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Prevention of SARS-CoV-2 infection in patients with decompensated cirrhosis

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For the Chinese translation see Online for appendix 1

We read the Comment by Chao Zhang and colleagues¹ in *The Lancet Gastroenterology & Hepatology* on liver injury in

coronavirus disease 2019 (COVID-19) with great interest. Given that patients with decompensated cirrhosis have a higher risk of, and mortality from, infection, preventing infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in this patient population is a challenging task.² We provide our experience of COVID-19 prevention in patients with decompensated cirrhosis in Wuhan, China.

111 patients with decompensated cirrhosis in the Department of Gastroenterology, Renmin Hospital of Wuhan University, Wuhan, China, were included, after approval from the ethics committee of the hospital and provision of written informed consent from each patient or their representative. 82 patients were outpatients (previously hospitalised and discharged between July, 2018, and April, 2019) and 29 were inpatients

Panel: Preventive messages and measures for patients with decompensated cirrhosis in our study

Precautions sent to outpatients with decompensated cirrhosis via WeChat

- Avoid visitors and parties
- Avoid areas where severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection or coronavirus disease 2019 (COVID-19) has occurred and avoid individuals with fever
- Reduce going out; wear a cap and a mask correctly if unavoidable, especially in places with a mobile population or high population density, or both
- When returning home, remove your coat and hang it on the balcony or in a special area for ventilation; thoroughly wash your hands and face (including eyes, nostrils, and ears)
- Wash your hands before and after meals for no less than 20 s
- Open windows and ventilate your room twice a day for 15–30 min
- Eat a light and balanced diet, and predominantly soft foods to reduce the risk of bleeding from oesophageal and gastric varices; eat alone
- Face the challenge with equanimity and caution, exercise properly, and avoid catching a cold after exercise
- Monitor blood pressure, heart rate, and urine volume, especially for those taking non-selective β blockers as secondary prevention
- Take medications on time, including antiviral drugs and non-selective beta β blockers
- After endoscopic treatment of gastro-oesophageal varices, continue to take oral proton pump inhibitors for 2 months
- Intervals between re-examinations can be extended if necessary
- Purchase necessary medications online or offline after contacting your doctor on WeChat
- If you have any questions, or you are not feeling well, please contact your doctor on WeChat

Measures taken for inpatients with decompensated cirrhosis

- Training about COVID-19 provided for health-care workers
- Each patient was taken care of by one attending doctor and one nurse
- Rounds changed from three times a day to once a day, except for severely ill patients
- Communication between patients and medical staff should be done online
- Hospital staff advised to carry out strict hand hygiene and disinfection
- One room for each patient, or use of isolation curtain in bigger rooms
- Air to be disinfected three times per day by medical electrostatic adsorption air steriliser
- Central air-conditioning system shut down
- Doors to be closed, except for normal medical work; windows opened regularly for ventilation
- Patients and their companions provided training on how to use surgical masks properly
- Only one companion allowed for critical patients; no companions allowed for non-critical patients
- Establish a clean area and buffer zone in the ward
- Patients and their companions not permitted to leave the ward; if unavoidable, disposable surgical caps and masks were to be worn, and hands washed on return
- Invasive examinations to be avoided; mandatory protection and disinfection according to relevant regulations if necessary
- After stabilisation, patients were encouraged to be discharged and to receive online follow-up
- Establish an emergency plan for when patients with cirrhosis are confirmed or suspected to be infected with SARS-CoV-2, including: a rapid reporting system; building multidisciplinary teams that include specialists in gastroenterology, hepatology, interventional therapy, endoscopy, infection, and intensive care; rapid transfer channel; and a quarantine observation system for close contacts

(hospitalised between Jan 1, 2020, and Feb 4, 2020). All patients had been diagnosed with cirrhosis by abdominal CT scan, CT during arterial portography, or liver biopsy.

Between Jan 1, and Feb 3, 2020, messages relating to precautions to take against COVID-19, including protective measures aimed at preventing patient infections and precautions for cirrhotic complications (panel), were sent to outpatients via WeChat every 3 days for a total of 12 times. Feedback from the patient was collected every day via WeChat. For inpatients, new precautionary procedures were implemented, including hospital staff training, health education for patients and their companions, new processes for diagnosis and treatment, emergency plans, and suggestions for discharging patients (panel). After 14 days, on Feb 18, 2020, a questionnaire was sent to all participants to investigate their symptoms and satisfaction with the messaging system.

Of the 111 patients, the mean age was 58.7 years (SD 10.7) (appendix 2, pp 1–2), most of whom came from Wuhan, the city hardest hit by the outbreak (appendix 2, p 3). One patient died after 19 days in hospital because of multiple organ failure.

At follow-up, none of our participants had clinical symptoms suggestive of SARS-CoV-2 infection. By contrast, five (2%) of 250 patients without cirrhosis and six (16%) of 38 health-care workers were diagnosed with COVID-19 by casual testing in our ward. Several outpatients complained about mild gastrointestinal and respiratory symptoms, which were resolved by rest, proton pump inhibitors, and probiotics (appendix 2, p 2).

As an additional comparator, we calculated the incidence of COVID-19 among 101 inpatients with decompensated cirrhosis at five other hospitals in Wuhan over the same period, where our approach had not been implemented. 17 (17%) of these

101 patients were diagnosed with COVID-19 ($p=0.018$ vs our group; appendix 2, p 4). This simple approach could be an effective means of preventing COVID-19 in patients with decompensated cirrhosis. However, our sample size is small and larger studies are needed.

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- 1 Zhang C, Shi L, Wang F. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol* 2020; published online March 4. DOI:10.1016/S2468-1253(20)30057-1.
- 2 Strnad P, Tacke F, Koch A, Trautwein C. Liver—guardian, modifier and target of sepsis. *Nat Rev Gastroenterol Hepatol* 2017; **14**: 55–66.

COVID-19 and the liver: little cause for concern

The largest study on COVID-19 to date¹ showed that the prevalence of elevated aminotransferases and bilirubin in people faring worst was at least double that of others. Although clinically significant liver dysfunction was not quantified, this and other studies have led some to suggest that this finding might present clinical challenges.² Close inspection of the available data supports a higher prevalence of abnormal aminotransferase levels in

severe COVID-19 disease, but these studies actually suggest that clinically significant liver injury is uncommon, even when data for the most severely ill patients are selected (table).

Although high levels of positive end expiratory pressure can contribute to hepatic congestion by increasing right atrial pressure and impeding venous return, data suggest that many patients admitted to hospital with COVID-19 have liver blood test abnormalities without mechanical ventilation. Furthermore, the distribution of aminotransferase levels among patients with COVID-19 do not support hypoxic hepatitis being a common phenomenon, according to the published literature. Drug-induced liver injury is a possible contributing factor to the observed abnormal liver blood test abnormalities after therapeutics begin and should be considered by clinicians, but mild liver test derangement is present at baseline in many patients with COVID-19 before significant medication use. Several studies have reported elevated levels of creatinine kinase and lactate dehydrogenase or myoglobin in association with COVID-19 severity (table). It is therefore possible that aminotransferase elevations do not necessarily arise from the liver alone and that COVID-19 infection might induce a myositis similar to that observed in severe influenza infections.

It has been proposed that COVID-19 causes direct liver injury via a viral hepatitis, but we believe that there are alternative explanations. First, the derangement of liver function is clearly mild. Second, when liver function tests for patients with different durations of symptoms are examined, there is no evidence that later presentation is associated with greater liver function derangement.³ The only post-mortem liver biopsy from a patient with COVID-19 showed only microvesicular steatosis, a common finding in sepsis.⁴ Most

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