ORIGINAL RESEARCH

Liver dysfunction and its correlation with the severity and mortality of coronavirus disease 2019

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ABSTRACT

Background: Since the emergence of coronavirus disease 2019 (COVID-19), the impact of the disease on various organs, including the liver, has been a subject of investigation. Reports have shown liver dysfunction in COVID-19 patients, and its association with severity and mortality remains of interest. **Aim:**To evaluate the prevalence of liver dysfunction and its correlation with severity and mortality in patients with COVID-19 infection. **Methods:** This cross-sectional observational study was conducted between June 2021 and December 2022 in a hospital setting. Patients diagnosed with moderate to severe COVID-19 were included and categorized into two groups based on disease severity. Data of liver function tests, viral markers, inflammatory markers, and patient mortality were recorded at regular intervals during hospitalization and post-discharge. **Results:** A total of 500 COVID-19 patients, with a mean age of 46.12 years were included in the study.Sixty four percent of patients had severe COVID-19 infection, while 36% had moderate infection.Liver dysfunction were significantly higher in patients with severe COVID-19 infection compared to those with moderate infection($p<0.001$).The moderate COVID-19 group had 80.34% of survivors (143/178) whereas, the severe COVID-19 group had 21.74% of survivors (70/322).Serum bilirubin, direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and prothrombin time-international normalized ratio (PT-INR) exhibited a significant correlation with the inflammatory markers C-reactive protein (CRP) and ferritin ($p\leq0.001$ for each). **Conclusion:**The present study indicates a higher prevalence of liver dysfunction among patients with COVID-19, especially among those with severe infection. Patients with liver dysfunction might hold higher odds of severity and mortality of COVID-19 infection.

Keywords: COVID-19, liver dysfunction, severity, mortality, inflammatory markers

INTRODUCTION

In December 2019, a highly contagious severe acute respiratory syndrome emerged in China, caused by a new type of coronavirus. Initially labelled as 2019 novel coronavirus (2019-nCoV), it was later designated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1,2]On 11 March 2020, the World Health Organization (WHO) declared the coronavirus disease of 2019(COVID-19) as a pandemic, which has resulted in more than 760 million infections, with 6,952,522 deaths worldwide.In India,44 million are infected, with 531,915 deaths until 26 July 2023.[3,4]

Although the respiratory system is the primary target of SARS-CoV-2, it has the ability to impact other significant organ systems, including the gastrointestinal tract (GI), liver, cardiovascular system, central nervous system, and kidneys.[5]These occurrences indicate a broader immunopathological response or the spread and replication of the SARS-CoV-2 outside of the lungs.

Several reports have emerged regarding the impact of COVID-19 on various organs, with some studies highlighting the presence of liver disease at different levels in affected patients. A recent investigation demonstrated that the SARS-CoV-2 virus binds to angiotensin-converting enzyme-2 receptors on cholangiocytes, leading to their dysfunction. This process has the potential to cause liver injury by triggering a systemic inflammatory response.[6]According to a systematic review conducted in September 2020, the cumulative prevalence of acute liver injury was estimated at 23.7 per 100 patients with COVID-19.[7]Severalstudies

conducted in hospitals have documented liver injury in COVID-19 patients, characterized by increased levels of liver enzymes, namely, aspartate aminotransferase (AST) and alanine aminotransferase (ALT). These enzyme levels have been found to rise by 14% to 53% compared to their standard levels.[8-11]Moreover, liver biopsy samples from a deceased COVID-19 patients revealed the presence of moderate microvesicular steatosis, along with mild lobular and portal activity, suggesting the potential involvement of SARS-CoV-2 in causing liver damage.[12]Therefore, this study aimed to evaluate the prevalence of liver dysfunction and its correlation with severity and mortality in patients with COVID-19 infection.

MATERIAL AND METHODS

Study design

This cross-sectional, observational study was conducted at the Department of Gastroenterology, IGIMS, Patna fromJune 2021 to December 2022. The study was conducted in accordance with the principles of the Declaration of Helsinki. The study protocol also metthe requirements of the Ethical Guidelines for Medical and Health Research and was approved by the Institutional Ethics Committee. Writteninformed consent was obtained from each patient prior to the study commencement.

Study population

Patients of either sex (≥18 years of age), diagnosed with moderate to severe COVID-19 and confirmed by reverse transcription-polymerase chain reaction (RT-PCR) from nasopharyngeal swab were included. Patients with history of liver disease, alcoholism, viral hepatitis, malignancy and pregnant women were excluded from the study. Patients on drugs causing liver dysfunction were also excluded.

Data collection

The eligible patients were divided into two groups; those with moderate COVID-19 infection and those with severe COVID-19 infection. Patients were treated as per the national guidelines of treatment for COVID-19 (COVID-19 Management Protocol AIIMS, New Delhi). Data of laboratory examinations including liver function test (LFT), viral markers, inflammatory markers[C-reactive protein (CRP), lactate dehydrogenase (LDH), D-dimer and ferritin]and patient mortalitywererecordedevery alternate date till discharge. Patients were followed during the entirehospitalization course and once weekly after discharge for a month.

Definitions

a) Moderate COVID-19: Patients with pneumonia and no signs of severe disease, but exhibiting clinical features of dyspnea and/or hypoxia, fever, cough, including oxygen saturation <94% (range 90–94%) on room air, respiratory rate ≥24 breaths/min.
b) Severe COVID-19: Patients with respiration rate ≥30 breath/min, oxygen saturation ≤93%, partial pressure of oxygen/fraction of inspired oxygen ≤300 mmHg, or multiple organ or respiratory failure that requires intensive care unit (ICU) monitoring and treatment.

Statistical analysis

Statistical analysis was done using Statistical Package for theSocial Sciences (SPSS) software, version 20. Descriptive statistics summarized categorical variables using frequency and percentages, while continuous variables were presented as mean and standard deviation (SD). Correlation of liver dysfunction with severity, mortality of COVID-19 and with inflammatory markers was studied.A p-value of ≤0.05 was considered as statistically significant.

RESULTS

The study included a total of 500 patients with COVID-19, with a mean age of 46.12 years. The majority ofpatients were men (81.0%). Most of the patients aged >47 years (48.0%). In terms of COVID-19 severity, 64.0% of patients had severe disease, while 36.0% had moderate disease. The mean levels of the inflammatory markers namely, CRP, LDH, D-dimer, and ferritin were 30.25 mg/L, 333.35 U/L, 4.24 µg/mL, and 419.33 ng/mL, respectively (Table 1).

Table 2 represents the prevalence of liver dysfunction in patients with COVID-19. A higher proportion of patients with COVID-19 exhibited LFT abnormalities with elevation in serum bilirubin >1mg/dL (98.60%), direct bilirubin >0.20 mg/dL (89.20%), AST >40 U/L (100%), ALT >45 U/L (100%),alkaline phosphate >120 U/L (100%), prothrombin time-international normalized ratio (PT-INR) >1.5 (99.40%), and decrease in serum albumin <3.5 g/dL (89.00%).

Among the patients with moderate COVID-19 (n=178), 143 patients (80.34%) were survivors, while 35 (19.66%) were non-survivors. In contrast, the severe COVID-19 group (n=322)had 70 survivors (21.74%) and 252 non-survivors (78.26%). Table 3 shows the LFT of survivors with moderate and severe COVID-19. Throughout the study period, the mean levels of serum bilirubin, direct bilirubin, AST, ALT, alkaline phosphate, and PT-INR were significantly higher in patients with severe COVID-19 compared to those with moderate COVID-19 ($p<0.001$, each).Additionally, the mean serum albumin levels were significantly lower in patientswith severe COVID-19 than in patientswith moderate COVID-19($p<0.001$).Table 4 shows the LFT of non-survivors with moderate and severe COVID-19. Among the non-survivors, a similar trend of significantly higher mean serum bilirubin, direct bilirubin, AST, ALT, alkaline phosphate, and PT-INR were observed in patients with severe COVID-19 compared to those with moderate COVID-19 ($p<0.0001$, each).

Supplementary table 1 represents the comparison of LFT between COVID-19 survivors and non-survivors on day 1,day 3, and day 5 of hospitalization. The non-survivors exhibited significantly higher levels of serum bilirubin, PT-INR, AST, ALT, and alkaline phosphate than the survivors ($p<0.001$ for all).

A correlation analysis to investigate the relationship between liver dysfunction and various inflammatory markers in patients with COVID-19 is presented in Table 5. Serum bilirubin, an important liver function indicator, showed positive correlation with CRP (Pearson correlation coefficient, $r=0.567$, $p<0.001$), LDH ($r = 0.367$, $p<0.001$), and ferritin ($r=0.433$, $p<0.001$). Similarly, the liver function parameters direct bilirubin, ALT, AST, and PT-INR exhibited a significant correlation with the inflammatory markers CRP and ferritin ($p\leq0.001$, each).

Table 1: Baseline characteristics of the study population

Parameters	Number of patients (N=500)
Age (years), mean(SD)	46.12 (15.23)
Age group (years)	
18-27	77 (15.40)
28-37	92 (18.40)
38-47	91 (18.20)
Above 47	240 (48.00)
Gender	
Men	403 (81.00)
Women	97 (19.00)
Severity of COVID-19	
Severe	322 (64.00)
Moderate	178 (36.00)
Inflammatory markers, mean (SD)	
CRP, mg/L	30.25 (16.29)
LDH, U/L	333.35 (102.65)
D-Dimer, µg/mL	4.24 (6.54)
Ferritin, ng/mL	419.33 (113.33)
Data presented as n (%), unless otherwise specified. COVID-19, coronavirus disease 2019; CRP, C-reactive protein;D-dimer, dimerized plasmin fragment D; LDH, lactate dehydrogenase;SD, standard deviation.	

Table 2: Prevalence of liver dysfunction in patients with COVID-19

LFT Parameters	Number of patients (N=500)
Serum bilirubin (mg/dL), mean (SD)	2.23 (0.63)
<1	7 (1.40)
>1	493 (98.60)
Direct bilirubin (mg/dL), mean (SD)	0.83 (0.42)
<0.20	54 (10.80)
>0.20	446 (89.20)
AST (U/L), mean (SD)	220.99 (76.02)
<40	0
>40	500 (100.00)
ALT (U/L), mean (SD)	242.78 (108.19)
<45	0
>45	500 (100.00)
Alkaline phosphate (U/L), mean (SD)	223.28 (51.09)
<120	0
>120	500 (100.00)
PT-INR, mean (SD)	2.43 (0.58)
<1.5	3 (0.60)
>1.5	497 (99.40)
Total protein (g/dL), mean (SD)	6.98 (0.66)
<6	20 (4.00)
>6	480 (96.0)
Serum albumin (g/dL), mean (SD)	3.87 (0.31)
<3.5	445 (89.00)

>3.5	55 (11.00)
Data presented as n (%), unless otherwise specified. ALT, alanine aminotransferase; AST, aspartate aminotransferase; LFT, liver function test; PT-INR,prothrombin time-international normalized ratio.	

Table 3: Liver function tests of survivors among patients with moderate and severe COVID-19

Liver parameter	COVID-19 severity	Day 1	Day 3	Day 5	Day 7	1 Week	2 Week	3 Week	4 Week	p-value
Serum bilirubin (mg/dL)	Moderate	1.58 (0.42)	1.48 (0.38)	1.35 (0.40)	1.26 (0.25)	1.12 (0.10)	0.97 (0.16)	1.02 (0.15)	0.98 (0.15)	<0.001
	Severe	2.59 (0.36)	2.83 (0.40)	2.88 (0.50)	2.76 (0.59)	2.48 (0.64)	2.24 (0.65)	1.76 (0.67)	1.49 (0.77)	
Direct bilirubin (mg/dL)	Moderate	0.49 (0.30)	0.50 (0.35)	0.32 (0.24)	0.37 (0.25)	0.27 (0.10)	0.23 (0.07)	0.21 (0.05)	0.22 (0.04)	<0.001
	Severe	1.05 (0.28)	1.25 (0.44)	1.12 (0.49	1.07 (0.54)	1.00 (0.56)	0.89 (0.66)	0.72 (0.61)	0.50 (0.49)	
AST, U/L	Moderate	145.48 (29.60)	134.27 (27.50)	125.96 (32.83)	104.34 (18.98)	94.26 (28.70)	86.03 (28.56)	77.08 (30.73)	56.05 (26.49)	<0.001
	Severe	280.55 (52.71)	280.75 (29.66)	278.60 (23.37)	268.50 (48.79)	232.05 (62.73)	176.51 (70.08)	140.64 (66.23)	92.93 (50.93)	
ALT, U/L	Moderate	131.03 (57.87)	106.03 (36.06)	112.43 (41.43)	86.79 (29.88)	80.24 (15.91)	80.68 (15.43)	75.03 (16.76)	65.15 (18.32)	<0.001
	Severe	301.85 (76.09)	309.69 (64.69)	319.39 (86.74)	282.43 (63.05)	266.04 (71.57)	187.87 (83.65)	141.09 (54.75)	97.44 (36.93)	
PT-INR	Moderate	1.91 (0.96)	2.38 (0.93)	1.78 (0.78)	1.64 (0.84)	1.68 (0.69)	1.54 (0.43)	1.62 (0.34)	1.65 (0.28)	<0.001
	Severe	3.28 (0.37)	3.64 (0.63)	3.21 (0.81)	2.69 (0.63)	2.57 (0.91)	2.23 (0.47)	2.14 (0.24)	2.08 (0.36)	
Alkaline phosphate, U/L	Moderate	207.37 (62.40)	215.28 (58.60)	191.78 (52.21)	183.82 (51.17)	169.27 (37.73)	157.54 (37.42)	155.42 (31.56)	142.92 (29.09)	<0.001
	Severe	237.01 (41.09)	242.98 (51.06)	250.50 (46.34)	239.85 (55.84)	211.20 (49.38)	184.10 (52.20)	151.90 (42.69)	127.47 (24.57)	
Total protein, g/dL	Moderate	7.02 (0.17)	7.04 (0.15)	7.01 (0.19)	7.07 (0.12)	7.08 (0.11)	7.03 (0.11)	6.96 (0.10)	6.99 (0.15)	<0.001
	Severe	6.83 (0.87)	6.69 (0.78)	6.70 (0.78)	6.61 (0.82)	6.51 (0.84)	6.61 (0.83)	6.57 (1.15)	6.54 (1.35)	
Serum albumin,g/dL	Moderate	4.05 (0.10)	3.90 (0.08)	3.89 (0.09)	3.85 (0.14)	3.82 (0.19)	3.79 (0.16)	3.64 (0.26)	3.71 (0.31)	<0.001
	Severe	3.92 (0.27)	3.79 (0.29)	3.77 (0.33)	3.67 (0.39)	3.62 (0.54)	3.62 (0.58)	3.57 (0.64)	3.60 (0.70)	
Data presented as mean (SD). ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; PT-INR,prothrombin time-international normalized ratio.										

Table 4: Liver function tests of non-survivors among patients with moderate and severe COVID-19

Liver parameters	COVID-19 severity	Day 1	Day 3	Day 5	p-value
Serum bilirubin(mg/dL)	Moderate	1.80 (0.37)	1.57 (0.40)	1.37 (0.39)	<0.0001
	Severe	2.60 (0.50)	2.80 (0.40)	2.34 (0.55)	
Direct bilirubin (mg/dL)	Moderate	0.43 (0.14)	0.41 (0.14)	0.27 (0.06)	<0.0001
	Severe	0.95 (0.55)	1.35 (0.45)	0.70 (0.40)	
AST(U/L)	Moderate	134.34 (10.96)	97.14 (22.26)	98.06 (21.82)	<0.0001
	Severe	206 (28.22)	270 (72.51)	322 (112.81)	
ALT(U/L)	Moderate	130.80 (27.77)	80.74 (19.09)	83.57 (11.55)	<0.0001
	Severe	252.24 (97.89)	271.24 (92.89)	304.72 (142.35)	
PT-INR	Moderate	2.21 (0.49)	2.36 (0.56)	1.90 (0.44)	<0.0001
	Severe	3.41 (1.12)	2.95 (0.99)	2.18 (0.38)	

Alkaline phosphate(U/L)	Moderate	167.71 (24.56)	154.40 (23.19)	142.71 (17.41)	<0.0001
	Severe	228 (50.36)	271.50 (74.03)	283 (73.53)	
Total protein (g/dL)	Moderate	7.38 (0.54)	7.46 (0.48)	7.87 (0.71)	<0.0001
	Severe	7.25 (0.15)	6.75 (0.05)	6.79 (0.21)	
Serum albumin(g/dL)	Moderate	3.59 (1.01)	3.75 (1.05)	3.82 (1.30)	<0.0001
	Severe	3.62 (0.17)	3.70 (0.10)	3.55 (0.05)	
Data presented as mean (SD). ALT, alanine aminotransferase; AST, aspartate aminotransferase; COVID-19, coronavirus disease 2019; PT-INR,prothrombin time-international normalized ratio.					

Table 5: Correlation between liver dysfunction and inflammatory markers

Liver Parameters	CRP	LDH	D-dimer	Ferritin
Serum bilirubin	**0.567****	0.367**	0.009	**0.433****
Direct bilirubin	**0.415****	0.480**	0.169**	**0.378****
AST	**0.308****	0.160**	0.047	**0.238****
ALT	**0.492****	0.108*	-0.031	**0.218****
PT-INR	**0.315****	0.232*	0.157	**0.356****
Alkaline phosphate	0.243**	-0.089*	-0.248**	0.053
Totalprotein	-0.246**	-0.129*	0.045	-0.343**
Serumalbumin	-0.031	0.236**	0.198**	-0.145**
Data presented asPearson correlation coefficient. *,p<0.05; **, p≤0.001. ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein, D-dimer, dimerized plasmin fragment D; LDH, lactate dehydrogenase; PT-INR,prothrombin time-international normalized ratio.				

Supplementary Table 1: Liver function tests according to survival in patients with COVID-19

LiverParameters	Survival	Day 1	Day 3	Day 5	p-value
Serum bilirubin, mg/dL	Survivor	0.96 (0.31)	0.57 (0.40)	0.37 (0.09)	<0.001
	Non-Survivor	3.12 (0.47)	2.63 (0.61)	2.15 (0.57)	
PT-INR	Survivor	2.34 (0.11)	1.43 (0.24)	1.27 (0.04)	<0.001
	Non-Survivor	3.54 (0.45)	3.65 (0.54)	4.10 (0.23)	
AST (U/L)	Survivor	121.14 (15.23)	101.12 (12.26)	97.35 (12.39)	<0.001
	Non-Survivor	197.12 (18.22)	212.22 (52.51)	252.14 (82.18)	
ALT (U/L)	Survivor	127.14 (17.77)	71.47 (09.90)	51.28 (13.57)	<0.001
	Non-Survivor	152.24 (87.52)	171.24 (42.69)	274.27 (92.83)	
Alkaline phosphate (U/L)	Survivor	117.31 (14.62)	93.40 (33.24)	67.17 (18.34)	<0.001
	Non-Survivor	158.28 (29.24)	178.96.37 (36.25)	189.34 (53.73)	
Total protein (g/dL)	Survivor	8.34 (0.34)	7.69 (0.57)	7.97 (0.39)	<0.001
	Non-Survivor	8.95 (0.39)	7.12 (0.13)	6.58 (0.12)	
Serum albumin (g/dL)	Survivor	4.89 (0.96)	3.12 (1.21)	2.86 (0.67)	<0.001
	Non-Survivor	3.87 (0.27)	3.29 (0.28)	3.14 (0.0.19)	
Data presented as mean (SD). ALT, alanine aminotransferase; AST, aspartate aminotransferase; PT-INR,prothrombin time-international normalized ratio.					

DISCUSSION

In December 2019, a new type of coronavirus was discovered, belonging to the same family of viruses that are responsible for SARS, Middle East respiratory syndrome (MERS), and the four human coronaviruses that commonly cause the common cold. On 11 March 2020, the WHO declared COVID-19 as a pandemic.[3]After this, the literature was flooded with the impact of this virus on vital organs of the body.

COVID-19 can cause liver damage through multiple pathways: immune-mediated inflammation (cytokine storms and hypoxia), direct viral cytotoxicity, drug-induced hepatotoxicity, reactivation of pre-existing liver disease, and potential hepatitis B reactivation with certain drugs.[13] Hence, the primary objective of this study was to investigate the prevalence of liver dysfunction and its correlation with disease severity and mortality in patients with COVID-19 infection.

The findings of this study were as follows: i) Majority of the patients were men and above 47 years of age; ii) Most of the patients had severe COVID-19 than the

moderate disease; iii) The mean levels of CRP,LDH, D-dimer and ferritin were 30.25 mg/L, 333.35 U/L, 4.24 µg/mL, and 419.33 ng/mL, respectively; iv) A large majority of patients with COVID-19 showed elevation in liver parameters including serum bilirubin, direct bilirubin, AST, ALT alkaline phosphate, PT-INR; v)Among the survivors and non-survivors, the liver function abnormalities were significantly higher in patients with severe COVID-19 than those with moderate COVID-19; vi)The non-survivors exhibited significantly higher levels of serum bilirubin, PT-INR, AST, ALT, and alkaline phosphate compared to survivors; vii)A significant correlation between serum bilirubin, direct bilirubin, AST, ALT, and PT-INR withthe inflammatory markers CRP and ferritin were established ($p \leq 0.001$, each).

In the current study, 81.0% of patients were men. The majority of patients were greater the 45 years of age. On similar lines, ameta-analysis of3062 COVID-19 patients showed that a higher proportion of infected patients were male (56.9%) [14]. Also, in a study by Satapathy SKet al.,[15] the majority of patients were male (59.0%), and aged 60 years or older (63.1%).

The present study exhibited a higher prevalence of liver dysfunction in patients with COVID-19.According to a study by Peiris JSM et al.,[16]liver impairment is common and has been stated in up to 60% of patients suffering from SARS. In a systematic review conducted in September 2020, the cumulative prevalence of acute liver injury was estimated at 23.7 per 100 patients with COVID-19[7]. Patients with COVID-19, particularly those with the severe form, frequently experience LFT abnormalities.[17] The criteria for abnormal liver function include ALT >40 U/L, AST >40 U/L, gamma-glutamyltransferase (GGT) >49 U/L, alkaline phosphatase (ALP) >135 U/L, and total bilirubin (TBIL) >17.1 µmol/L.[18]Likewise, in the present study, AST>40U/L, ALT >45 U/L, alkaline phosphate >120 U/L was found in all the patients followed by serum bilirubin>1mg/dL in 98.60%of patients. Many studies have reported abnormal laboratory test results in patients with COVID-19 disease. Chen et al.[19]reported that 43 out of 99 patients had varying degrees of liver function abnormality, with ALT or AST above the normal range; one patient with severe liver function damage showed ALT 7590 U/L and AST 1445 U/L. In a systematic review and meta-analysisof 128 studies by Kumar et al.,[7]the pooled prevalence of ALT, AST, and hypoalbuminemia was 23.28% (19.92–27.01), 23.41% (18.84–28.70), and 61.27% (48.24–72.87), respectively.Cai et al.[11]reported abnormal liver test in 318 patients with COVID-19 within 2 weeks of hospitalization; with 23.4%, 14.8%, and 11.5% of patients having ALT, AST, and TBIL levels elevated to more than 3×the upper limit of normal, respectively.

In the present study, patients with severe COVID-19, both survivors and non-survivors, exhibited significantly elevated levels of serum bilirubin, direct bilirubin, AST, ALT, PT-INR, and alkaline phosphate compared to those with moderate COVID-19($p<0.001$ for all parameters). Similar observations were made by Abdelrahman et al.,[17] who reported that LFT abnormalities including AST, TBIL, and INR were significantly higher among patients with severe COVID-19 than those with non-severe infection. In a retrospective study by Wang et al.,[20] 56.2% of patients had abnormal ALT, AST, or total bilirubin during the illness; the percentage of patients with elevated both ALT and AST was 12.7% in mild cases vs 46.2% in severe cases.In another meta-analysis by Parohan et al.[21] that included 20 retrospective studies with 3428 COVID-19 infected patients, showed that the incidence of liver injury assessed by AST, ALT, TBIL, and albumin levels seemed to be higher in patients with severe COVID-19 infection.Cai et al. found that serum biochemical indexes of the liver (ALT, AST, and ALP) were significantly higheramong severe patients at admission.During the course of hospitalization,the peak values of ALT (34.5% vs. 7.9%), AST (24.1% vs. 4.6%), and TBIL (24.1% vs. 6.7%) were increased significantly among severe patients compared with non-severe patients.[11]

The massive pro-inflammatory cytokine release caused by SARS-CoV-2 is characterized by elevated CRP, IL-6, LDH, and ferritin concentrations that can result in liver failure and progressive liver damage.[22]In the present study, a significant positive correlation between the liver function parameters (serum bilirubin, direct bilirubin, AST, ALT, and PT-INR) and inflammatory markers (CRP, ferritin) was established ($p \leq 0.001$, each).These findings were supported by Devang et al.,[23] who reported a significant correlation of the inflammatory markers CRP and ferritin with liver enzymes such as AST and ALT ($p<0.05$); ferritin also showed a positive correlation with alkaline phosphate ($p=0.005$). Moreover, Abdelrahman et al.[17] reported that levels of CRP, serum ferritin, and D-dimer were higher in COVID-19 patients with LFT abnormalities than those with normal LFT; high serum ferritin levels might be potential risk factors for LFT abnormalities.

LIMITATIONS

The age distribution of the participants skewed towards older age groups, potentially limiting the generalizability of the findings to younger populations. Additionally, the high worldwide prevalence of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis could confound the interpretation of liver dysfunction specific to COVID-19. Lastly, the small sample size underscores the importance of conducting larger studies to gain a comprehensive understanding of liver enzyme responses and inflammatory markers in moderate and severe COVID-19 cases, enabling more effective prognostication and treatment approaches.

CONCLUSION

The present study indicates a higher prevalence of liver dysfunction among patients with COVID-19, irrespective of their survival. Abnormal liver function was especially more prevalent among those with severe COVID-19 infection, suggesting its potential as a prognostic indicator. The correlation analysis showed positive associations between liver dysfunction and inflammatory markers; suggesting inflammatory markers as valuable biomarkers in the prognosis of COVID-19.Overall, the study suggests that patients with liver dysfunction hold higher odds of severity and mortality of COVID-19 infection. Monitoring liver function is therefore crucial in severe COVID-19 cases, and further research is needed to understand mechanisms and develop targeted interventions for better outcomes.

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