Original Article

Medical Journal of Viral Hepatitis (MJVH)

Impact of COVID-19 on mortality rate in patients with chronic liver diseases, single-centre observational study

Samar El-sayed[1], Mohamed El-Sabbagh[2], Ahmed Abdelrazik[1], Mona Arafa[1], Ahmed Yassen[1].

[1] Tropical Medicine Department, Mansoura University, Egypt. [2] Medical Microbiology and Immunology Department, Mansoura University, Egypt.

Abstract

Background: Coronavirus induced disease-19 (COVID-19), is a serious disease induced by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Liver cirrhosis and its complications are currently the ninth most common cause of death worldwide. This work aims to evaluate the impact of COVID-19 on mortality rate in patients with CLD.

Patients and methods: The current study included 120 patients with COVID-19 who were distributed according to the state of the liver affection into two groups; group 1 included 60 patients with combined COVID-19 and CLD and group 2 included 60 with COVID-19 free from CLD. All the included cases were reviewed to obtain data about general history, clinical examination laboratory investigations and mortality rate. **Results:** Compared to COVID-19 patients without chronic liver diseases, patients with COVID-19 and chronic liver diseases had a significant mortality rate (60% versus 20% respectively). Among patients with chronic liver diseases, the mortality rate was statistically significantly higher in decompensated cirrhosis (100%) followed by patients with hepatocellular carcinoma (80%) and the lowest mortality rate was found in decompensated cirrhosis (46.7%). Multivariate regression analysis showed that increasing age, decreased albumin concentration, and increasing INR and PT were independent predictors for mortality in patients with chronic liver diseases. **Conclusion:** COVID-19 in patients with chronic liver diseases had worse outcomes compared to COVID -19 in patients without chronic liver diseases. Among the chronic liver diseases decompensated liver disease was linked to the worst outcome.

Introduction

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus-2) a novel coronavirus causing COVID-19 was identified in December 2019 [1]. The virus spread around the whole world in a short time and World Health Organization (WHO) declared the pandemic status on 11 March 2020 [2]. COVID-19 is a serious respiratory infection marked by fever, dry cough, and dyspnea [3]. While mild symptoms are encountered by most infected people, who do not need hospitalization, a considerable proportion of admitted patients were complicated with acute hypoxemia and needed assisted ventilation in ICU [3-5]. COVID-19 is primarily a respiratory illness. The coronavirus spike (S) protein attaches to ACE2 receptors [6] found on the surface of many human cells, including those in the lungs and liver cholangiocytes. This allows viral entry which may be responsible for hepatic dysfunction.

Chronic liver disease (CLD) is a major cause of mortality, morbidity, and resource utilization worldwide [7]. At present, liver cirrhosis with its related complications is the ninth most common cause of death globally. The most common etiologies of CLD include non-alcoholic fatty liver disease (NAFLD), alcohol-related liver disease (ALD), viral hepatitis B (HBV) and hepatitis C virus (HCV) [8]. it has been reported that up to 50% of patients with COVID-19 can develop some form of hepatic dysfunction that may eventually result in poor outcomes [9, 10].

Understanding the conditions that lead to severe disease and death among COVID-19–infected people is critical with the evolving pandemic. COVID-19 infection highlights the pre-existing weaknesses of the individual organ systems, making it logical to postulate that people with chronic liver disease may be susceptible to more severe respiratory infections or be at increased risk of death [11, 12]. Although COVID-19 patients with chronic liver disease have been deemed to be at an increased risk for serious illness in many studies, little is known about the impact of COVID-19 on the natural history and outcome of COVID-19 in patients with CLD. Therefore, the current work was conducted to study the impact of COVID-19 on patients with CLD compared to the cases without CLD.

Patients and methods

This is a prospective observational study that was conducted at Mansoura University Hospital, Mansoura, Egypt. The study included 120 patients with COVID-19 who were distributed into two groups according to the state of the liver, Group 1 (60 patients with CLD) and Group 2 (60 patients without CLD). The diagnosis of COVID-19 based on clinical symptoms and signs (fever, cough, breathing difficulties or organ failures [13], laboratory findings (elevation of inflammatory biomarkers as (CRP, ferritin, lactate dehydrogenase, D-dimer and INR, decrease in lymphocyte count and decrease in serum K level [14], positive result of reverse transcription polymerase chain

Keywords: COVID-19, chronic liver disease, mortality.
Received: 25-7-2023 ; Accepted: 05-8-2023
* Corresponding author. email: elmessery2005@hotmail.com

reaction (RT-PCR) in nasopharyngeal swab specimens [15] and CT chest finding (patchy ground glass opacities (GGO) and patchy consolidation which were mainly distributed in the middle and outer zone of the lung [16]. The cases with the following criteria were excluded; age < 18 years, negative for COVID-19, and patients with no available clinical or laboratory data confirming the diagnosis of COVID-19.

The cases were subjected to the following: history taking (including the demographic data and history of present illness) and clinical examination and body mass index measurement.

1. Laboratory investigations: Were done including complete blood count, liver and kidney function tests, serum level of D-dimer, serum ferritin, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum creatinine, total cholesterol, triglyceride, HDL and LDL, prothrombin time (PT) and HbA1c and blood glucose levels, anti-HCV antibody and HBsAg.

2. Radiological studies: Included chest x-ray and chest computerized tomography (CT). The study outcomes included the primary outcome (mortality rates) and secondary outcomes (disease severity, duration of hospitalization, need for ICU admission, need for mechanical ventilation, and duration of ICU admission).

The study is conducted following Helsinki Standards as revised in 2013 [17]. The study was conducted after obtaining approval from the local ethics committee, Faculty of Medicine, Mansoura University and after obtaining written/oral informed consent from the included cases (or their relatives). Research ethics committee: Ms.5.3.2021.

Statistical analysis

The data collected were coded, processed and analyzed with SPSS version 26 for Windows® (Statistical Package for Social Sciences) (IBM, SPSS Inc, Chicago, IL, USA). Qualitative data as number (frequency) and % were presented. The Kolmogorov-Smirnov test tested quantitative data for normality. Data was shown as median ± SD or median (interquartile range) according to normality. To compare two or more groups with categorical variables, the Chi-Square test (or Fisher's exact test/Monte Carlo test) was used. To compare two groups with normally distributed quantitative variables, independent samples (student's) t-test was used and Mann-Whitney U-test was used if the data were abnormally distributed. To compare three or more groups with abnormally distributed quantitative variables, the Kruskal-Wallis test was used. Univariate and multivariate logistic regression analyses were used for the prediction of risk factors for categorical outcomes. For all tests, P values <0.05 are considered significant.

Results

Table (1) shows that there was no statistically significant difference between the cases in the two groups regarding age and sex distribution. The mean age was 62.07± 15.01 years and 57.18 ± 13.69 years in group 1 and group 2 respectively. Males represented 63.3% and 58.3% in group 1 and group 2 respectively. There was no statistically significant difference between the two groups regarding BMI. There was no statistically significant difference between the two groups regarding the associated comorbidities. Hypertension was reported in 36.7% and 28.3% in group 1 and group 2 respectively. DM was reported in 23.3% and 25% of group 1 and group 2 respectively. In the cases of group 1, there were 14 cases (23.3%) with HCV. According to the ultrasound examinations, fatty liver disease was reported in 12 cases (20%), compensated cirrhosis in 30 cases (50%), decompensated cirrhosis in 8 cases (13.3%) and HCC in 10 cases (16.7%). **Table (2)** shows that at the index admission, the haemoglobin level, platelets count and albumin level were statistically significantly lower in the COVID-19 cases with CLD. On the other hand, leucocytic count, ALT, AST, INR, PT, lactate dehydrogenase and d-dimer were statistically significantly higher in the COVID-19 cases with CLD. There was no statistically significant difference between the two groups regarding the total bilirubin level, creatinine, ferritin and CRP. The percentage of cases with positive d-dimer was statistically significantly higher in the COVID-19 cases with CLD. There was no statistically significant difference between the two groups regarding the respiratory parameters including PO2 and PCO2. There was no statistically significant difference between the two groups regarding the radiological findings. The most common findings in the two groups were the GGO which was detected in 53.3% and 68.3% in group 1 and group 2 respectively. The second most common findings were consolidation which was detected in 20% and 16.7% of the cases. **Table (3)** shows that, no statistically significant difference between the two groups regarding oxygen therapy. In the cases of group 1, IMV was required in 20% while it was required in 16.7% in the cases within group 2. While NIMV was required in 16.7% and 15% of group 1 and group 2 respectively. The duration of hospital admission was statistically significantly lower in the COVID-19 cases with CLD. The incidence of mortality in the COVID-19 cases with CLD was 60% which was statistically significantly higher compared to the Covid-19 without CLD (20%). **Table (4)** shows that with univariate regression analysis, increasing age, decrease haemoglobin level, decrease albumin concentration, decrease platelet count, increasing leucocytic count, bilirubin level, serum creatinine, INR, PT and CRP were shown as predictors of mortality. However, with multivariate regression analysis, increasing age, decreased albumin concentration, and increasing INR and PT were shown as independent predictors for mortality. **Table (5)** shows that in the COVID-19 with CLD, there was no statistically significant difference in the duration of hospitalization according to the pathological condition of the liver. However, there was a statistically significant difference in the mortality rate between the different liver conditions with the highest mortality reported in the decompensated cirrhosis (100%) followed by the HCC group (80%).

Table 1. Analysis of demographic and clinical data in the two study groups.

	Group 1 [Covid-19 with CLD] (N=60)	Group 2 [Covid-19 without CLD] (N=60)	Test of significance	P value
Age (Years)	62.07 ± 15.01	57.18±13.69	t = 1.862	0.065
Sex				
Male	38 (63.3%)	35 (58.3%)	$\chi 2$= 0.315	0.575
Female	22 (36.7%)	25 (41.7%)		
BMI (kg/m2)	27.01 ± 3.48	29.50 ± 3.69	t = - 1.862	0.065
HTN	22 (36.7%)	17 (28.3%)	$\chi 2$= 1.677	0.195
DM	14 (23.3%)	15 (25%)	$\chi 2$= 0.950	0.330
Virology				
Negative	14 (23.3%)			
HCV	14 (23.3%)			
Cured HCV	32 (53.3%)			
Ultrasound				
Fatty liver	12 (20%)			
Cirrhotic(compensated)	30 (50%)			
Cirrhotic (De-compensated)	8 (13.3%)			
HCC	10 (16.7%)			

$\chi 2$: Chi-square test: Independent samples t-test

CLD, chronic liver disease; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; HCV, hepatitis C virus; HCC, hepatocellular carcinoma.

Table 2: Analysis of laboratory and radiological data in the two study groups (on admission)

	Group 1 [COVID-19 with CLD] (N=60)	Group 2 [COVID-19 without CLD] (N=60)	Test of significance	P-value
HGB (gm/dl)	11.50 ± 2.68	12.71 ± 2.11	t = -2.733	0.007
WBCs (103/cmm)	10.6 (1-26.6)	7.9 (1.9-25)	z = - 2.772	0.006
PLTs (103/cmm)	140 (47-715)	225 (100-634)	z = - 4.451	< 0.001
ALT (U/L)	37 (14-224)	25 (3-136)	z = - 2.605	0.009
AST (U/L)	61 (17-215)	33 (9-155)	z = - 5.250	< 0.001
Albumin (gm/dl)	2.71 ± 0.71	3.06 ± 0.37	t = -3.341	0.001
Total bilirubin (mg/dl)	0.87 (0.29-4.9)	0.5 (0.12-1.8)	z = - 3.926	0.749
INR	1.25 ± 0.25	1.13 ± 0.15	t = 3.359	0.001
PT (Seconds)	16.23 ± 2.71	15.13 ± 2.19	t = 2.460	0.015
LDH	385 (172-3446)	312 (58-969)	z = - 1.916	0.050

Creatinine	0.9 (0.4-2)	0.8 (0.5-1.8)	z = - 0.713	0.476
Ferritin	398 (29-2655)	434 (2-2600)	z = - 0.136	0.891
CRP	96 (6-312)	95 (12-372)	z = - 0.861	0.389
CRP				
Negative **Positive**	6 (10%) 54 (90%)	2 (3.3%) 58 (96.7%)	FET = 2.143	0.143
D-dimer	0.4 (0.2-1.6)	0.3 (0.2-1.6)	z = -2.228	0.022*
D-dimer				
Negative **Positive**	16 (26.7%) 44 (73.3%)	38 (63.3%) 22 (36.7%)	$\chi 2$= 16.296	< 0.001*
Respiratory parameters				
PO2	50 (20-137)	47 (20-105)	z = -0.850	0.359
PCO2	38.21 ± 11.65	37.38 ± 8.69	t = 0.445	0.657
Radiology findings				
Consolidation	12 (20%)	10 (16.7%)	$\chi 2$= 0.223	0.637
Fibrous stripes	10 (16.7%)	9 (15%)	$\chi 2$= 0.063	0.803
GGO	32 (53.3%)	41 (68.3%)	$\chi 2$= 2.883	0.092

t: Independent samples t-tests: Mann-Whitney U-test

LDH, lactate dehydrogenase; CRP: C-reactive protein; PO2, partial pressure of oxygen; PCO2, partial pressure of carbon dioxide; GGO, ground glass opacity.

Table 3: Analysis of the outcomes in the two study groups

	Group 1 [Covid-19 with CLD] (N=60)	**Group 2 [Covid-19 without CLD] (N=60)**	**P value**
IMV	18 (20%)	7 (16.7%)	0.648
NIMV	8 (16.7%)	7 (15%)	0.803
Oxygen	32 (53.3%)	41 (68.3%)	0.092
No Oxygen	2 (3.3%)	5 (8.3%)	0.458
A disease of hospital stay (Days)	8 (3-26)	10 (0-40)	0.003*
Discharged	24 (40%)	48 (80%)	< 0.001*
Mortality	36 (60%)	12 (20%)	

IMV, intermittent mandatory ventilation; NIMV, noninvasive mechanical ventilation

Table 4: Univariate and multivariate regression analysis for prediction of mortality in the included cases (n=48).

Predictors	**Univariate regression**				**Multivariate regression**			
	Odds ratio	**95% C.I. for odds ratio**		**P value**	**Odds ratio**	**95% C.I. for odds ratio**		**P value**
		Lower	**Upper**			**Lower**	**Upper**	
Age	4.361	2.804	6.319	<0.001	2.875	1.889	3.534	0.001
Male gender	1.167	0.825	1.391	0.760				

BMI	1.432	0.746	1.450	0.436				
DM	1.085	0.537	1.269	0.260				
HTN	1.621	0.922	1.911	0.874				
HCV	1.437	0.873	1.670	0.870				
Fatty liver (NASH)	1.203	0.756	1.439	0.397				
Cirrhotic (compensated)	1.174	0.622	1.572	0.157				
Cirrhotic (De-compensated)	1.940	0.929	2.130	0.081				
HCC	1.386	0.728	1.654	0.106				
Haemoglobin	0.726	0.432	0.958	**0.016***	1.009	0.716	1.487	0.204
WBCs	1.962	1.234	2.672	**0.٠13***	0.884	0.627	1.156	0.169
Platelets	0.648	0.533	0.817	**0.003***	1.599	.736	1.763	0.122
D-dimer	1.240	0.823	1.636	0.153				
Ferritin	1.152	0.706	1.972	0.434				
ALT	1.254	0.630	1.245	0.532				
AST	1.327	0.580	1.397	0.452				
Albumin	**0.642**	**0.359**	**0.873**	**<0.001***	0.740	0.425	0.907	**<0.001**
Bilirubin	1.648	1.255	2.187	**0.003***	1.23	0.71	1.46	0.214
Creatinine	2.147	1.479	2.436	**0.006***	1.124	0.735	1.800	0.553
INR	**2.692**	**1.584**	**3.172**	**<0.001***	2.002	1.604	2.964	**0.001**
PT	**3.715**	**2.172**	**4.122**	**<0.001***	2.364	1.11	3.78	**<0.001**
CRP	1.648	1.127	2.348	**0.034***	0.733	0.541	1.276	0.238
LDH	1.512	0.844	1.707	0.576				
PCO2	1.301	0.750	1.569	0.340				
PO2	0.871	0.520	1.167	0.242				
Hospital stays	1.456	0.860	1.835	0.756				
CI: Confidence interval					**OR: Odd's ratio**			

CLD, chronic liver disease; BMI, body mass index; HTN, hypertension; DM, diabetes mellitus; HCV, hepatitis C virus; HCC, hepatocellular carcinoma; NASH, non-alcoholic steatohepatitis; LDH, lactate dehydrogenase; CRP, C-reactive protein; PO2, partial pressure of oxygen; PCO2, partial pressure of carbon dioxide.

Table 5: Analysis of the outcomes in the Covid-19 with CLD according to the aetiology of CLD.

	NASH (N=12)	**Compensated cirrhotic (N=30)**	**Decompensated cirrhosis (N=8)**	**HCC (N=10)**	**Test of significance**	**P value**
A disease of hospital stay (Days)	9 (4-12)	7 (3-24)	8 (4-13)	8 (4-26)	KW= 1.345	0.719
Outcome						
Discharged	6 (50%)	16 (53.3%)	0 (0%)	2 (20%)	MC= 9.772	0.021*
Dead	6 (50%)	14 (46.7%)	8 (100%)	8 (80%)		

MC, Monte Carlo test; KW, Kruskal Wallis.

Discussion

According to this study, the mortality rate in COVID-19 cases with CLD was found to be 60%, which was statistically higher than the mortality rate in COVID-19 cases without CLD, which was 20%. These results are corroborated by an important meta-analysis conducted by Nagarajan that included 40 studies and 908,032 subjects. Nagarajan found that COVID-19 severity and death risk were twice as likely to occur in CLD patients as they were in controls[11].

Many earlier studies that found that hospitalized COVID-19 patients with pre-existing liver disease had an increased risk of death and severe illness 18, 19 supported our findings that patients with CLD in the COVID-19 study group had a high rate of death and risk of developing severe disease. Additionally, according to other studies, cirrhotic individuals in particular those with CLD have more severe COVID-19 and a higher COVID-19 mortality rate [20-22]. On the other hand, Garrido et al. reported that mortality occurred in patients with and without chronic liver disease was 28.6 % and 22.5 % of cases respectively with no appreciable difference between the two groups [23].

In the current study, there was a statistically significant difference in mortality rates among the different liver disorders, with the decompensated cirrhotic group reporting the greatest mortality (100%) and the HCC group reporting the second-highest mortality (80%). This result was in line with the results of one of the largest studies on the effects of SARS-CoV-2 in patients with CLDs who had cirrhosis or not. According to this research, persons with CLDs who were infected with SARS-CoV-2 had a 3.31 times higher risk of dying from cirrhosis than those who weren't. [24]. In a different study, there were 745 individuals from 29 different nations; 386 of them had cirrhosis, whereas the other 359 did not. Patients with cirrhosis had a mortality rate of 32% compared to those without the condition, which was just 8%. When compared to patients without liver disease, the mortality rate for cirrhotic patients with CTP-B and CTP-C was significantly greater [25]. In a different study, mortality in cirrhosis increased following Child-Turcotte-Pugh classes, CTP-A was 19%, CTP-B was 35%, and CTP-C was 51%. Along with old age, diabetes, hypertension, chronic and current smoking, and alcoholic liver disease, respiratory failure contributed to 71% of deaths. The presence of decompensated cirrhosis and Hispanic ethnicity were independent risk factors for severe COVID-19 [26].

According to Zhang et al., cancer patients have a worse prognosis than the general population. The patients' ages, associated comorbidities, and underlying cirrhosis were risk factors. Anaemia and hypoproteinemia have an impact on their nutritional state, which reduces their immunity and makes them more vulnerable to dangerous diseases. Co-infection with COVID-19 and cancer increased a patient's vulnerability to serious disease, their chance of passing away, and their requirement for ICU care [27].

According to this study's Kaplan Meier survival analysis, cases with NASH have the second-lowest mean survival after cirrhotic compensation The complicated interaction between chronic active inflammatory pathways linked to NAFLD and the COVID-19-associated cytokine storm may increase the risk of severe NAFLD [28]. By intensifying the cytokine storm, damage caused by the accumulation of fat in the liver may exacerbate patient prognoses [29]. In COVID-19 patients, MAFLD was discovered to exacerbate the virus-induced inflammatory cytokine storm by a similar mechanism, with enhanced reactive oxygen generation and hepatic release of the proinflammatory cytokines [30, 31].

The current study's Covid-19 subjects with CLD had considerably shorter hospital stays. Patients with and without CLD had median hospitalization times of 11.5 and 10 days, respectively, according to Garrido et al. [23]. There was little difference between the two groups. This was in contrast to Frager et al.'s findings, which stated that statistical analysis demonstrated that the length of hospital stays for patients with and without liver illness was equal at mean values of 8.21 and 7.8 days [32]. Hashemi et al. also noted that patients with chronic liver illness have lengthier hospital stays (13.4 days compared to 10.1 days in those without liver disease) [33].

The current study found several variables as predictors of death, including increased age, decreased haemoglobin level, decreased albumin concentration, decreased platelet count, increased leucocyte count, bilirubin level, serum creatinine, INR, PT, and CRP were all identified in the current study as predictors of mortality. Multivariate regression analysis after adjusting for multiple confounders showed that the elderly, lower albumin concentrations, higher INRs, and higher PTs were all shown to be independent predictors for mortality. However, there is no consensus on the prognostic factors for COVID-19 patients with preexisting liver diseases [34]. A previous study reported that severe COVID-19 was linked to increased age and pre-existing comorbidities in an American study of CLD patients [26,35]. After adjusting for age and sex, preliminary findings from a meta-analysis of 88 studies including 6653207 cases of COVID-19 across Europe indicate that liver disease is linked to hospital admission and death [36]. The current COVID-19 outbreak has been associated with mortality, extended hospital admissions, the requirement for life-sustaining care, and liver dysfunction [37].

Hypoalbuminemia was a significant predictor of mortality in the COVID-19 individuals with CLD in this research. Samir et al.'s findings that COVID-19 patients with chronic hepatitis and cirrhotic liver had statistically significantly lower albumin levels than COVID-19 patients without indications of CLD are consistent with these findings [38]. In the current study, higher blood bilirubin levels were found to be a significant predictor of death in COVID-19 participants with CLD, but not in multivariate analysis. However, a study indicated that patients with liver disease had significantly higher bilirubin levels (0.66 vs. 0.4 mg/dl, respectively) than those without the ailment [23]. Hashemi et al. reported no significant difference in relating this item [23].

In our study, in patient with CLD INR were significantly high versus non-CLD patients. According to Samir et al study, COVID-19 patients with chronic liver disease had statistically significantly higher INR values than COVID-19 patients without CLD [38]. However, this is in contrast to the findings of Hashemi et al., who demonstrated that there was no statistically significant difference between patients with and without liver disease in terms of INR [33]. Serum creatinine levels in the current study show no discernible difference between the two groups. Similarly to this, Hashemi et al. reported that patients with and without chronic liver disease had no statistically significant difference regarding serum

creatinine [33]. Also, serum CRP levels show no statistically significant difference between both groups. Similarly to this, another study found that patients with and without chronic liver disease had no statistically significant difference between the two groups [23]. On the other hand, according to a different study, CRP significantly rises in patients with liver disease (84.7 mg/l compared to 66.9 mg/l in patients without liver disease) [39].

In the current study, the proportion of COVID-19 cases with CLD that had positive d-dimer results was statistically significantly higher. In accordance Samir et al., demonstrated that COVID-19 patients with chronic liver disease had statistically significantly higher d-dimers than COVID-19 patients without CLD [38]. In most cases, D-Dimer is absent from human blood plasma. It only exists when the coagulation system is engaged. D-dimer, prothrombin time, and activated partial thromboplastin time are three of the most frequently used laboratory coagulation indicators (APTT) [40]. In the current investigation, there was no statistically significant difference between the two groups concerning the related comorbidities. 36.7% and 28.3% of the individuals in groups 1 and 2, respectively, had hypertension. Groups 1 and 2 reported DM at 23,3% and 25%, respectively. Another study discovered that all systemic comorbidities were statistically equivalent across patients with and without chronic liver disease, except for chronic kidney disease, which significantly increased in conjunction with chronic liver disease [23]. Hashemi et al. also observed that the patient's comorbidities, which included lung disease, coronary artery disease, diabetes, hypertension, and hyperlipidemia, did not significantly differ between the two groups [33]. This study has some drawbacks. Patients from a single institution were also included in the study population. To address the prior limitations, more research needs to be done in the future.

Conclusion

There was a significant effect on the healthcare system and the economy from the COVID-19 pandemic. Patients in the COVID-19 study who also suffered from chronic liver disease had poorer outcomes than those who did not. Of all the causes of liver affection, cirrhosis with liver decompensation had the worst prognosis.

References

1. Guan, W. J., Ni, Z. Y., Hu, Y. (2020). Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine, 382(18), 1708-1720.
2. Wang, C., Horby, P. W., Hayden, F. G. (2020). A novel coronavirus outbreak of global health concern. The lancet, 395(10223), 470-473.
3. Huang, C., Wang, Y., Li, X. (2020). Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet, 395(10223), 497-506.
4. Murk, J. L., van de Biggelaar, R., Stohr, J. (2020). Dutch.[The first 100 admitted COVID-19 patients in the Elisabeth-Tweesteden hospital]. NTVG, 164, D5002.
5. Grasselli, G., Pesenti, A., and Cecconi, M. (2020). Critical care utilization for the COVID-19 outbreak in Lombardy, Italy: early experience and forecast during an emergency response. Jama, 323(16), 1545-1546.
6. Hu, X., Sun, L., Guo, Z. (2022). Management of COVID-19 patients with chronic liver diseases and liver transplants. Annals of hepatology, 27(1), 100653.
7. Younossi, Z. M., Stepanova, M., Younossi, Y. (2020). Epidemiology of chronic liver diseases in the USA in the past three decades. Gut, 69(3), 564-568.
8. Paik, J. M., Golabi, P., Younossi, Y. (2020). Changes in the global burden of chronic liver diseases from 2012 to 2017: the growing impact of NAFLD. Hepatology, 72(5), 1605-1616.
9. Méndez-Sánchez, N., Valencia-Rodríguez, A., Qi, X. (2020). What has the COVID-19 pandemic taught us so far? Addressing the problem from a hepatologist's perspective. Journal of clinical and translational hepatology, 8(2), 109.
10. Younossi, Z. M., Stepanova, M., Lam, B. (2022). Independent predictors of mortality among patients with NAFLD hospitalized with COVID-19 infection. Hepatology Communications, 6(11), 3062-3072.
11. Bertagnolio, S., Thwin, S. S., Silva, R. (2022). Clinical features of, and risk factors for, severe or fatal COVID-19 among people living with HIV admitted to hospital: analysis of data from the WHO Global Clinical Platform of COVID-19. The Lancet HIV, 9(7), e486-e495.
12. Berenguer, J., Ryan, P., Rodriguez-Bano, J. (2020). Characteristics and predictors of death among 4035 consecutively hospitalized patients with COVID-19 in Spain. Clinical Microbiology and Infection, 26(11), 1525-1536.
13. Fang, Y., Nie, Y., and Penny, M. (2020). Transmission dynamics of the COVID-19 outbreak and effectiveness of government interventions: A data-driven analysis. Journal of medical virology, 92(6), 645-659.
14. Ali, M. R., Haroon, M., Samayyah, R. (2022). Prognostic Significance of ALT/AST in diabetic patients having Myocarditis secondary to COVID Pneumonia. Pakistan Journal of Medical & Health Sciences, 16(07), 121-121.
15. Hanson, K. E., Altayar, O., Caliendo, A. M. (2021). The Infectious Diseases Society of America guidelines on the diagnosis of coronavirus disease 2019 (COVID-19): antigen testing. Clinical Infectious Diseases, ciab557.
16. Pan, Y., Guan, H., Zhou, S. (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.
17. Shrestha, B., and Dunn, L. (2019). The declaration of Helsinki on medical research involving human subjects: a review of seventh revision. Journal of Nepal Health Research Council, 17(4), 548-552.
18. Wu, Z. H., and Yang, D. L. (2020). A meta-analysis of the impact of COVID-19 on liver dysfunction. European Journal of Medical Research, 25, 1-9.

19. Sharma, A., Jaiswal, P., Kerakhan, Y. (2021). Liver disease and outcomes among COVID-19 hospitalized patients–a systematic review and meta-analysis. Annals of hepatology, 21, 100273.
20. Azwar, M. K., Setiati, S., Rizka, A. (2020). Clinical profile of elderly patients with COVID-19 hospitalised in Indonesia's National General Hospital. Acta Medica Indonesiana, 52(3), 199.
21. Singh, S., and Khan, A. (2020). Clinical characteristics and outcomes of coronavirus disease 2019 among patients with preexisting liver disease in the United States: a multicenter research network study. Gastroenterology, 159(2), 768-771.
22. Bajaj, J. S., Garcia-Tsao, G., Biggins, S. W. (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.
23. Garrido, M., Pereira Guedes, T., Alves Silva, J. (2021). Impact of liver test abnormalities and chronic liver disease on the clinical outcomes of patients hospitalized with covid-19. GE-Portuguese Journal of Gastroenterology, 28(4), 253-264.
24. Ge, J., Pletcher, M. J., Lai, J. C. (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.
25. Marjot, T., Moon, A. M., Cook, J. A. (2021). Outcomes following SARS-CoV-2 infection in patients with chronic liver disease: an international registry study. Journal of hepatology, 74(3), 567-577.
26. Kim, D., Adeniji, N., Latt, N. (2021). Predictors of outcomes of COVID-19 in patients with chronic liver disease: US multi-center study. Clinical Gastroenterology and Hepatology, 19(7), 1469-1479.
27. Zhang, L., Zhu, F., Xie, L. (2020). Clinical characteristics of COVID-19-infected cancer patients: a retrospective case study in three hospitals within Wuhan, China. Annals of oncology, 31(7), 894-901.
28. Sachdeva, S., Khandait, H., Kopel, J. (2020). NAFLD and COVID-19: a pooled analysis. SN Comprehensive Clinical Medicine, 2, 2726-2729.
29. Roca-Fernandez, A., Dennis, A., Nicolls, R. (2020). High liver fat associates with higher risk of developing symptomatic covid-19 infection-initial UK biobank observations. medRxiv, 2020-06.
30. Hegyi, P. J., Váncsa, S., Ocskay, K. (2021). Metabolic associated fatty liver disease is associated with an increased risk of severe COVID-19: a systematic review with meta-analysis. Frontiers in medicine, 8, 626425.
31. Assante, G., Williams, R., and Youngson, N. A. (2021). Is the increased risk for MAFLD patients to develop severe COVID-19 linked to perturbation of the gut-liver axis?. Journal of Hepatology, 74(2), 487-488.
32. Frager, S. Z., Szymanski, J., Schwartz, J. M. (2021). Hepatic predictors of mortality in severe acute respiratory syndrome coronavirus 2: role of initial aspartate aminotransferase/alanine aminotransferase and preexisting cirrhosis. Hepatology communications, 5(3), 424-433.
33. Hashemi, N., Viveiros, K., Redd, W. D. (2020). Impact of chronic liver disease on outcomes of hospitalized patients with COVID-19: A multicentre United States experience. Liver international : official journal of the International Association for the Study of the Liver, 40(10), 2515–2521.
34. Bahardoust, M., Heiat, M., Khodabandeh, M. (2021). Predictors for the severe coronavirus disease 2019 (COVID-19) infection in patients with underlying liver disease: a retrospective analytical study in Iran. Scientific Reports, 11(1), 3066.
35. Krishnan, A., Prichett, L., Liu, Y. (2022). Risk of Severe Illness and Risk Factors of Outcomes of COVID-19 in Hospitalized Patients with Chronic Liver Disease in a Major US Hospital Network. Canadian Journal of Gastroenterology and Hepatology.
36. Vardavas, C. I., Mathioudakis, A. G., Nikitara, K. (2022). Prognostic factors for mortality, intensive care unit and hospital admission due to SARS-CoV-2: a systematic review and meta-analysis of cohort studies in Europe. European Respiratory Review, 31(166).
37. Ortega-Quiroz, R. J. (2022). COVID-19 and Liver Disease: A panorama that is being clarified. Rev Colomb Gastroenterol, 37(2), 131-135.
38. Samir, A., Nabil, F., Ashour, M. (2022). Impact of chronic liver disease on COVID-9 infection at Zagazig University Hospitals. African Journal of Gastroenterology and Hepatology, 5(2), 16-31.
39. Vrsaljko, N., Samadan, L., Viskovic, K. (2022, April). Association of nonalcoholic fatty liver disease with COVID-19 severity and pulmonary thrombosis: CovidFAT, a prospective, observational cohort study. In Open forum infectious diseases (Vol. 9, No. 4, p. ofac073). US: Oxford University Press.
40. Chen, T., Wu, D. I., Chen, H. (2020). Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. bmj, 368.