



# COVID-19 in patients with preexisting liver disease: Clinical features and outcomes from Northern Iran

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## ABSTRACT

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People living with chronic liver disease (CLD) may experience more severe consequences when infected with coronavirus disease 2019 (COVID-19). However, information from Middle Eastern populations is still limited. The present research examined the presentation and outcomes of COVID-19 among patients with underlying liver disorders in Northern Iran. To achieve this, a retrospective cross-sectional review was carried out in a major referral hospital between March 2020 and March 2023. Adult patients with confirmed COVID-19 and documented preexisting liver disease were included. Demographic, clinical, and outcome data were extracted and analyzed. Among 83 identified patients, common symptoms were myalgia (59%), cough (56.6%), and respiratory distress (49.4%). Hypoxemia (25.3%) was significantly associated with mortality (47.4% vs. 18.8%,  $P = 0.017$ ). Altered consciousness also predicted poor outcomes (31.6% vs. 9.4%,  $P = 0.016$ ). COVID-19 patients with preexisting liver disease had increased risk of adverse outcomes, with hypoxemia and altered mental status serving as key mortality predictors. Early recognition and tailored management are essential for this vulnerable group.

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## 1. Introduction

The emergence of coronavirus disease 2019 (COVID-19), triggered by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has quickly developed into a worldwide health emergency, resulting in significant illness and death [1,2]. While the infection primarily targets the respiratory tract, it is now clear that various other organs may also be affected, especially in individuals with underlying health conditions [3]. Among these, liver disease and liver transplantation have attracted increasing attention due to their potential impact on the severity and outcomes of COVID-19 [4,5]. Peoples with underlying liver disorders represent a vulnerable population, as the underlying hepatic dysfunction, impaired immune response, and coexisting metabolic or viral conditions may predispose them to adverse clinical outcomes [6, 7]. Several studies have reported that individuals with preexisting liver disorders, including cirrhosis, viral hepatitis, and nonalcoholic fatty liver disease, are at higher risk of complications, prolonged hospitalization, and increased mortality when infected with SARS-CoV-2 [8-10]. In addition, this viral disease itself can contribute to liver injury through direct viral cytopathic effects, systemic inflammatory responses, hypoxia, and drug-induced hepatotoxicity [11]. Although an increasing number of studies have explored the interaction between liver disease and coronavirus infection, information on the clinical progression and outcomes of COVID-19 in this patient group is still scarce [12,13], particularly across Middle Eastern populations. Gaining insight into how chronic liver disorders influence the severity and prognosis of COVID-19 is essential for refining risk assessment, optimizing therapeutic decisions, and determining public health strategies. In this context, the present investigation examined the clinical profile and outcomes of COVID-19 patients with preexisting liver disease in Northern Iran.

## 2. Materials and Methods

### 2.1 Study protocol

This research employed a retrospective cross-sectional design at Razi Teaching Hospital, a major referral center located in Rasht, Northern Iran. Medical files of patients admitted with a confirmed diagnosis of COVID-19 between March 2020 and March 2023 were reviewed. The study protocol received approval from the Ethics Committee of Guilan University of Medical Sciences (approval code: IR.GUMS.REC.1402.304). Given the retrospective design, the ethics committee waived the requirement for obtaining informed consent.

### 2.2 Enrollment criteria and variables

Patients eligible for the study were adults ( $\geq 18$  years) who had a confirmed COVID-19 diagnosis verified by reverse transcriptase-polymerase chain reaction (RT-

PCR) testing. Individuals presenting with underlying chronic illnesses other than liver-related conditions, incomplete medical records, or those transferred from other hospitals were excluded. Individuals with a prior diagnosis of liver disease, such as cirrhosis, hepatitis of viral origin, nonalcoholic fatty liver disease, and similar disorders, were included in the study population. Patient information was retrieved retrospectively from electronic health records using a structured form. The collected data covered demographic variables (age, sex), presenting symptoms, coexisting medical conditions, and vital signs at admission. Details on treatment measures, such as oxygen use, and intensive care admission, together with outcomes like hospital stay duration, need for mechanical ventilation, and mortality were documented.

### 2.3 Data analysis

All statistical procedures were conducted with SPSS software (version 22, IBM Corp., Armonk, NY, USA). Continuous data were reported as mean values with corresponding standard deviations. Categorical data were presented as counts and percentages, with group differences assessed using either the chi-square test or Fisher's exact test, depending on suitability. Statistical significance was defined as a p-value below 0.05.

## 3. Results

Eighty-three patients with documented liver disorders and confirmed COVID-19 infection were analyzed. The distribution of baseline clinical manifestations is summarized in Table 1. Myalgia was reported in 49 patients (59%), followed by cough in 47 (56.6%), respiratory distress in 41 (49.4%), and fever in 31 (37.3%). Gastrointestinal symptoms were less frequent, with nausea in 7 patients (8.4%) and diarrhea in 4 patients (4.8%). Anosmia and dysgeusia were uncommon, reported in 4 (4.8%) and 5 (6%) cases, respectively. Hypoxemia ( $\text{SpO}_2 < 93\%$ ) was present in 21 patients (25.3%). The association between baseline characteristics (age, sex, and comorbidities) as well as COVID-19 symptoms and hospitalization outcomes was evaluated. Statistical analysis revealed no significant associations between these variables and length of hospital stay ( $P > 0.05$ ). Similarly, none of the demographic or clinical factors were significantly correlated with the need for ICU admission ( $P > 0.05$ ) or mechanical ventilation ( $P > 0.05$ ). In contrast, the mortality analysis identified significant associations with two clinical factors. An altered level of consciousness was more frequently observed in patients who died compared with those who recovered (31.6% vs. 9.4%,  $P = 0.016$ ). Likewise, hypoxemia ( $\text{SpO}_2 < 93\%$ ) was significantly more common among patients with fatal outcomes than among survivors (47.4% vs. 18.8%,  $P = 0.017$ ). No other baseline or clinical variables were significantly associated with mortality ( $P > 0.05$ ).

**Table 1.** Demographic, symptoms at admission, and treatment measures of COVID-19 patients with preexisting liver disease.

Variable	Group	Frequency	Percentage
Fever	No	52	62.7
	Yes	31	37.3
Cough	No	36	43.4
	Yes	47	56.6
Myalgia	No	34	41
	Yes	49	59
Respiratory distress	No	42	50.6
	Yes	41	49.4
Altered level of consciousness	No	71	85.5
	Yes	12	14.5
Anosmia	No	79	95.2
	Yes	4	4.8
Dysgeusia	No	78	94
	Yes	5	6
Nausea	No	76	91.6
	Yes	7	8.4
Diarrhea	No	79	95.2
	Yes	4	4.8
SpO <sub>2</sub>	<93	21	25.3
	≥93	62	74.8
Respiratory rate	4-18	6	8.3
	18-22	55	76.4
	22-28	9	12.5
	>28	2	2.8
Oxygen therapy	No	27	32.5
	Yes	56	67.5

#### 4. Discussion

This research provides insights into the interaction concerning chronic liver disease (CLD) and COVID-19 in a Middle Eastern setting, contributing to the global body of evidence on this important issue. Consistent with global evidence, our findings underscore that CLD is linked with a higher risk of severe COVID-19 and mortality. A meta-analysis of 40 studies including over 900,000 participants demonstrated that CLD significantly elevates the odds of severe COVID-19 (pooled OR = 2.44; 95% CI, 1.89–3.16) and death (pooled OR = 2.35; 95% CI, 1.85–3.00) compared with non-CLD patients [14]. Similarly, data from a large US cohort (n = 2780) indicated that patients with CLD had a nearly three-fold higher risk of mortality (RR = 2.8; 95% CI, 1.9–4.0; P < 0.001), which persisted even after score matching (RR = 3.0; 95% CI, 1.5–6.0; P = 0.001) [2]. Moreover, mortality risk was substantially higher in cirrhotic patients (RR = 4.6; 95% CI, 2.6–8.3; P < 0.001) [15]. The mechanisms underlying these adverse outcomes are multifactorial. CLD and cirrhosis may predispose patients to immune dysregulation, rendering them vulnerable to severe SARS-CoV-2 infection [16]. The virus can infect liver cells via the ACE2 receptor, potentially causing direct cytopathic effects, and systemic hypoxia associated with respiratory failure may aggravate hepatic injury [15]. During systemic conditions, those with cirrhosis show a higher likelihood of progressing to acute-on-chronic liver failure [17]. Although our study did not differentiate by liver disease etiology or severity, the evidence indicates that severity of liver disease, particularly cirrhosis further increases

the risk of poor outcomes [18,19]. Regarding specific liver-related conditions, data are heterogeneous. Regional and etiological differences, along with comorbidities like diabetes and obesity, likely modulate these risks. Multicenter analyses from the U.S. have identified ALD, decompensated cirrhosis, and hepatocellular carcinoma as independent predictors of higher mortality in COVID-19 patients with CLD [20].

Limitations of our study include its retrospective cross-sectional design, modest sample size, and absence of stratification by liver disease etiology, or severity, which limited multivariable analysis. Future studies incorporating larger samples with detailed liver staging and CLD-specific scores could better elucidate risk gradients and guide management protocols.

In conclusion, our findings confirm that preexisting liver disease is an important risk factor for adverse COVID-19 outcomes. Clinical awareness should include monitoring for early neurological changes and hypoxaemia in this vulnerable group. Integration of CLD severity indices and tailored therapeutic strategies may improve prognostication and resource allocation, especially in regions with high CLD prevalence. These data warrant incorporation into clinical guidelines and public health policies to optimize outcomes for patients with CLD during COVID-19.

#### Authors' contributions

Study supervision, Design, and Resources: TY, PS; Data collection, Analysis and Interpretation: SA, MS; Writing draft and Editing: SA, TY, MS, PS. All authors have read and approved the final version of manuscript.

## Conflict of interest

No potential conflict of interest was reported by the authors.

## Ethical declarations

The study protocol received approval from the Ethics Committee of Guilan University of Medical Sciences (approval code: IR.GUMS.REC.1402.304). Given the retrospective design, the ethics committee waived the requirement for obtaining informed consent.

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