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Multicenter study of some liver and heart function tests in SARS-Cov-2 patients from three ethnic groups in Iran

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Abstract

The liver and cardiovascular system disorders are not common in COVID-19 patients, but the patients suffering from these complications are exposed to a higher rate of mortality and disease progression. Hepatic injuries can drive to increased levels of liver enzymes, including ALT, AST, and LDH. Abundant levels of AST, LDH, and CPK can be indicators of cardiac injuries. The current study compares 366 individuals who are divided into COVID-19 patients and healthy individuals groups, in which we have examined hepatic and cardiac function parameters. Moreover, the clinical characteristics of the participants, ethnicities, and their difference with studied parameters were assessed. The results showed Fars individuals are more susceptible to the disease progression, including liver and heart damage. COVID-19 infection is associated with aging, which indicates that the mean age of the case group is ten years older than the control group ($P < 0.001$). The blood sugar in the case group (140.50) was higher than in the control group (131.66), although there was no difference between the infection and BS ($P = 0.505$). Similarly, the increased mean of the ALT level in the case group (102.369) compared with the control group (68.324) resulted in no significant difference ($P = 0.318$). Other parameters, including CPK, LDH, and AST showed an increase in the control group values compared to the case group; however, the differences were not significant ($P = 0.264$, $P = 0.795$, $P = 0.417$). Considering the involvement of cardiac and hepatic organs by SARS-CoV-2, paying particular attention to the disorders of these organs through assessing the hepatic and cardiac function parameters can enhance the patient's recovery and survival. However, in this study, we not observed significant differences, except for the Fars people. There is need for further assessment of this issue.

Keywords SARS-CoV-2 · COVID-19 · Liver function test · Heart function test

Seyed Majid Fatahi and Hadi Razavi Nikoo contributed equally for this work.

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Introduction

Coronavirus is one of the viruses which can cause respiratory and gastrointestinal diseases among humans and other mammals. The members of the Coronaviridae family tend to invade the upper respiratory tract and drive to diseases varying from mild to severe such as common cold and pneumonia. In December 2019, the number of patients experiencing the symptoms of pneumonia of unknown origin started to rise rapidly in Wuhan, China; this was the outset of a global health emergency that caused coronavirus disease (COVID-19) [8]. Most COVID-19-infected individuals experience mild complications, but some develop severe pneumonia, acute respiratory distress syndrome (ARDS), septic shock, multiple-organ failure (MOF). Involvements of the gastrointestinal tract, liver, and cardiovascular system disorders also occur [4, 14].

The receptor of SARS-CoV-2 is angiotensin-converting enzyme 2 (ACE2), expressing vastly on the alveolar cells. ACE2 is also expressed substantially in the gastrointestinal tract and cardiovascular systems [1].

Hepatic dysfunctions have been diagnosed by a slight rise in bilirubin and increased levels of the alanine aminotransferase (ALT), also called serum glutamic-oxaloacetic transaminase (SGPT), and the aspartate aminotransferase (AST), also called serum glutamic-oxaloacetic transaminase (SGOT), in COVID-19 patients and some severe hepatic injuries were also reported [4]. Patients infected by SARS-CoV-2 exhibit complications, including diarrhea, decreased levels of lymphocytes, and increased liver enzymes. During the initial stages of SARS-CoV-2 infection, RNA belonging to this virus was detected in stool and blood samples from 2 to 10% of the patients suffering from gastrointestinal symptoms such as diarrhea, abdominal pain, nausea, and vomiting [18]. Cytokine storm resulting from the over-activation of the immune system against SARS-CoV-2 infection is one of the paths that may affect the liver [3]. The abnormal increase of pro-inflammatory cytokines, including IL-1, IL-2, IL-6, IL-8, IL-10, IL-17, and interferon- γ in the COVID-19 patient's serum, may indicate the disease severity. Patients with severe COVID-19 experience diminished lymphocytes and increased neutrophil levels [10].

Heart disease symptoms such as heart palpitations or chest pain have been reported in COVID-19 patients. Previous studies have shown that 40% of COVID-19 patients are afflicted by underlying heart diseases [4]. Moreover, 26% of COVID-19 patients who require intensive cardiovascular care are suffering from arrhythmia (16.7%) and acute coronary syndrome (7.2%), in addition to other complications [12]. The patients suffering from myocardial injury originating from SARS-CoV-2 infection are exposed to a substantially higher rate of mortality [6].

Lactate dehydrogenase (LDH) is an intracellular enzyme found in many organs, including the liver and heart; thus, its rise is detectable in cardiac injuries. Creatine kinase (CK) is another factor that increases are associated with cardiac injury; CK owns three isozymes, and among them, CK-MB is highly associated with cardiac cells. On the other hand, high levels of ALT and AST were reported in COVID-19 patients; increased levels of these enzymes correlate with liver injury [11].

The current study aims to assess the mentioned liver and heart function parameters of the patients affected by the novel coronavirus and compare them with the healthy individuals to pave the way for choosing and following efficient therapeutic directions for COVID-19 patients who are suffering from cardiac and hepatic injuries.

Methods

Subjects and methods

The participants of the case group in the current study were chosen among the COVID-19 patients suffering from respiratory disorders and referred to the Shohada Ashayer hospital of Khorramabad city (Lorestan, Iran) and 5 Azar hospital of Gorgan city (Golestan, Iran) between 20th of March 2020 to 20th of June 2020. All of the patients in this study with history of liver/heart function abnormalities, diabetes or other underlying diseases be excluded. PCR-based laboratory tests and CT scans confirmed the infection of these patients. The control group participants were selected among individuals referred to the hospitals for being suspected of infection but got negative PCR tests and CT scans for COVID-19. The participant's ethnicities comprise Lor, Fars, and Turkmen races. The Lor live in the Zagros Mount in the midwest of Iran, the Turkoman tribes live to the northeast near the border of Turkomanstan, and Fars are the dominant people scattered across the country.

After consenting to the enter study, 5 ml venous blood was collected in EDTA-containing tubes, and 5 ml venous blood was collected without EDTA. Blood samples containing EDTA were employed for the spectrophotometric measurements performed at 340 nm for LDH and 320 nm for ALT, AST, and CPK using Man company kits (Iran); The BS of the EDTA-free blood sample was assessed using a BS test kit (Man company, Iran) and the AutoAnalyzer.

Statistical analysis

All the statistical analyses were performed using IBM SPSS V.26, and the descriptive statistics were presented. The Kolmogorov–Smirnov test was employed to evaluate the normality of data. The independent t-test, fisher's exact test,

and chi-squared test were applied to analyze the data. A *P* value < 0.05 was considered statistically significant for all tests.

Results

The current study includes 366 participants; 195 patients were diagnosed with confirmed COVID-19, and 171 controls were negative for COVID-19 PCR-based laboratory tests and CT scans. The number of female participants was 170, of which 98 tested positive for COVID-19 comprising 50.25% of the case group, whereas 72 participants owned negative tests for COVID-19, accounting for 42% of the control group. Our study includes 196 male participants; 97 participants tested positive for COVID-19 comprising 49% of the case group, while the COVID-19 tests and CT scans were negative for 99 cases, accounting for 57.9% of the control group.

In the current study, 71.7% of COVID-19 patients were hospitalized in the general ward, whereas this percentage was dramatically lower for the patients hospitalized in ICU (18.2%) and infection (isolation) ward (10.1%). Accordingly, their hospitalization mean duration were 4.8, 7.4, and 11.6 days.

Clinical manifestations and underlying diseases of the participants belonging to both cases and control groups have been assessed during the current study, and the results have been presented in Table 1. According to Table 1, there is a significant difference between the clinical manifestations, including fever (*P* < 0.001), respiratory distress (*P* < 0.001), and diabetes (*P* = 0.014) of patients and healthy individuals. The muscle pain indicates no differences between these two groups, but this clinical manifestation was common amongst patients afflicted by severe COVID-19. Anosmia and ageusia were observed in some patients, but no significant difference between both groups was found. In fact, none of the individuals belonging to the control group exhibited such clinical manifestation. Moreover, the assessment of the declined level of consciousness demonstrated that none of the participants experienced this clinical presentation in both groups, except one in the case group. Any participants did not exhibit dizziness and abdominal pain. Underlying diseases, including liver, chronic cardiac diseases, and hypertension, were also evaluated, and there were no significant differences regarding such diseases between both groups. Although, participants who have diabetes exhibited significant differences between both case and control groups (*P* = 0.014) (Table 1).

The results of heart function tests, including ALT, AST, LDH, CPK, and age of the participants, have been compared in Table 2. According to Table 2, there is a significant age difference (*P* < 0.001); the mean age of the case

Table 1 Comparisons between the clinical manifestations of cases and control groups

Variable		Groups		<i>P</i> value*
		Control n(%)	Case n(%)	
Fever	No	105 (68.2)	96 (48.2)	<0.001
	Yes	49(31.8)	103 (51.8)	
Cough	No	99 (64.3)	112 (56.3)	0.155
	Yes	55 (35.7)	87 (43.7)	
Muscle pain	No	137 (89.0)	162 (81.4)	0.054
	Yes	17 (11.0)	37 (18.6)	
Respiratory distress	No	106 (68.8)	91 (45.7)	<0.001
	Yes	48 (31.2)	108 (54.3)	
Anosmia	No	82 (100)	190 (95.5)	0.063
	Yes	0 (0.00)	9 (4.5)	
Ageusia	No	82 (100)	189 (95.5)	0.062
	Yes	0 (0.00)	9 (4.5)	
Nausea	No	63 (100)	165 (97.1)	0.327
	Yes	0 (0.00)	5 (2.9)	
Vomiting	No	63 (100)	166 (97.6)	0.576
	Yes	0 (0.00)	4 (2.4)	
Diarrhea	No	133 (98.5)	164 (96.5)	0.309
	Yes	2 (1.5)	6 (3.5)	
Diabetes	No	145 (94.2)	171 (85.9)	0.014
	Yes	9 (5.8)	28 (14.1)	
Chronic liver disease	No	82 (100)	195 (98.0)	0.325
	Yes	0 (0)	4 (2.0)	
Chronic cardiac disease	No	143 (92.9)	181 (91.0)	0.563
	Yes	11 (7.1)	18 (9.0)	
Hypertension	No	146 (94.8)	186 (93.5)	0.656
	Yes	8 (5.2)	13 (6.5)	

*Fisher Exact Test

Table 2 The comparisons of some liver and heart function tests between case and control groups

Variable	Group	N	Mean	Sd	<i>P</i> value
Age	Control	172	45.85	21.075	<0.001
	Case	194	55.75	18.017	
BS	Control	65	131.66	81.322	0.505
	Case	82	140.50	78.339	
CPK	Control	78	395.10	1281.833	0.264
	Case	99	238.04	486.868	
LDH	Control	89	676.31	928.328	0.795
	Case	104	650.87	338.670	
SGOT (AST)	Control	37	52.86	85.912	0.417
	Case	69	40.81	34.076	
SGPT (ALT)	Control	37	68.324	140.8273	0.31 8
	Case	65	102.369	176.7854	

group is ten years more than the control group. The BS faces higher levels in the case group than the control one, whereas no significant difference is determined between BS and COVID-19. Similarly, the higher mean of ALT in the case group (102.369) compared to the control group (68.324) does not drive to a significant difference. Other parameters, including CPK, LDH, and AST, experience higher levels in the control group, although no significant difference is determined.

The comparisons between liver function tests of the case and control groups are illustrated in Table 3. The results indicated in Table 3 regarding male participants share many similarities with Table 2; only BS showed an increase in the control group, although this increase was insignificant. Among the female participants, the mean age difference exceeds 12 years between the case and control groups (Table 3). Unlike differences between the male participants, BS of the female case participants group demonstrated higher levels than in the control group; however, this rise was not statistically significant (Table 3). Moreover, the mean LDH level of the female group was higher in the case

group than in the control, although these differences were not significant.

The liver and heart function tests of COVID-19 patients based on their underlying diseases, including diabetes and heart disease, have been assessed in Table 4. According to Table 4, the BS levels belonging to diabetic patients are higher than non-diabetic patients, demonstrating a significant difference ($P=0.017$). Patients afflicted by underlying heart disease experienced higher levels of BS than patients without such underlying disease. LDH levels face an increase in diabetic patients and patients suffering from underlying heart disease. Although, none of these parameters except the BS of diabetic patients indicate a significant difference. Non-diabetic patients and individuals without underlying heart disease experienced increased ALT levels than patients afflicted by both underlying diseases. Non-diabetic patients experienced increased AST levels compared with diabetic patients, whereas AST levels demonstrate a decline in individuals without underlying heart disease compared to those afflicted by this underlying disease; however, both AST and ALT determined no significant difference.

Table 3 The sex-disaggregated comparison of some liver and heart function tests between case and control groups

Variable	Group	Male				Female			
		N	Mean	Sd	P value	N	Mean	Sd	P value
Age	Control	99	46.51	20.866	0.010	72	44.46	21.186	<0.001
	Case	95	54.00	19.228		97	57.13	16.486	
BS	Control	39	134.82	60.485	0.453	26	126.92	106.443	0.274
	Case	36	124.56	57.148		46	152.98	90.243	
CPK	Control	48	371.88	856.692	0.537	30	432.27	1780.709	0.372
	Case	46	282.74	478.000		53	199.25	495.683	
LDH	Control	54	767.17	1159.059	0.518	35	536.14	320.991	0.185
	Case	49	657.53	242.442		55	644.93	407.984	
SGOT (AST)	Control	22	62.91	97.340	0.571	15	38.13	66.147	0.546
	Case	32	50.25	42.085		34	27.47	13.178	
SGPT (ALT)	Control	22	90.136	176.5115	0.450	15	36.333	49.1814	0.410
	Case	30	135.833	237.3130		32	50.000	53.9061	

Table 4 Some liver and heart function tests of COVID-19 patients based on diabetes and heart disease

Variable	Diabetes	N	Mean	Sd	P value	Cardiac disease	N	Mean	Sd	P value
BS	No	69	126.38	58.088	0.017	No	75	142.51	80.728	0.575
	Yes	12	225.83	122.123		Yes	6	123.67	45.579	
CPK	No	83	236.72	482.362	0.336	No	87	184.69	302.525	0.363
	Yes	15	115.33	93.508		Yes	11	482.73	1032.016	
LDH	No	85	636.41	350.867	0.423	No	93	615.23	255.785	0.165
	Yes	18	707.39	282.109		Yes	10	961.20	720.252	
SGOT (AST)	No	61	41.51	35.469	0.752	No	63	39.05	23.409	0.580
	Yes	7	37.14	22.623		Yes	5	66.40	101.530	
SGPT (ALT)	No	58	110.707	185.5312	0.322	No	59	105.356	183.0688	0.784
	Yes	6	34.500	11.4149		Yes	5	82.400	109.5687	

During the current study, the effects of underlying liver disease on the hepatic and cardiac function parameters revealed no significant difference; however, being affected by underlying liver disease leads to higher levels of these parameters. Moreover, with an increase in the disease severity, the levels of these parameters also get augmented.

The patients belonging to the case group were hospitalized in regular isolation and ICU wards. The hepatic and cardiac function parameters were elevated in the patients hospitalized in the ICU and isolation wards. Although none of the patient parameters except LDH ($P < 0.001$) demonstrate a significant difference, the levels of LDH were 565.75, 987.79, and 671.67 in the normal, ICU, and isolation wards, respectively. 70% of the patients suffering from underlying heart disease must be hospitalized in ICU or isolation wards.

Our results show significant differences between the levels of AST, ALT, and BS among the ethnicities of the patients affected by this novel coronavirus. Patients with Fars ethnicity experienced higher levels of BS, which showed a significant difference between Lor and Fars ethnicities ($P < 0.001$). The AST and ALT levels of Fars ethnicity were significantly higher than that of Lor ethnicity and slightly higher than Turkmen ethnicity. These variables determined significant differences between Lor and Fars ethnicities (AST $P < 0.001$ and ALT $P < 0.001$). On the other hand, the ALT levels of Turkmen ethnicity differ significantly from ALT levels of Fars ethnicity ($P = 0.004$). Among all variables that led to significant difference, the variables belonging to Fars ethnicity were higher. Furthermore, Fars ethnicity demonstrated increased levels of LDH; however, the difference was not significant ($P \geq 0.05$).

Discussion

We have illustrated that age is associated with COVID-19 infection and its severity. Underlying liver and heart diseases and hypertension did not correlate significantly with COVID-19 infection, whereas diabetes indicated a significant difference with the outcome of this disease.

Moreover, BS belonging to the case group showed an increase in level compared to the control group, although no significant difference was detected. This increased BS may associate with disorders of the gastrointestinal tract. Patients affected by high BS were also experiencing high LDH levels associated with intensified ALT and AST levels. A previous study on 69 patients has depicted that 33 and 28% of COVID-19 patients experienced high levels of ALT and AST, respectively [13]. Our study confirms the increase of ALT and AST in 19.4 and 16.4% of COVID-19 patients, respectively. It has been demonstrated that among 298 COVID-19 patients, 44 patients (14.8%) were afflicted by liver injury, and these patients were more susceptible to

the complications of COVID-19 [2]. It has been revealed that there are no difference between ALT, AST, alkaline phosphatase, total bilirubin, albumin, and other liver function parameters and the severity of COVID-19 [20]. In other studies the ALT levels, AST total bilirubin, and other liver function parameters grow substantially in the patients affected by severe COVID-19 compared with those experiencing mild symptoms. The liver injury of the patients with mild COVID-19 may heal without any specific treatment, and mostly it is a temporary complication [15, 19]. In the current study, despite the increase of some liver function parameters of the case group when compared with the control group, no significant difference between these parameters was found.

In COVID-19 patients, lymphopenia and increased C-reactive protein (CRP) are associated with liver injury. This fact signifies that cytokine storm may be the main mechanism of liver injury. Furthermore, severe cytokine storms can induce injuries to various organs, including the lung, liver, heart, and kidney [10].

The drugs used for SARS treatment include ribavirin, steroids and antibiotics (Macrolides and Quinolones), usually lead to liver injury [16]. Some of these drugs are being administrated for COVID-19 treatment, which can result in the potential injury of the liver [17]. The dose and duration of lopinavir-ritonavir used as an antiviral treatment for SARS-COV-2 infection correlate with the severity of the liver injury. Thus, the utilization of these medications may lead to a significant increase in liver injury in hospitalized patients. Moreover, liver dysfunction can extend the duration of a patient's hospitalization [5]. Previous studies have elucidated that 62% of COVID-19 patients hospitalized in ICU experience elevated AST levels, whereas this percentage diminishes to 25% of the patients hospitalized in a general ward. The cause of this phenomenon can attribute to the long duration and high dose of antiviral medications such as arbidol, lopinavir-ritonavir, and other drugs for the patients afflicted by severe COVID-19 [7, 15]. During the current study, the duration of hospitalization in ICU and isolation wards and the utilization of antiviral medications could drive to elevated levels of liver function parameters.

There is a higher risk of mortality rate in Covid-19 patients with myocardial injury caused by the virus [6]. In the current study, heart function parameters including AST, CPK, and LDH demonstrated elevated levels in the patients afflicted by the novel coronavirus and underlying heart disease simultaneously. However, no significant difference was found in the patients without underlying heart disease. Some studies demonstrated the underlying cardiovascular disease (CVD) as a risk factor for being infected by severe COVID-19 [9], but we did not find a significant difference between COVID-19 infection and underlying heart disease. Chinese Center for Disease Control and Prevention (China CDC) has

reported that the mortality rate of the patients affected by the novel coronavirus and CVD simultaneously is 10.5%, whereas the total rate of mortality drops to 2.4% [14].

A study conducted on 1527 Chinese COVID-19 patients has elucidated that hypertension, cardiac and cerebrovascular diseases, and diabetes were witnessed in 17.1%, 16.4%, and 9.7%, respectively, among these patients [9]. During the current study, 70% of COVID-19 patients affected by the underlying cardiac disease must be hospitalized in ICU. Potentiating the severity of these patients' diseases was accompanied by increasing levels of LDH and CPK. Increased LDH and CPK were also detected in the patients hospitalized in ICU. It has been reported that 36 out of 138 patients requiring ICU admission experienced substantial rises in CK-MB levels [12].

During the current assessment of the liver and heart function parameters, clinical manifestations, and disease severity of COVID-19 patients belonging to varied ethnicities, including Lur, Fars, and Turkmen, individuals from Fars ethnicity were the most susceptible ethnicity to COVID-19 complications such as liver and cardiac injury and being afflicted by the severe type of COVID-19. The complications of COVID-19 were correlated with disease severity of Fars ethnicity, resulting in more required clinical support. Although, some members of all three ethnicities suffered from severe cardiac and hepatic complications originating from COVID-19.

Conclusion

Infecting by SARS-CoV-2 can lead to complications including respiratory, hepatic, gastrointestinal, and cardiovascular dysfunctions. Giving special attention to the dysfunctions of these organs through the assessment of hepatic and cardiac function parameters can accelerate the treatment and hinder disease development. The administration of medications leading to the slightest liver injury, considering symptoms and clinical complications, and constant monitoring of the liver and heart function parameters can play considerable roles in choosing promising therapeutic approaches. It seems that liver injury of some COVID-19 patients originates from long and extensive utilization of medications such as ribavirin, steroids, and antibiotics (Macrolides and Quinolones). Thus, it can prevent possible hepatic disorders by employing medications with less hepatotoxicity.

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Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical approval Ethical approval for this study was obtained from the Ethics Committee of Biomedical Research at Lorestan University of Medical Sciences (LUMS) (Approval number: IR.LUMS.REC.1400.075).

References

1. Beyerstedt S, Casaro EB, Rangel ÉB. COVID-19: angiotensin-converting enzyme 2 (ACE2) expression and tissue susceptibility to SARS-CoV-2 infection. *Eur J Clin Microbiol Infect Dis*. 2021;40(5):905–19.
2. Cai Q, Huang D, Qu P, Yu H, Zhu Z, Xia Z, et al. COVID-19 in a designated infectious diseases hospital outside Hubei Province, China. *Allergy*. 2020;75(7):1742–52.
3. Cao X. COVID-19: immunopathology and its implications for therapy. *Nat Rev Immunol*. 2020;20(5):269–70.
4. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020;395(10223):507–13.
5. Fan Z, Chen L, Li J, Cheng X, Yang J, Tian C, et al. Clinical features of COVID-19-related liver functional abnormality. *Clin Gastroenterol Hepatol*. 2020;18(7):1561–6.
6. He XW, Lai JS, Cheng J, Wang MW, Liu YJ, Xiao ZC, et al. Impact of complicated myocardial injury on the clinical outcome of severe or critically ill COVID-19 patients. *Zhonghua Xin Xue Guan Bing Za Zhi*. 2020;48(6):456–60.
7. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506.
8. Li H, Liu SM, Yu XH, Tang SL, Tang CK. Coronavirus disease 2019 (COVID-19): current status and future perspectives. *Int J Antimicrob Agents*. 2020;55(5):105951.
9. Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol*. 2020;109(5):531–8.
10. Liu J, Li S, Liu J, Liang B, Wang X, Wang H, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. *EBio-Medicine*. 2020;55:102763.
11. Ponti G, Maccaferri M, Ruini C, Tomasi A, Ozben T. Biomarkers associated with COVID-19 disease progression. *Crit Rev Clin Lab Sci*. 2020;57(6):389–99.
12. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *Jama*. 2020;323(11):1061–9.
13. Wang Z, Yang B, Li Q, Wen L, Zhang R. Clinical features of 69 cases with coronavirus disease 2019 in Wuhan, China. *Clin Infect Dis*. 2020;71(15):769–77.
14. Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese center for disease control and prevention. *JAMA*. 2020;323(13):1239–42.
15. Wu J, Song S, Cao HC, Li LJ. Liver diseases in COVID-19: etiology, treatment and prognosis. *World J Gastroenterol*. 2020;26(19):2286–93.
16. Yang Z, Xu M, Yi JQ, Jia WD. Clinical characteristics and mechanism of liver damage in patients with severe acute respiratory syndrome. *Hepatobiliary Pancreat Dis Int*. 2005;4(1):60–3.
17. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia

- in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med.* 2020;8(5):475–81.
18. Yeo C, Kaushal S, Yeo D. Enteric involvement of coronaviruses: is faecal-oral transmission of SARS-CoV-2 possible? *Lancet Gastroenterol Hepatol.* 2020;5(4):335–7.
 19. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol.* 2020;5(5):428–30.
 20. Zhang Y, Zheng L, Liu L, Zhao M, Xiao J, Zhao Q. Liver impairment in COVID-19 patients: a retrospective analysis of 115 cases from a single centre in Wuhan city, China. *Liver Int.* 2020;40(9):2095–103.

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