Received: 19 May 2020 | Revised: 17 June 2020 | Accepted: 20 June 2020

DOI: 10.1111/liv.14583

BRIEF DEFINITIVE REPORT

Liver INTERNATIONAL WILEY

Impact of chronic liver disease on outcomes of hospitalized patients with COVID-19: A multicentre United States experience

Nikroo Hashemi[1,2] | Kathleen Viveiros[1,2] | Walker D. Redd[2,3] | Joyce C. Zhou[2] | Thomas R. McCarty[1,2] | Ahmad N. Bazarbashi[1,2] | Kelly E. Hathorn[1,2] | Danny Wong[2,3] | Cheikh Njie[2,3] | Lin Shen[1,2] | Walter W. Chan[1,2]

[1]Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, Boston, MA, USA

[2]Harvard Medical School, Boston, MA, USA

[3]Department of Medicine, Brigham and Women's Hospital, Boston, MA, USA

Correspondence
Walter W. Chan, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, 75 Francis Street, Boston, MA 02115, USA.
Email: wwchan@bwh.harvard.edu

Funding information
This work was funded, at least in part, by the NIH grant T32 DK007533-35.

Handling Editor: Jian Sun

Abstract

Liver injury has been described with COVID-19, and early reports suggested 2%-11% of patients had chronic liver disease (CLD). In this multicentre retrospective study, we evaluated hospitalized adults with laboratory-confirmed COVID-19 and the impact of CLD on relevant clinical outcomes. Of 363 patients included, 19% had CLD, including 15.2% with NAFLD. Patients with CLD had longer length of stay. After controlling for age, gender, obesity, cardiac diseases, hypertension, hyperlipidaemia, diabetes and pulmonary disorders, CLD and NAFLD were independently associated with ICU admission ([aOR 1.77, 95% CI 1.03-3.04] and [aOR 2.30, 95% CI 1.27-4.17]) and mechanical ventilation ([aOR 2.08, 95% CI 1.20-3.60] and [aOR 2.15, 95% CI 1.18-3.91]). Presence of cirrhosis was an independent predictor of mortality (aOR 12.5, 95% CI 2.16-72.5). Overall, nearly one-fifth of hospitalized COVID-19 patients had CLD, which was associated with more critical illness. Future studies are needed to identify interventions to improve clinical outcomes.

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) first emerged in the fall of 2019 and has since become a global pandemic. This virus, which causes coronavirus disease 2019 (COVID-19), has led to over 4.8 million infections and 316,000 deaths worldwide to date.[1] Prior studies have demonstrated advanced age, chronic cardiopulmonary diseases, immunosuppression and obesity as potential risk factors for worse clinical outcomes among patients with COVID-19 – with mortality often driven by disease-associated cardiopulmonary failure.[2,3] While the virus primarily affects the lungs, experience from China and the USA also suggests that SARS-CoV-2 may impact extra-pulmonary systems, including the gastrointestinal and hepatobiliary systems.[4,5]

Chronic liver disease (CLD), including non-alcoholic fatty liver disease (NAFLD), alcohol-related liver disease and chronic viral hepatitis, comprise a large global burden of disease.[6] Published reports indicate that up to half of adults hospitalized with COVID-19 have abnormal aminotransferase levels and 2%-11% have underlying liver conditions.[7–12] A meta-analysis of 11 observational studies of 2034 adults with COVID-19 from China revealed an overall CLD prevalence of 3%.[13] However, there are limited reports on the nature of liver disease among COVID-19 patients and it remains unclear how underlying CLD influences hepatic injury and clinical outcomes in these patients. Higher rates of liver dysfunction have been observed in patients with more severe cases of COVID-19 and among those requiring admission to the intensive care unit (ICU).[12,14] Given the high prevalence of NAFLD in the USA, as well as metabolic syndrome and

obesity being potential poor prognostic factors for COVID-19, we hypothesized that CLD, particularly NAFLD, may be associated with more severe clinical course and worse outcomes among patients with COVID-19. We therefore aimed to describe the characteristics of CLD and study the effect of existing liver-related comorbidities on the manifestations and outcomes of hospitalized adult patients with COVID-19.

1.1 | METHODS

1.1.1 | Study Design and Population

We performed a retrospective cohort study of all consecutive adult patients hospitalized with a positive SARS-CoV-2 infection via polymerase chain reaction (PCR) nasopharyngeal swab or tracheal aspirate from 11 March to 2 April 2020. Centres included were nine hospitals (two large tertiary centres and seven community hospitals) in a single healthcare system in Massachusetts, USA. All patients were followed to hospital discharge or death. Patient demographics, presence and type of CLD, comorbid conditions, laboratory data and clinically relevant hospitalization outcomes (including ICU admission, need for mechanical ventilation and in-hospital mortality) were obtained from electronic medical records. The presence of CLD was identified and confirmed through manual review of laboratory, imaging and/or histopathological data by the study investigators. NAFLD was defined by the presence of diffuse hepatic steatosis on any prior imaging studies or liver histology in the absence of secondary causes of hepatic fat accumulation including significant alcohol use, long-term use of steatogenic medications or hereditary disorders. Data on alcohol consumption and, when available, quantification were extracted through chart review. Chronic hepatitis B virus (HBV) was defined as presence of hepatitis B surface antigen for greater than 6 months, with or without detectable viremia. Chronic hepatitis C virus (HCV) was defined as history of HCV viremia, including those with cured infection who have evidence of liver fibrosis on histology or non-invasive testing. Among patients with underlying CLD, cirrhosis was defined by the presence of morphological features of cirrhosis with or without portal hypertension on abdominal imaging and/or liver histology. Decompensation was defined as the presence of ascites or hepatic encephalopathy on active treatment or history of variceal bleeding.

1.1.2 | Outcome Measures

The primary outcomes were measurements of disease severity among hospitalized COVID-19 patients with and without CLD, including the mean hospital length of stay, prevalence of ICU admission, rate of need for mechanical ventilation and all-cause in-hospital mortality. Secondary outcomes included patient characteristics (age, gender, BMI and race), prevalence of medical comorbidities (hypertension, diabetes, cardiac conditions and pulmonary disease), and laboratory results on admission (including alanine aminotransferases [ALT], aspartate aminotransferase [AST], total and direct bilirubin and alkaline phosphatase) among patients with CLD versus those without. Further analyses on clinical outcomes were also performed by stratifying patients with CLD into those with and without cirrhosis, and into NAFLD and non-NAFLD.

1.2 | Statistical Analyses

Continuous variables were reported as means and standard deviations and categorical variables were expressed using numbers and frequencies. Student's t test and Fisher's Exact test were performed for univariate analyses for continuous and categorical variables respectively. Multivariable analyses were performed using logistic regression. All statistical analyses were performed using Statistical Analysis Software version 9.4 (SAS Institute Inc, Cary, NC, USA). The study protocol was approved by the Partners Healthcare Institutional Review Board (2020P00000983).

1.3 | RESULTS

1.3.1 | Study population

A total of 363 patients hospitalized with confirmed COVID-19 were included, with a mean age of 63.4 years (SD ± 16.5) and 201 (55.4%) men. The mean body mass index (BMI) was 30.3 kg/m^2 (SD ± 6.6). Conditions associated with metabolic syndrome were prevalent, including 117 (32.3%) patients with diabetes, 169 (46.6%) patients with dyslipidaemia and 212 (58.4%) patients with hypertension. Overall, 69 (19%) patients were found to have underlying CLD: 55 (15.2%) patients had NAFLD, 6 (1.7%) had compensated cirrhosis (including one with NAFLD, one with alcohol-related liver disease, three with HCV, one with HBV; two patients also had hepatocellular carcinoma [HCC]) and three (0.8%) patients had decompensated cirrhosis (two alcohol-related liver disease and one with previously treated HCV) (Table 1). The cohort did not include any liver transplant recipients.

1.3.2 | Impact of chronic liver disease

Patients with CLD had a greater prevalence of elevated aminotransferases ([AST 66.2% vs 38.8%, $P < .0001$] and [ALT 38.2% vs 26.9%, $P = .06$]) on admission. Additionally, patients with underlying CLD had higher mean AST, ALT and alkaline phosphatase on admission compared to those without CLD. There was no difference in mean total bilirubin, platelet count, creatinine and international normalized ratio (INR) values on admission between the two groups. Peak AST and ALT values during hospitalization were not statistically higher among the CLD group. No significant differences in inflammatory makers on admission, including lactate dehydrogenase and ferritin,

TABLE 1 Baseline characteristics and admission laboratory data of patients hospitalized with CLD with COVID-19

Variable	Chronic Liver Disease, n = 69	No Chronic Liver Disease, n = 294	*P* value
Age (years)	64.8 ± 15.0	63.0 ± 16.9	.42
Male (%)	37 (53.6)	164 (55.8)	.75
White (%)	35 (53.0)	142 (49.8)	.84
Black (%)	6 (9.0)	41 (14.4)	
Hispanic (%)	20 (30.3)	81 (28.4)	
Asian (%)	3 (4.6)	11 (3.9)	
Other (%)	2 (3.0)	10 (3.5)	
Tobacco Use (%)	10 (14.5)	31 (10.5)	.35
Alcohol Use (%)	13 (18.8)	34 (11.6)	.11
BMI	32.0 ± 6.8	29.9 ± 6.6	**.018**
Length of Stay (days)	13.4 ± 11.0	10.1 ± 8.0	**.038**
Chronic liver disease			
NAFLD (%)	55 (79.7)		
NAFLD and ALD (%)	1 (1.4)		
HCV (%)[a]	6 (8.7)		
HBV (%)	2 (2.9)		
PBC (%)	1 (1.4)		
Compensated cirrhosis: NAFLD (1), viral (4), alcohol (1); includes 2 hepatocellular carcinoma (1 HBV, 1 HCV), (%)	6 (8.7)		
Decompensated cirrhosis: alcohol (2), HCV (1) (%)	3 (4.3)		
Comorbidities			
Hypertension (%)	45 (65.2)	167 (56.8)	.20
Diabetes mellitus (%)	28 (40.6)	89 (30.4)	.10
Hyperlipidaemia (%)	32 (46.4)	137 (46.6)	.97
Coronary artery disease (%)	10 (14.5)	42 (14.3)	.96
Congestive heart disease (%)	7 (10.1)	32 (10.9)	.85
Pulmonary disease[b] (%)	20 (29.0)	56 (19.1)	.07
Laboratory data on admission			
Abnormal AST, n (%)			
Admission	45 (66.2)	111 (38.8)	**<.0001**
Peak[c]	59 (86.6)	195 (67.2)	**.0014**
Abnormal ALT, n (%)			
Admission	26 (38.2)	77 (26.9)	.06
Peak[c]	44 (64.7)	169 (58.1)	.32
AST (U/L)			
Admission	73.5 ± 83.2	45.5 ± 49.2	**.0003**
Peak[c]	153.8 ± 179.7	106.8 ± 213.5	.09
ALT (U/L)			
Admission	49.0 ± 45.6	33.8 ± 28.3	**.0006**
Peak[c]	95.3 ± 89.0	78.5 ± 114.7	.26
Alkaline phosphatase (U/L)	92.4 ± 54.2	79.2 ± 39.3	**.02**
Total bilirubin (mg/dL)	0.95 ± 2.12	0.54 ± 0.48	.12
Platelet count (K/μL)	186.0 ± 74.7	200.1 ± 82.8	.20
Ferritin (ng/mL)	825.0 ± 850.0	843.5 ± 1117.1	.90

(Continues)

TABLE 1 (Continued)

Variable	Chronic Liver Disease, n = 69	No Chronic Liver Disease, n = 294	*P* value
Lactate dehydrogenase (U/L)	381.2 ± 144.8	342.0 ± 187.4	.06
Peak creatinine phosphokinase[c] (U/L)	2810.3 ± 14 056	2517.2 ± 18 300	.90
International normalized ratio (INR)	1.22 ± 0.46	1.26 ± 0.48	.55
Creatinine (mg/dL)	1.18 ± 0.63	2.43 ± 15.1	.16

Abbreviations: ALD, alcoholic liver disease; BMI, body mass index (kg/m^2); HBV, hepatitis B virus; HCV, hepatitis C virus; NAFLD, non-alcoholic fatty liver disease; PBC, primary biliary cholangitis.

All the bold values highlight those with $P < .05$.

[a]1 untreated, 5 cured (4 cirrhosis, 1 stage 3 fibrosis)

[b]chronic obstructive lung disease, asthma, pulmonary hypertension, interstitial lung disease

[c]Peak laboratory values throughout hospitalization

and peak creatinine phosphokinase (CPK) were noted between those with and without CLD (Table 1).

In the assessment of hospitalization course and outcomes, patients with CLD had higher rates of ICU stay (49.3% vs 35.0%, $P = .028$), need for mechanical ventilation (47.8% vs 30.3%, $P = .0055$) and in-hospital, all-cause mortality (23.9% vs 13.2%, $P = .029$). The mean length of stay was also longer among those with CLD compared to those without (13.4 ± 10.5 vs 10.1 ± 8.0, $P = .038$). Patients with cirrhosis had higher mortality than those without cirrhosis (55.6% vs 13.2%, $P = .0004$). On multivariable analyses controlling for age, gender, BMI, cardiac disease, hypertension, diabetes and pulmonary disorders, CLD remained an independent predictor for ICU admission (adjusted OR 1.77, 95% CI 1.03-3.04, $P = .04$) and for need for mechanical ventilation (adjusted OR 2.08, 95% CI 1.20-3.60, $P = .0092$), but not for death (adjusted OR 2.00, 95% CI 0.94-4.28, $P = .07$) (Table 2). When CLD was stratified into two groups (those with cirrhosis and those without cirrhosis), cirrhosis was an independent predictor for mortality on multivariable analysis (adjusted OR 12.5, 95% CI 2.16-72.5, $P = .009$) compared to patients without CLD, but not for mechanical ventilation or ICU admission. Non-cirrhosis CLD, on the other hand, was not associated with mortality (adjusted OR 1.47, 95% CI: 0.64-3.38, $P = .13$).

1.3.3 | Impact of non-alcoholic fatty liver disease

On secondary analyses, we stratified CLD patients into those with NAFLD versus other aetiologies of CLD. The BMI was significantly higher among patients with NAFLD compared to those with non-NAFLD CLD (32.9 ± 6.9 vs 28.2 ± 4.9, $P = .024$). A significantly higher proportion of non-NAFLD CLD patients had cirrhosis compared to NAFLD patients (61.5% vs 1.8%, $P < .0001$). On univariate analyses, when compared to patients without CLD, those with NAFLD had significantly higher rates of ICU admission (50.9% vs 35.2%, $P = .0095$) and need for mechanical ventilation (49.1% vs 30.4%, $P = .006$). On the other hand, there were no differences between patients with non-NAFLD CLD and those with no CLD in ICU admission (38.5% vs 33.7%, $P = .81$) and need for mechanical ventilation (38.5% vs 30.4%, $P = .54$). In-hospital mortality was significantly higher among patients with non-NAFLD CLD (53.9% vs 13.2%, $P < .0001$) but not among NAFLD patients (16.4% vs 13.2%, $P = .54$), when compared to individuals without CLD. Notably, four of seven (57%) patients who died in the non-NAFLD CLD group had cirrhosis compared to one of nine (11%) patients who died in the NAFLD group.

On multivariate analyses controlling for age, gender, BMI, cardiac disease, hypertension, diabetes mellitus, hyperlipidaemia and pulmonary disorders, CLD as a result of NAFLD remained significantly associated with ICU admission (adjusted OR 2.30, 95% CI 1.27-4.17, $P = .03$) and with needing mechanical ventilation (adjusted OR 2.15, 95% CI 1.18-3.91, $P = .02$). Neither NAFLD nor non-NAFLD CLD was predictive for death on multivariate model.

1.4 | DISCUSSION

In this multicentre study of two tertiary and seven community hospitals in the Northeastern United States, we found that 19% of adult patients hospitalized with COVID-19 had pre-existing CLD. This is higher than published reports thus far from China and the USA. In the largest study to date from China, only the prevalence of HBV (2.1%) was reported.[12] The causes of 'liver disease' in another study, where CLD was present among 5% of patients, included NAFLD, HBV or alcohol-related.[9] In the first recently published large case series of hospitalized patients in the USA, only a few patients had underlying liver disease (cirrhosis 0.4%, HBV 0.1%, HCV < 0.1%). Other CLD including NAFLD was not reported, despite the high prevalence of metabolic comorbidities in the cohort.[15] Considering the high prevalence of NAFLD in the USA and the mean BMI of 30.3 kg/m^2 in our cohort, our prevalence rate of CLD may reflect a more accurate representation of the US population. Additionally, our systematically performed, manual review of each patient's prior medical records may have allowed us to better capture and ascertain the presence and type of CLD compared to some prior retrospective studies, which may have mostly relied on diagnosis codes and admission documentation in the electronic medical records. Notably, our robust chart review and data-gathering process

TABLE 2 Multivariate analyses for (A) the need for mechanical ventilation, (B) ICU admission and (C) death

Covariates	Odds Ratio	95% Confidence Interval	*P*-value
(A) Multivariate regression models for need for mechanical ventilation			
CLD vs no CLD	**2.08**	**1.20-3.60**	**.0092**
Age	1.01	0.99-1.03	.27
Obesity	1.23	0.77-1.98	.39
Male	**1.59**	**0.99-2.56**	**.054**
Cardiac diseases	0.64	0.34-1.19	.16
Hypertension	0.77	0.44-1.34	.35
Diabetes	1.39	0.84-2.33	.20
Hyperlipidaemia	1.08	0.66-1.76	.76
Pulmonary disorders	1.04	0.58-1.85	.90
(B) Multivariate regression models for **ICU Admission**			
CLD vs no CLD	**1.77**	**1.03-3.04**	**.04**
Age	1.01	0.99-1.02	.57
Obesity	1.26	0.79-1.98	.33
Male	1.51	0.96-2.38	.08
Cardiac diseases	0.88	0.49-1.58	.66
Hypertension	0.93	0.55-1.60	.80
Diabetes	1.22	0.74-2.00	.44
Hyperlipidaemia	1.01	0.63-1.63	.96
Pulmonary disorders	0.88	0.50-1.54	.65
(C) Multivariate regression models for **death**			
CLD vs no CLD	2.00	0.94-4.28	.07
Age	**1.08**	**1.05-1.12**	**<.0001**
Obesity	1.03	0.51-2.09	.94
Male	1.62	0.80-3.26	.18
Cardiac diseases	0.98	0.46-2.09	.96
Hypertension	2.20	0.88-5.52	.09
Diabetes	1.38	0.68-2.79	.37
Hyperlipidaemia	0.91	0.46-1.81	.78
Pulmonary disorders	2.01	0.95-4.25	.07

All the bold values highlight those with $P < .05$.

allowed us to identify cases of fatty liver which may not have been captured through diagnosis codes or simple review of admission/discharge problem lists. Furthermore, another reason for the higher prevalence of baseline CLD observed in our study versus those of previously reported cohorts may be the relatively higher mean age of our study population.

Patients with CLD had an increased prevalence of abnormal AST and ALT levels, as well as higher mean values of AST, ALT and alkaline phosphatase on admission. However, interestingly, peak AST and ALT values during hospitalization did not differ between patients with and without CLD, possibly due to a variety of factors. The first may be due to drug hepatotoxicity, as many patients received antiviral and anti-inflammatory medications against COVID-19 during hospitalization. Second, immune-mediated inflammation, cytokine release, ischemia and congestion related to positive pressure ventilation may also contribute to liver injury among critically ill patients. Additionally, underlying liver injury or inflammation may also result in a lower hepatic reserve and lower threshold for significant injury induced by direct viral effect, immune-mediated inflammation or medications.

Patients with CLD had increased length of stay, higher rates of ICU stay and need for mechanical ventilation compared to those without CLD, even after controlling for comorbidities. Interestingly, this association was observed in patients with NAFLD but not among those with non-NAFLD CLD, although this may be potentially influenced by small sample size of the non-NAFLD CLD group. This difference might also, in part, be secondary to the association between NAFLD and obesity, as the mean BMI of NAFLD patients was significantly higher compared to that of non-NAFLD CLD patients. Prior studies have identified increased morbidity in patients with obesity in the ICU.[16] There was also an observed higher rate of mechanical ventilation among severely obese hospitalized patients with COVID-19 in a recent US study.[3] The pro-inflammatory state associated with obesity may contribute to the increased disease severity associated with COVID-19, with potentially higher risk for complications such as acute respiratory distress syndrome (ARDS), as has previously been observed among non-COVID-19 populations.[17,18] However, the increased rates of clinical severity among NAFLD patients were observed even after controlling for the presence of obesity, suggesting that the effect of NAFLD on disease severity may be due to more than increased BMI alone. A prior study found liver fat to be associated with higher serum markers of inflammation and oxidative stress.[19] NAFLD has also been linked to reduction in lung function measured on pulmonary function test.[20] These suggest possible pathways through which NAFLD may impact the clinical course of COVID-19, which often manifests with hypoxemic respiratory failure, progressive systemic inflammatory response and ARDS.

We found that compared to patients without CLD, those with cirrhosis had increased mortality, even after adjusting for other comorbidities. This relationship with mortality was not seen with non-cirrhotic CLD. On the other hand, mechanical ventilation and ICU admission were significantly associated with non-cirrhotic CLD, but not cirrhosis. The majority of patients with cirrhosis in our cohort had non-NAFLD CLD. These results may be explained by the observation that all patients with cirrhosis who required ICU care in our cohort died. This was substantially higher than the mortality rate (28%) among patients with non-cirrhosis CLD who required ICU admission, suggesting that presence of cirrhosis is associated with significant mortality among critically ill COVID-19 patients. More specifically, of the two patients with cirrhosis and HCC, one died of multi-organ failure and the other was discharged on home hospice. Our outcome results are compatible with those of a recent study analysing electronic medical records based on diagnosis codes of a large number of COVID-19 patients aged 10 years or older from healthcare centres across the USA.

The prevalence of pre-existing liver disease in that cohort was 9% (cirrhosis 1.8%) and was associated with a significantly higher risk of mortality and hospitalizations especially among those with cirrhosis.[21]

Our study has several limitations. First is the retrospective design. Secondly, the diagnosis of CLD was determined based on prior evaluations such as imaging studies or histopathology. It is, therefore, possible that some patients with undiagnosed CLD may be misclassified. Second, our cohort focuses on hospitalized patients and precludes the evaluation of patients with perhaps milder courses of COVID-19, potentially over-estimating the effects of SARS-CoV-2 on the liver. Finally, as this study includes data from multiple hospitals, the criteria for ICU admission and usage of mechanical ventilation may not be uniform. However, decisions for escalation to critical care are based mainly on clinician judgement, as there are no set guidelines at individual sites. In addition, as all nine hospitals belong to a single healthcare system, patients are often transferred between sites if ICU overcapacity at any individual site occurred, thereby decreasing potential influence of non-clinical factors in decisions of care. Despite the above limitations, this is one of the first and largest US studies to date to systematically evaluate the effect of underlying liver disease on manifestations and outcomes of COVID-19. Moreover, the CLD status was classified independently by two experienced liver specialists based on careful manual review of each patient's record, including all available imaging studies and histopathologic reports. Our study also included patients hospitalized in both tertiary medical centres and community settings, thereby improving the generalizability of our results.

In summary, in our cohort of hospitalized US adults with COVID-19, approximately one in five patients had underlying CLD, of whom 13% had confirmed cirrhosis. While patients with NAFLD were more likely to be admitted to the ICU and require mechanical ventilation, only those with cirrhosis, which were mostly secondary to non-NAFLD CLD in our cohort, had an increased risk of mortality. Further research is needed to better understand the effect of underlying CLD, specifically NAFLD, on the severity of COVID-19 and identify interventions to improve patient outcomes.

CONFLICTS OF INTEREST

Nikroo Hashemi has no conflicts to disclose. Kathleen Viveiros has no conflicts to disclose. Walker D. Redd has no conflicts to disclose. Joyce C. Zhou has no conflicts to disclose. Thomas R. McCarty has no conflicts to disclose. Ahmad Najdat Bazarbashi has no conflicts to disclose. Kelly E. Hathorn has no conflicts to disclose. Danny Wong has no conflicts to disclose. Cheikh Njie has no conflicts to disclose. Lin Shen has no conflicts to disclose. Walter W. Chan has no conflicts to disclose.

AUTHOR CONTRIBUTIONS

Study concept and design: NH, KV and WWC. Data Acquisition: NH, KV, WDR, JCZ, TRM, ANB, KEH, DW, CN and LS. Paper preparation and statistical analysis: NH, KV and WWC. Critical revisions – NH, KV, WDR, JCZ, TRM, ANB, KEH, DW, CN, LS and WWC. Administrative support and overall study supervision – WWC.

ORCID

Walter W. Chan https://orcid.org/0000-0002-1709-8230

REFERENCES

1. Coronavirus disease (COVID-19) pandemic. Latest updates. World Health Organization. 2020. https://www.who.int/emergencies/diseasees/novel-coronaviru-2019. Updated Mat 1st 2020. Accessed May 1, 2020
2. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054-1062.
3. Kalligeros M, Shehadeh F, Mylona EK, et al. Association of obesity with disease severity among patients with COVID-19. *Obesity (Silver Spring)*. 2020.
4. Zhou Z, Zhao N, Shu Y, Han S, Chen B, Shu X. Effect of gastrointestinal symptoms on patients infected with coronavirus disease 2019. *Gastroenterology*. 2020.
5. Jin XI, Lian J-S, Hu J-H, et al. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. *Gut*. 2020;69:1002-1009.
6. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. *J Hepatol*. 2019;70:151-171.
7. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol*. 2020;5:428-430.
8. Fan Z, Chen L, Li J, et al. Clinical features of COVID-19-Related Liver Damage. *Clin Gastroenterol Hepatol*. 2020.
9. Cai Q, Huang D, Yu H, et al. COVID-19: Abnormal liver function tests. *J Hepatol*. 2020.
10. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected Pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061.
11. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis*. 2020;20:425-434.
12. Guan W-J, Ni Z-Y, Hu YU, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382:1708-1720.
13. Mantovani A, Beatrice G, Dalbeni A. Coronavirus disease 2019 and prevalence of chronic liver disease: a meta-analysis. *Liver Int*. 2020;40:1316-1320.
14. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395:497-506.
15. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting characteristics, comorbidities, and outcomes among 5700 patients hospitalized with COVID-19 in the New York City Area. *JAMA*. 2020.
16. Schetz M, De Jong A, Deane AM, et al. Obesity in the critically ill: a narrative review. *Intensive Care Med*. 2019;45:757-769.
17. Gong MN, Bajwa EK, Thompson BT, Christiani DC. Body mass index is associated with the development of acute respiratory distress syndrome. *Thorax*. 2010;65:44-50.
18. Karnatovskaia LV, Lee AS, Bender SP, et al. Obstructive sleep apnea, obesity, and the development of acute respiratory distress syndrome. *J Clin Sleep Med*. 2014;10:657-662.
19. Fricker ZP, Pedley A, Massaro JM, et al. Liver fat is associated with markers of inflammation and oxidative stress in analysis of data from the framingham heart study. *Clin Gastroenterol Hepatol*. 2019;17(1157–64):e4.
20. Mantovani A, Lonardo A, Vinco G, et al. Association between non-alcoholic fatty liver disease and decreased lung function in

adults: a systematic review and meta-analysis. *Diabetes Metab*. 2019;45:536-544.

21. Singh S, Khan A. Clinical characteristics and outcomes of COVID-19 among patients with pre-existing liver disease in United States: a multi-center research network study. *Gastroenterology*. 2020.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Hashemi N, Viveiros K, Redd WD, et al. Impact of chronic liver disease on outcomes of hospitalized patients with COVID-19: A multicentre United States experience. *Liver Int*. 2020;40:2515–2521. https://doi.org/10.1111/liv.14583