between the two groups was statistically significant (p<0.001). Two hundred and three of the study participants had elevated ALT levels at admission. The mean ALT level in the non-survived group (82.34 ± 81.05 U/L) was higher than the survived group (71.44 ± 69.41 U/L). On comparing the ALT levels at different levels between the two study groups, no significant difference was observed (p<0.765). The mean total bilirubin was. 36±0.60 mg/dl and. 60±0.68 mg/dl in survived and non-survived groups (p < 0.065). Serum ALP was elevated in 81 patients out of 344. The mean serum ALP was 114.439 ± 68.984 IU/L in the study participants. The difference in the distribution of serum ALP at different levels between the two study groups was significant (p=0.005). The mean serum albumin was decreased in both the survived group (3.49±.63) as well as the non-survived group (3.31±.52). However, the decrease in the mean serum albumin in the non-survived group was more and statistically significant (p =0.011). as compared survived group [Table 4].

Discussion

After the respective analysis of clinical parameters and liver function results in patients admitted at DCH Mandi, Himachal Pradesh, we found that moderate to severe COVID-19 pneumonia affected the people more in the age group of 45-75 years (56.4%) with male predominance and high mortality rate (61.17%). At admission, 78.49% of the study population had abnormal liver function tests with high mortality compared to the group with normal liver functions. Liver dysfunction was more in males and in patients <55 years of age. Prevalence of elevated AST, ALP and hypoalbuminemia was more common in the non-survived group.

Liver dysfunction was more common in younger patients with COVID-19 illness as compared to older patients with a higher elevation in ALT levels in patients with age <55 years in our study, which is in accordance with previous studies.[11-13] However, several other studies have shown contradictory results.[14-17] Higher incidence of abnormal liver functions in younger patients can be attributed to overwhelming immune and inflammatory responses to infection.[16] Median age in non-survivors with liver dysfunction is >55 years. This finding is similar to previous studies worldwide.[18,19]

A male predominance was observed in the abnormal liver function group as well as in the non-survivors group in our study, and

Table 3: Baseline characteristics of severe COVID-19 pneumonia patients admitted in DCH

Variable	Total (*n*=344)	Survived (*n*=241)	Non-survived (*n*=103)
Age (years, SD)	54.69±16.05	53.04±16.329	58.56±14.75
Sex			
Male (*n*, %)	206 (59.9%)	143 (59.34%)	63 (61.17%)
Female (*n*, %)	138 (40.1%)	98 (40.67%)	40 (38.83%)
Symptoms duration before admission	4.34±3.38	4.38±3.43	4.25±3.29
Duration of hospital stay (days)	9.74±7.34	10.5±7.7	7.97±6.08
Fever (*n*, %)	186 (54.1%)	133 (55.2%)	53 (51.5%)
Cough (*n*, %)	180 (52.3%)	129 (53.5%)	51 (49.5%)
Shortness of breath (*n*, %)	260 (75.6%)	179 (74.3%)	81 (78.4%)
Myalgias (*n*, %)	21 (6.1%)	15 (6.2%)	6 (5.8%)
Gastrointestinal symptoms (*n*,%)	12 (3.49%)	7 (2.9%)	5 (4.9%)
DM† (*n*, %)	76 (22.1%)	56 (23.2%)	20 (19.4%)
HTN‡ (*n*, %)	98 (28.5%)	67 (27.8%)	31 (30.1%)
CAD§ (*n*, %)	14 (4.1%)	9 (3.7%)	5 (4.9%)
CKD‖ (*n*, %)	9 (2.6%)	7 (2.9%)	2 (1.9%)
Hypothyroidism (*n*, %)	10 (2.9%)	6 (2.5%)	4 (3.9%)
Parameters			
Serum total bilirubin	0.577±0.449	0.36±0.60	0.60±0.68
Aspartate aminotransferase	73.677±68.402	66.39±58.62	90.72±85.04
Alanine aminotransferase	74.701±73.142	71.44±69.41	82.34±81.05
Alkaline phosphasphatase	114.439±68.984	109±67.51	126.31±71.12
Serum albumin	3.422±0.502	3.49±0.63	3.31±0.52

*LFT: liver function tests, †DM: Diabetes mellitus, ‡HTN: Hypertension, §CAD: coronary artery disease, ‖CKD: chronic kidney disease

this finding was consistent with previous studies.[8,11,13,15] On the contrary, Zhang *et al.*[20] have reported a female dominance (53%) in their study with a higher risk of cumulative liver biochemistry abnormality or injury in females than in males (OR = 2.09; 95% CI: 1.46 to 3.06).

In our study, a higher incidence of elevated AST and ALT and hypoalbuminemia were observed in the study participants. More than three-fourths of our study population (78.49%) had abnormal liver function at admission. In previous studies, an overall incidence of abnormal liver chemistries has been reported in 2.5%-76.3% of hospitalised patients.[4] The incidence of abnormal liver functions ranges from 1.1%-68% in COVID-19 pneumonia at initial presentation.[21] In our study, we also observed that 83% (p<0.001) and 74.8% (p<0.001) of the patients had significantly raised levels of AST at admission and in non-survivors, respectively. ALT was also significantly elevated in patients with abnormal liver function (75.19%, p<0.001). Among both the transaminases, aspartate and alanine, elevation in AST levels was a dominant finding in our study, similar to the previous clinical data. Kaushik *et al.*[15] have found that AST was elevated in 45.71% of the patients with COVID-19. The multicentric retrospective study by Fang Lei *et al.*[22] found significantly elevated levels of AST at admission and in severe patients as compared to non-severe patients. These higher AST levels were associated with a significantly increased risk of all-cause mortality.[10,16,22] In a meta-analysis, the pooled incidence of AST elevation was 22.5% at admission.[21] Prevalence of elevated AST was 4%-53% and 58% in the Chinese cohorts and US cohorts, respectively.[4] The higher incidence of raised AST in our study may be due to the inclusion of patients with severe COVID-19 illness only.

Hepatocellular liver injury (83.95%) was more common in our study. This was in concordance with previous studies where hepatocellular injury was more common.[23] Mixed-type liver injury (43.4%) was more common, followed by cholestatic (29.25%) and hepatocellular injury (20.7%) in the study conducted by Cai Q *et al.*[10]

In our study, 54.9% of the study population had hypoalbuminemia at the initial presentation. In a meta-analysis, 80.4% of the patients had hypoalbuminemia.[13] We found that patients with hypoalbuminemia had a higher mortality rate of 65% vs. 35% in the normal albumin group (p=0.011). Huang *et al.*[24] had found an inverse association between the level of albumin and risk of death independent of age and other complications in patients with COVID-19 illness. Albumin is a negative acute phase reactant indicative of severe disease. Poor nutritional status and uncontrolled release of acute-phase cytokines in severe COVID-19 illness may play an important role in decreased synthesis of albumin in liver.[23] However, the mean time from onset of symptom to admission is 4.34 ± 3.38 days in our study which is less than the half-life of serum albumin and, therefore, less likely to explain the decreased synthesis of albumin in COVID-19. On the other hand, increased capillary permeability resulting in the escape of albumin to interstitial space can explain hypoalbuminemia in severe COVID-19. This is also a common finding in many inflammatory diseases.[24]

Inflammatory cytokine storm is one of the proposed mechanisms in the pathophysiology of COVID-19. Several studies showed that inflammatory markers like ESR, CRP, serum ferritin, IL-6 and D-dimer levels correlated with the severity of illness. Hwaiz *et al.*[25]

Table 4: Comparison of liver function tests at admission between survived and non-survived COVID-19 patients

Variable	Survived (*n*=241)	Non-survived (*n*=103)	*P*
Age (years)			
<30	17 (7.1%)	1 (1%)	0.027
31-45	70 (29.0%)	22 (21.4%)	
46-60	73 (30.3%)	30 (29.1%)	
61-75	56 (23.2%)	35 (34.01%)	
>75	25 (10.4%)	15 (14.6%)	
Sex			
Male	143 (59.3%)	63 (61.02%)	0.300
Female	98 (40.7%)	40 (38.8%)	
Abnormal liver functions	181 (75.1%)	89 (86.4%)	0.019
Aspartate aminotransferase (U/L)			
<40	94 (39.0%)	26 (25.2%)	0.001
1-2 ULN*	90 (37.7%)	39 (37.9%)	
2-3 ULN	34 (14.1%)	12 (11.7%)	
>3 ULN	23 (9.5%)	26 (25.2%)	
Alanine aminotransferase (U/L)			
<40	103 (42.7%)	38 (36.9%)	0.765
1-2 ULN	70 (29%)	32 (31.1%)	
2-3 ULN	33 (13.7%)	15 (14.6%)	
>3 ULN	35 (14.5%)	18 (17.5%)	
Total serum bilirubin (mg/dl)			
<1	91 (88.3%)	321 (93%)	0.065
1-2	10 (9.7%)	18 (5.2%)	
2-3	2 (1.9%)	4 (1.2%)	
>3	0 (0%)	1 (0.3%)	
Alkaline phosphatase (IU/L)			
<135	195 (81.2%)	68 (66.0%)	0.005
1-2 ULN	35 (14.6%)	32 (31.1%)	
2-3 ULN	8 (3.3%)	2 (1.9%)	
>3 ULN	2 (.81%)	1 (1%)	
Serum albumin (g/dl)			
<3.5	121 (50.2%)	67 (65.0%)	0.011
>3.5	120 (49.8%)	36 (35%)	

*ULN: Upper limit of normal

reported higher levels of CRP and IL-6 in patients with abnormal liver functions. Abdelrahman *et al.*[26] showed that higher ferritin levels could be potential risk factors for LFT abnormalities. So, it can be concluded that inflammatory cytokine storm could be responsible for liver function derangement too.

Our study's mortality rate was 29.9%, with significantly higher mortality in patients with abnormal liver function on admission compared to those with normal liver functions (33% vs. 18.9%; p<0.022). Mendizabal *et al.*[11] had also reported a significantly higher mortality rate in patients with elevated liver test results on admission than those with normal liver tests. (18.7% vs. 12.2%; p<0.0001). In a recent meta-analysis, non-survivors had a higher risk of presenting with abnormal liver functions on admissions than survivors (OR = 3.46).[21]

Limitations

This was a single-centre retrospective study. Patients with mild and asymptomatic COVID-19 illness were not included in the study because our institute was declared DCH by the state government. In contrast, only those with moderate to severe COVID-19 illness were admitted. Patients with underlying liver disease were excluded based on history only. Serial levels of LFTs were not included in the analysis.

Conclusion

Our study showed that liver dysfunction was present in more than three-fourths of patients at admission, more common in younger than older populations. Patients with deranged LFTs were at higher risk of severe illness and poor outcomes. LFT is widely available and cost-effective and can be used as an ancillary marker of severity and mortality especially when inflammatory markers could not be performed due to infrastructural/affordability issues.

Take home message

LFT can be utilised as diagnostic and prognostic marker in severe COVID-19 illness. Further research is required to validate the results.

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Conflicts of interest

There are no conflicts of interest.

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