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Mortality risk and associated factors in cirrhosis patients with SARS-CoV-2 infection

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Abstract

Background: *The SARS-CoV-2 virus causes the severe illness known as COVID-19. Globally, liver cirrhosis is a leading cause of death. This study seeks to evaluate the severity of COVID-19 and identify factors that predict mortality in patients with cirrhosis.* ***Patients and methods:*** *The study involved 156 COVID-19 patients, with 78 in the liver cirrhosis group (group 1) and 78 in the non-cirrhosis group (group 2). Each case underwent a clinical examination, general history taking, laboratory and radiological investigations. The severity of liver disease was assessed in cirrhosis patients using the Child-Pugh and MELD scores. Data were collected at presentation and upon ICU admission included mortality rate.* ***Results:*** *The mortality rate was significantly higher in cirrhotic group group (56.4%) compared to non-cirrhotic group (32.1%) (p=0.002). In cirrhotic group, the Child-Pugh and MELD scores were significantly higher in the dead cases compared to the survivors. Multivariate regression analysis identified older age, ICU duration, and presence of chronic kidney disease, cardiovascular disease, hepatoma, dyspnea, ascites, respiratory rate, WBCs, D-dimer level, CRP, serum albumin, and CT CORADS as independent risk factors for mortality in cirrhotic group.* ***Conclusion:*** *Patients with chronic liver diseases had a higher risk of poor outcomes when they got COVID-19 compared to those without liver diseases. Among patients with liver cirrhosis, those who died had significantly higher Child-Pugh and MELD scores than survivors.*

Introduction

The newly discovered severe acute respiratory syndrome coronavirus-2019 (SARS-CoV-2) causes COVID-19, which has infected millions worldwide since December 2019. The disease has a significant morbidity and mortality rate. COVID-19 can manifest in different forms, ranging from mild, self-limiting illness to life-threatening pneumonia. Up to 10% of patients with COVID-19 are thought to experience gastrointestinal symptoms[2]. Global, chronic liver disease (CLD) is one of the top causes of mortality, illness, and resource depletion[3]. Liver cirrhosis and its associated complications currently rank as one of the most common cause of death worldwide. The leading causes of chronic liver disease include hepatitis B and C viruses, alcohol-related liver disease (, and non-alcoholic fatty liver disease (NAFLD)[4]. It has been documented that up to 50% of COVID-19 patients may experience some form of liver dysfunction, which could ultimately lead to unfavourable outcomes [5, 6]. Therefore, it is important to study the impact of COVID-19 on individuals with liver disease to develop better strategies for managing and treating these patients. Understanding the specific risk factors and mechanisms of severe illness in this population can help improve outcomes and reduce mortality[7,8]. This study aimed to determine the severity and predictors of mortality in patients with liver cirrhosis who have contracted SARS-CoV-2.

Patients and Methods

This prospective cohort study was conducted at Minouf Hospital in Menoufia, Egypt, in the gastroenterology, hepatology, and fever departments. The study included 156 SARS-CoV-2-infected individuals of both sexes aged 18 and above. Patients were diagnosed based on clinical presentation (fever, cough, breathing difficulties, or organ failures)[9], laboratory findings (elevation of inflammatory biomarkers such as CRP, ferritin, lactate dehydrogenase, D-dimer, and INR, decreased lymphocyte count, and decreased serum K level)[10], positive RT-PCR result in nasopharyngeal swab specimens[11], and CT chest findings showing patchy consolidation and ground glass opacities (GGO) in the middle and outer zones of the lung[12]. The patients were divided into two groups; Group 1 consisted of 78 patients with liver cirrhosis and Group 2 consisted of 78 patients without cirrhosis.

Exclusion criteria

We excluded cases under 18 years, patients without confirmed clinical or laboratory data for COVID-19 diagnosis, and individuals with contraindications to radiation exposure, such as pregnant women. The research was conducted in accordance with the 2013 revised Helsinki Standards[13]. Approval to conduct the study was obtained from the local ethics committee at the Faculty of Medicine, Benha University (Ms39-3-2022). The medical records were reviewed to gather information including the patient's demographics, current illness history and clinical examination. Patients were assigned to COVID-19 units based on the severity of their admission with the goal of maintaining an acceptable SO2 (>93 percent) and respiratory rate[14]. Laboratory tests

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included complete blood count, liver and kidney functions, serum electrolytes, arterial blood gas (ABG), serum d-dimer level, serum ferritin, and CRP. The Child-Pugh[15], The Model for End-stage Liver Disease (MELD)[16], were used to assessed the severity of liver disease. The study measured hospital stay, time of referral to the Intensive Care Unit (ICU), reasons for ICU referral, ICU stay duration, and patient outcomes (death or survival).

Sample collection

Blood samples were collected following standard venipuncture procedures. Serum was prepared by centrifuging the blood samples at 3000 rpm after collection in a standard vacutainer tube.

Radiological examination

Including chest x-rays and computed tomography (CT), were conducted to assess the severity of COVID-19. Severity was categorized as mild (constitutional and/or upper respiratory tract symptoms with minimal changes on imaging), moderate to severe (lower respiratory tract symptoms, evidence of pneumonia, and/or signs of respiratory failure) and critical (severe pneumonia and respiratory or other organ failure requiring ICU admission[17].

Statistical analysis

We coded, processed, and analyzed the data using the Statistical Package for the Social Sciences (SPSS) version 26 for Windows® (IBM, SPSS Inc, Chicago, IL, USA). Quantitative data, such as percentages and frequencies, were shown. The Kolmogorov-Smirnov test examined the normality of quantitative data. The data was presented as median (interquartile range) or median ± SD based on normalcy. A Chi-Square test, Fisher's exact test, or Monte-carlo test was utilized to compare two groups with categorical variables. With normally distributed quantitative variables, the independent samples (student's) t-test was utilized for group comparisons; in cases where the data did not follow a normal distribution, the Mann-Whitney U-test was employed. For all tests, P values <0.05 are considered significant.

Results

Table 1 shows that there were no significant differences between the two groups in terms of age and gender distribution. Additionally, there were no significant differences in the total duration of hospitalization or time spent in the intensive care unit (ICU). However, the length of non-ICU hospital admission was significantly longer in group II. There were no significant differences in the prevalence of smoking, diabetes mellitus, chronic kidney disease or lung diseases between the two groups. However, the prevalence of hypertension, coronary heart disease, and cerebrovascular diseases was significantly lower in the cirrhotic group compared to the non-cirrhotic group. On the other hand, the prevalence of hepatoma was significantly higher in cirrhotic group compared to non-cirrhotic group. There were no statistically significant differences in the prevalence of fever, sore throat, chest pain, myalgia and diarrhea between the two study groups. However, cough and dyspnea were significantly more prevalent in non-cirrhotic group, while chest tightness, vomiting, abdominal pain, and disturbed conscious level (DCL) were significantly more prevalent in cirrhotic group. In addition, 53.8% of patients in cirrhotic group had ascites. **Table 2** shows that, there were no significant differences in vital signs between the two groups, including temperature, blood pressure, respiratory rate, and heart rate. The only statistically significant differences in the complete blood count were a higher white blood cell count and a higher platelet count in non-cirrhotic compared to cirrhotic group. The levels of D-dimer, ferritin, LDH, ALT, serum creatinine, INR, sodium, potassium, and phosphorus were similar in both study groups. However, the CRP level was significantly higher in non-cirrhotic group. Furthermore, the AST, total bilirubin levels were significantly higher in cirrhotic group. Conversely, albumin level, calcium levels were higher in non-cirrhotic group. The two groups did not differ significantly with respect to the components of the ABG, including vital data such as PCO2, PO2, oxygen saturation, and HCO_3. There was, no statistically significant difference between the two groups in terms of CT chest for CORADS. The highest percentage of CORAD V was observed in both groups. In terms of Child-pugh class, 17 patients (21.8%) were in class A, 39 patients (50%) were in class B, and 22 patients (28.2%) were in class C. The mean MELD score was 18.52 ± 0.94. **Table 3** shows the outcomes in study groups. There was no statistically significant difference in ICU transfer and cause of ICU admission between the studied groups. Acute respiratory distress syndrome (ARDS) was the most common cause for ICU admission in both groups (81.6% in group I and 76.7% in group II). The need for respiratory support was higher in non-cirrhotic (87.2%) compared to cirrhotic (78.2%) group, but the difference was not statistically significant. There was also no significant difference between the two groups in terms of the type of respiratory support used. The mortality rate in group I was 56.4%, significantly higher than in group II (32.1%) (p=0.002). **Table 4** shows the outcome of cirrhotic patients based on clinical scores. There was a statistically significant difference between died patients and discharged patients as regard Child-Pugh class. In died patients, there were 7 patients (15.9%) class A, 19 patients (43.2%) class B and 18 patients (40.9%) class C. In discharged patients of cirrhotic group, there were 10 patients (29.4%) class A, 20 patients (58.8%) class B and 4 patients (11.8%) class C. Also, the MELD score was statistically significantly higher in the died cases as compared to the survived cases in the same group. **Table 5** shows logistic regression analysis for factors predictive of death in the cirrhotic cases. The univariate regression analysis showed that older age, longer ICU stay, presence of chronic kidney disease, cardiovascular disease, hepatoma, cough, dyspnea, diarrhea, DLC, ascites, respiratory rate, WBCs, D Dimer level, CRP, seum albumin, INR, CT CORADS were associated with higher odds of mortality. Conversely, longer stay in the non-ICU, serum albumin, PO2, SO2 (%), were associated with lower odds of mortality. Multivariate regression analysis identified older age, ICU duration, presence of chronic kidney disease, cardiovascular disease, hepatoma, cough, dyspnea, DCL, diarrhea, ascites respiratory rate, WBCs, D Dimer level, CRP, serum albumin and CT CORADS as independent risk factors for mortality.

Table 1. Baseline demographic and clinical data of study patients.

Variables		Group I (Cirrhotic) (N = 78)		Group II (Non-cirrhotic) (N = 78)		P-value
Demographic data						
Sex	▪ ***Male***	21	26.9%	30	38.5%	0.125
	▪ ***Female***	57	73.1%	48	61.5%	
Age	▪ ***Mean ±SD***	65.6	± 8.6	63.8	± 14.6	0.376
Non-ICU duration	▪ ***Mean ±SD***	3.8	± 4.6	6.0	± 4.5	0.001
ICU duration	▪ ***Mean ±SD***	3.03	± 4.3	2.1	± 4.1	0.075
Total hospital stays	▪ ***Mean ±SD***	6.9	± 4.8	8.03	± 4.8	0.056
Smoking		14	17.9%	19	24.4%	0.327
DM		42	53.8%	49	62.8%	0.256
HTN		32	41 %	46	59%	0.025
CVD		13	16.7%	26	33.3%	0.016
CKD		12	15.4%	10	12.8%	0.645
Lung diseases		7	9%	13	16.7%	2.06
Cerebro-vascular D		3	3.8%	10	13 %	0.04
Hepatoma		14	17.9%	4	5.1%	0.012
Clinical picture						
Fever		61	78.2%	57	73.1%	0.456
Cough		58	74.4%	69	88.5%	0.024
Sore throat		27	34.6%	25	32.1%	0.734
Dyspnea		35	45.5%	52	66.7%	0.008
Chest tightness		35	44.9%	23	29.5%	0.047
Myalgia		46	59%	44	56.4%	0.746
Vomiting		31	39.7%	17	21.8%	0.015
Diarrhea		23	29.5%	17	21.8%	0.271
Abdominal pain		48	61.5%	28	35.9%	0.001
Disturbed conscious level (DCL)		27	34.6%	13	16.7%	0.010
Ascites		42	53.8%			

DM: *diabetes mellitus;* ***CHvD:*** *cardio-vascular disease;* ***CKD:*** *chronic kidney disease;* ***DCL:*** *disturbed conscious level;* ***HTN:*** *hypertension.*

Table 2. Comparison between Baseline and laboratory data of study patients.

Variables	Group I (cirrhotic)	Group II (non-cirrhotic)	P-
Vital signs			
Temp (°C)	38.4± 1.0	38.2± 0.9	0.198
SBP (mmHg)	124.8± 21.4	120.9± 26.0	0.713
DBP (mmHg)	76.7± 11.0	73.5± 11.1	0.285
RR (/min)	23.6± 6.4	24.3± 5.0	0.365
Hb (mg/dl)	12.4± 2.4	12.0± 2.1	0.233
WBCs (10^3 cm^3)	8.8± 7.5	9.9± 5.0	0.019
Lymph (Abs) (10^9/L)	2.6± 6.0	1.8± 2.2	0.071
Lymph (%)	21.0± 16.3	19.4± 12.8	0.719
Neutrophil (%)	72.0± 17.2	87.4± 100.8	0.628
PLT (10^9/L)	106.4± 70.2	219.2± 85.2	<
D. Dimer (ng/mL)	1202.2± 1881.3	944.2± 1239.6	0.488
Ferritin (ng/ml)	660.6± 567.0	670.4± 527.7	0.719
CRP (mg/dL)	39.5± 28.7	77.2± 71.0	<
LDH (IU/L)	519.3± 441.6	475.7± 279.1	0.867

ESR(mm/hr)	62.7± 13.44	63.32± 17.31	0.226
ALT(IU/L)	20.4± 9.4	24.9± 13.01	0.063
AST(IU/L)	117.5± 31,6	25.3± 10.2	<
Albumin(g/dl)	3.1± 0.6	3.9± 0.7	<
T. Bilirubin (mg/dl)	1.8± 3.3	0.8± 0.8	0.002
INR	1.4± 0.5	1.3± 0.2	0.103
Creatinine (mg/dl)	1.6± 1.7	1.8± 2.0	0.794
Na (mEq/L)	132.7± 8.2	132.0± 4.9	0.260
K (mEq/L)	4.2± 0.9	4.3± 0.7	0.641
Ca (mEq/L)	8.7± 0.9	9.4± 1.0	<
ABG			
PH	7.4± 0.1	7.4± 0.1	0.140
PaCO2 (mmHg)	31.3± 9.6	29.8± 8.7	0.323
PaO2 (mmHg)	63.4± 15.9	61.2± 13.7	0.495
SO2(%)	89.4± 7.5	88.8± 6.4	0.524
HCO3 (mEq/L)	19.3± 3.8	44.8± 209.2	0.662
CT chest CORAD: II/ III/ IV/ V I	0/14/19/45 (0%/17.9%/24.4%/57.7%)	1/12/20/45 (1.3%/15.4%/25.6%/57.7%)	0.758
Child-pughclass: A/B/C	17/39/22		
MELD score Mean ± SD)	18.52± 0.94		

SBP: *systolic blood pressure;* ***DBP:*** *diastolic blood pressure;* ***Hb:*** *hemoglobin;* ***WBC:*** *white blood cells;* ***PLTS:*** *platelets;* ***CRP:*** *c-reactive protein;* ***LDH:*** *Serum Lactate Dehydrogenase;* ***ESR:*** *erythrocyte sedimentation rat;* ***ALT:*** *alanine aminotransferase enzyme;* ***AST:*** *aspartate aminotransferase;* ***INR:*** *international normalized ratio;* ***ABG:*** *arterial blood gases;* ***MELD:*** *model for end liver disease.*

Table 3. Clinical outcomes in study groups.

Variables		Group I (N = 78)		Group II (N = 78)		P-value
ICU transfer	***No***	40	51.3%	48	61.5%	0.196
	Yes	38	48.7%	30	38.5%	
ICU transfer Causes	***ARDS***	31	81.6%	23	76.7%	0.143
	AKI	1	2.6%	2	6.7%	
	DKA	2	5.3%	3	10%	
	ACLF	4	10.5%	0	0%	
Respiratory support	***No***	17	21.8%	10	12.8%	0.138
	Yes	61	78.2%	68	87.2%	
Final outcome	***Died***	44	56.4%	25	32.1%	0.002
	discharged	34	43.6%	53	67.9%	

ICU: *intensive care unit;* ***ARDS:*** *acute respiratory distress syndrome;* ***AKI:*** *acute kidney injury;* ***DKA:*** *diabetic ketoacidosis –* ***ACLF:*** *acute on top of chronic liver failure.*

Table 4. The outcome of cirrhotic patients based on clinical score.

Variables	Outcome				P-value
	Died (N = 44)		***Discharged (N = 34)***		
Child Pugh score	***A (1–6 points)***	7	15.9%	10	29.4%	0.016
	B (7–9 points)	19	43.2%	20	58.8%	
	C (10–15 points)	18	40.9%	4	11.8%	
MELD	***Mean ± SD***	19.44	± 1.02	17.34	± 2.19	0.005

MELD: *model for end liver disease*

Table 5. Logistic regression analysis for factors predictive of death in the cases in group I

Variables	Univariable OR (95% CI)	P value	Multivariable OR (95% CI)	P
Demographic data.				
▪ ***Age***	1.122 – 2.62	< 0.001	1.842 - 2.603	< 0.001

▪ ***Admission data***				
▪ ***Non-ICU duration***	0.394 – 0.706	< 0.001	0.543 - 1.318	0.246
▪ ***ICU Duration***	1.287 – 1.956	< 0.001	1.017- 1.885	0.030
Comorbidities.				
▪ ***CKD***	1.570 – 2.682	< 0.001	1.242 - 1.940	0.025
▪ ***CVD***	1.392 – 2.630	< 0.001	1.821 – 3.004	0.001
▪ ***Hepatoma***	1.959 – 3.407	< 0.001	2145 - 3.645	< 0.001
Clinical symptoms and signs.				
▪ ***Fever***	0.586 – 1.279	0.104		
▪ ***Cough***	1.628 – 2.330	< 0.001	1.062 - 1.842	0.039
▪ ***Sore Throat***	0.700- 1.485	0.166		
▪ ***Dyspnea***	1.890 – 3.682	< 0.001	1.584 - 4.66	< 0.001
▪ ***Chest Tightness***	0.459 – 1.352	0.132		
▪ ***Myalgia***	0.572 – 1.320	0.511		
▪ ***Vomiting***	0.527 – 2.470	0.380		
▪ ***Diarrhea***	1.256 – 2.170	0.018	1.136 - 2.472	0.032
▪ ***Abdominal Pain***	0.561 – 1.618	0.398		
▪ ***DCL***	1.740 – 2.819	< 0.001	1.459 – 5.206	< 0.001
▪ ***Ascites***	2.140 – 3.263	< 0.001	1.672 – 3.420	< 0.001
▪ ***Vital signs***				
▪ ***Temp (°C)***	0.518 – 1.228	0.179		
▪ ***SBP (mmHg)***	0.741 – 1.190	0.516		
▪ ***DBP (mmHg)***	0.826 – 1.310	0.842		
▪ ***RR (breath/min)***	1.256 – 1.552	0.006	1.662 - 2.741	0.001
Laboratory data (at admission)				
▪ ***Hb (mg/dl)***	0.792 – 1.877	0.180		
▪ ***WBCs (10^3/mm^3)***	1.262 – 1.597	0.002	1.130 - 1.852	0.032
▪ ***Lymph Abs (10^9/L)***	0.881 – 1.362	0.078		
▪ ***Lymph %***	0.698 – 1.250	0.748		
▪ ***Neutrophil %***	0.826 – 1.22	0.278		
▪ ***PLT (10^9/L)***	0.796 – 1.126	0.552		
Inflammatory markers				
▪ ***D Dimer (ng/mL)***	1.410 – 1.972	0.002	1.203 - 1.83	0.015
▪ ***Ferritin (ng/mL)***	0.877 – 1.145	0.086		
▪ ***CRP (mg/dl)***	1.273 – 1.846	0.010	1.175- 1.762	0.026
▪ ***ESR (mm/hr)***	0.867 – 1.674	0.593		
▪ ***LDH(IU/L)***	1.479 – 1.527	0.202		
▪ ***Liver functions***				
▪ ***ALT (IU/L)***	0.677 – 1.145	0.139		
▪ ***AST (IU/L)***	0 0.698 – 1.237	0.442		
▪ ***ALB (g/dl)***	0.621 – 0.995	0.001	0.473 - 0.814	0.001
▪ ***T. Bilirubin (mg/dl)***	0.739 – 1.348	0.379		
▪ ***INR***	1.146 – 1.692	0.022		
▪ ***Creatinine (mg/dl)***	0.798 – 1.242	0.311		
Serum Electrolytes				
▪ ***Na (mEq/L)***	0.8 – 1.016	0.826		
▪ ***K (mEq/L)***	0.974 – 1.248	0.412		
▪ ***Ca (mEq/L)***	0.46 – 1.074	0.382		
▪ ***ABG***				
▪ ***PH***	0.846 – 1.017	0.876		
▪ ***PCO2(mm/Hg)***	0.907 – 1.068	0.359		
▪ ***PO2 (mm/Hg)***	0.623 – 0.989	0.005	0.623 - 1.443	0.169

▪ ***ABG.SO2 (%)***	0.183-0.673	0.019	0.746 – 1.792	0.243
▪ ***HCO3 (mEq/L)***	0.39 – 1.118	0.591		
▪ ***CT CORADS***	1.226 – 2.978	< 0.001	1.086-2.45	< 0.001

DM: *diabetes mellitus;* ***CVD:*** *cardio-vascular disease;* ***CKD:*** *chronic kidney disease;* ***DCL:*** *disturbed conscious level;* ***HTN:*** *hypertension;* ***SBP:*** *systolic blood pressure;* ***DBP:*** *diastolic blood pressure;* ***RR:*** *respiratory rate;* ***Hb:*** *hemoglobin;* ***WBC:*** *white blood cells;* ***PLTS:*** *platelets;* ***CRP:*** *c-reactive protein;* ***ESR:*** *erythrocyte sedimentation rat;* ***LDH:*** *serum Lactate Dehydrogenase;* ***ALT:*** *a lanine amino trasferase enzyme;* ***AST:*** *aspartate amino transferase;* ***INR:*** *international normalized ratio ;* ***ABG:*** *arterial blood gase; MELD: model for end liver disease.*

Discussion

Patients with cirrhosis are at a higher risk of infection and have an increased mortality rate[18]. Our study showed a mortality rate of 56.4% in cirrhotic patients, significantly higher than the 32.1% mortality rate in non-cirrhotic patients. This aligns with a large meta-analysis by Nagarajan et al., which included 40 studies and 908,032 participants. The analysis found that patients with cirrhosis had double the risk of COVID-19 severity and mortality compared to those without cirrhosis[7]. This was consistent with the findings of a large study that compared the impact of SARS-CoV-2 infection on patients with chronic liver disease (CLD) with and without cirrhosis. The study revealed that the risk of mortality was 3.31 times higher in patients with cirrhosis and 2.38 times higher in patients with cirrhosis who were also infected with SARS-CoV-2[19]. Additionally, Wu and Yang's review showed that COVID-19 patients with CLD had a nearly twofold higher risk of death and over four times the risk of dev-eloping severe disease compared to non-CLD patients[20]. A previous pooled analysis found no association between chronic liver disease and severe COVID-19 (OR 0.96, 95% CI 0.36-2.52, I2= 0%, P= 0.86)[21]. The study used multivar-iate regression analysis to confirm that older age, longer ICU duration, chronic kidney disease, cardiovascular disease, hepatoma, cough, dyspnea, low lymphocyte count, diarrhea, ascites, respiratory rate, white blood cell count, D-dimer level, C-reactive protein level, serum albumin level, and CT CORADS were independent risk factors for mortality. Our study, like previous research, found a high mortality rate in cirrhotic patients with COVID-19. We also observed that elevated D-dimer levels were associated with higher mortality in the cirrhotic group[22]. Additionally, a study by Sohail et al. identified chronic kidney disease, cardiovascular diseases, and intensive care admission as predictors for mortality in cirrhotic patients hospitalized with COVID-19[23]. However, other studies have found that chronic kidney disease and cardiovascular diseases were not predictors for mortality in cirrhotic patients hospitalized with COVID-19 infection[24,25]. In this study, both WBC and serum albumin were found to be predictors of death in cirrhotic patients with COVID-19. Other studies have also identified WBC, total bilirubin, ALT, AST, INR, and creatinine as predictors of death in cirrhotic patients with COVID-19. Additionally, the CRP level was significantly elevated and identified as a predictor of death in the cirrhotic group compared to non-cirrhotic group[26,27]. This finding is consistent with a study by Vrsaljko et al who observed a significant increase in CRP in associa-tion with liver disease[28]. The study did not find a statistically significant difference between the cirrhotic and non-cirrhotic groups in terms of CT chest for CORADS. However, the grade of CORAD V was found to be a predictor for mortality in both groups. Previous studies have shown conflicting results regarding the association between chronic liver disease and the severity of COVID-19[29]. Some studies have reported no link between chronic liver disease and severe COVID-19, while others have found that chronic liver disease increases the risk of developing severe COVID-19. For example, Zhou et al. reported that chronic liver disease is associated with an increased risk of severe COVID-19[30]. In this study, the symptoms were similar in both groups, but the cirrhotic group had a higher risk of death, with cough, dyspnea, and diarrhea being significant predictors. This is consistent with a study by Bajaj et al, which found that most Covid-related symptoms were similar in patients with and without liver disease, except for diarrhea, vomiting, and body aches, which were more common in the latter group[31]. The rate of ICU transfer was 43% in cases with liver disease compared to 38% in cases without liver disease, Bajaj et al. agreed with our findings, stating that patients with liver disease had a higher rate of ICU transfers (43% versus 38% in cases without liver disease)[32]. In this study, patients with cirrhosis had significantly longer ward admission times. However, there was no significant difference in total hospital stay or length of stay in the intensive care unit between the two groups. This is consistent with a study by Pugh et al, which found that hospitalization periods for patients with and without cirrhosis were similar, with median lengths of 11.5 and 10 days, respectively[31]. Our study found that intensive care unit admission is a predictor of mortality in cirrhotic patients with COVID-19. On the other hand, ward admission (P < 0.001) and increased ward admission duration were shown to decrease the odds of mortality in the included cases. Similarly, it was found that found that intensive care unit admission and duration were predictors of mortality in cirrhotic patients[33]. One limitation of the study is the small sample size of patients with chronic liver disease. Additionally, the study only included patients from a single institution. To address these limitations, further research is needed.

Conclusion

The COVID-19 pandemic significantly impacted the local economy and healthcare system. Patients with liver cirrhosis who contracted COVID-19 experienced worse outcomes compared to those without cirrhosis.

Conflict of Interest

There are no conflicts of interest disclosed by the authors.

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References

1. Jewell, P., Bramham, K., Galloway, J., (2021). COVID-19-related acute kidney injury; incidence, risk factors and outcomes in a large UK cohort. ***BMC Nephrol***. 22: 1-12.
2. Gu, J., Han, B. & Wang J. (2020). COVID-19: Gastrointestinal manifestations and potential fecal–oral transmission. ***Gastroenterology***. 158 (6): 1518-1519.
3. Younossi, Z., Stepanova, M., Younossi, Y., et al. (2020). Epidemiology of chronic liver diseases in the USA in the past three decades. ***Gut***. 69 (3): 564-568.
4. Paik, J., Golabi, P., Younossi, Y., et al. (2021). Changes in the global burden of chronic liver diseases from 2012 to 2017: The growing impact of NAFLD. ***European J. of Gastroenterology & Hepatology***. 33 (1): 121-124.
5. Méndez-Sánchez, N., Valencia-Rodríguez, A., Qi, X., et al. (2020). What has the COVID-19 pandemic taught us so far? Addressing the problem from a hepatologist's perspective. ***J. of Clinical and Translational Hepatology***. 8 (2): 109.
6. Younossi, Z., Stepanova, M., Lam, B., (2022). Independent predictors of mortality among patients with NAFLD hospitalized with COVID-19 infection. ***Hepatology Communications***. 6 (11): 62-3072.
7. Nagarajan, R. (2022). COVID-19 severity and mortality among chronic liver disease patients: A systematic review and meta-analysis. ***Preventing Chronic Disease***. 19: E53.
8. Berenguer, J., Ryan, P., Rodriguez-Bano, J., et al. (2020). Characteristics and predictors of death among 4035 consecutively hospitalized patients with COVID-19 in Spain. ***Clinical Microbiology and Infection***. 26 (11): 1525-1536.
9. Fang, Y., Nie, Y. & Penny, M. (2020). Transmission dynamics of the COVID-19 outbreak and effectiveness of government interventions: A data-driven analysis. ***J. of Medical Virology***. 92 (6): 645-659.
10. Kordzadeh-Kermani, E., Khalili, H. & Karimzadeh, I. (2020). Pathogenesis, clinical manifestations and complications of coronavirus disease 2019 (COVID-19). Future microbiology. 15 (13): 1287-1305.
11. Hanson, K., Caliendo, A., Arias, C., et al. (2020). Infectious Diseases Society of America guidelines on the diagnosis of coronavirus disease 2019. ***Clinical Infectious Diseases***. 10.1093/cid/ciaa1343.
12. Pan, Y., Guan, H., Zhou, S., et al. (2020). Initial CT findings and temporal changes in patients with the novel coronavirus pneumonia (2019-nCoV): a study of 63 patients in Wuhan, China. ***European Radiology***. 30: 3306-3309.
13. Association, W. (2013). World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. ***Jama***. 310 (20): 2191-2194.
14. Winck, J. & Scala, R. (2021). Non-invasive respiratory support paths in hospitalized patients with COVID-19: Proposal of an algorithm. ***Pulmonology***. 27(4):305-312
15. Pugh, R., Murray-Lyon, I., Dawson, J., et al. (1973). Transection of the oesophagus for bleeding oesophageal varices. ***British J. of Surgery***. 60 (8): 646-649.
16. Kamath, P., Wiesner, R., Malinchoc, M., et al. (2001). A model to predict survival in patients with end-stage liver disease. ***Hepatology***. 33 (2): 464-470.
17. Garrido, M., Guedes, T., Silva, J., et al. (2021). Impact of liver test abnormalities and chronic liver disease on the clinical outcomes of patients hospitalized with covid-19. GE-Portuguese ***J. of Gastroenterology***. 28 (4): 253-264.
18. Su, H. & Hsu, Y. (2021). Patients with cirrhosis during the COVID-19 pandemic: Current evidence and future perspectives. ***World J Clin Cases***. 9 (13): 2951-2968.
19. Ge, J., Pletcher, M., Lai, J., et al. (2021). Outcomes of SARS-CoV-2 infection in patients with chronic liver disease and cirrhosis: A national COVID cohort collaborative study. ***Gastroenterology***. 161 (5): 1487-1501. e5.
20. Wu, Z-h. & Yang, D. (2020). A meta-analysis of the impact of COVID-19 on liver dysfunction. ***European J. of Medical Research***. 25: 1-9.
21. Lippi, G., De Oliveira, M. & Henry, B. (2020). Chronic liver disease is not associated with severity or mortality in Coronavirus disease 2019 (COVID-19): A pooled analysis. ***Eur J Gastroenterol Hepatol***. 33(1): 114-115.
22. Marjot, T., Moon, A., Cook, J., et al. (2021). Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: An international registry study**.** ***J Hepatol***.74 (3): 567-577.
23. Sohail, A., Naseem, K., Khan, A., et al. (2023). Predictors of inpatient outcomes of COVID-19 infection in patients with cirrhosis in the early pandemic phase: A nationwide survey. ***JGH Open***. 7: 889-898.
24. Grgurevic, I., Lucijanić, M., Pastrovic, F., et al. (2022). Short-term outcomes of patients with chronic liver disease hospitalised with COVID-19. ***Intern Med J***. 52 (11):1891-1899.
25. Walia, D., Saraya, A. & Gunjan, D. (2023). COVID-19 in patients with pre-existing chronic liver disease – predictors of outcomes. ***World J Virol***. 12 (1): 30-43.
26. Elhence, A., Vaishnav, M., Biswas, S., et al. (2022). Predictors of in-hospital Outcomes in Patients With Cirrhosis and Coronavirus Disease-2019. ***J Clin Exp Hepatol***. 12: 876-886.
27. Lempesis, I., Karlafti, E., Papalexis, P., et al. (2023). COVID-19 and liver injury in individuals with obesity. ***World J Gastroenterol***. 29 (6): 908-916.
28. Vrsaljko,. N, Samadan, L., Viskovic, K., et al. (eds.) (2022). ***Association of nonalcoholic fatty liver disease with COVID-19 severity and pulmonary thrombosis: Covid FAT, a prospective, observational cohort study. open forum infectious diseases***, Oxford University Press US, Oxford.
29. El-sayed, S., El-Sabbagh, M., Ahmed Abdelrazik, A. , et al. (2023). Impact of COVID-19 on mortality rate in patients with chronic liver diseases, single-centre observational study. ***Med J Viral Hepatitis***. 7 (2): 15-22

30. Garrido, I., Liberal, R. & Macedo G. (2020). COVID-19 and liver disease—what we know on 1st May 2020. ***Aliment Pharmacol Ther***. 52 (2): 267-275.

31. Zhou, Y., Zheng K., Wang, X., et al. (2020). Metabolic-associated fatty liver disease is associated with severity of COVID-19. ***Liver International***. 40 (9): 2160-2163.

32. Bajaj, J., Garcia-Tsao, G., Biggins, S., et al. (2021). Comparison of mortality risk in patients with cirrhosis and COVID-19 compared with patients with cirrhosis alone and COVID-19 alone: multicentre matched cohort. ***Gut***. 70 (3): 531-536.

33. Kaur, S., Hussain, S., Kolhe, K., et al. (2021). Elevated plasma ICAM1 levels predict 28-day mortality in cirrhotic patients with COVID-19 or bacterial sepsis. ***JHEP Rep***. 3 (4): 100303.