Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Characteristics and in-hospital outcomes of COVID-19 patients with acute or subacute liver failure ☆

To the Editor,

A recent review paper by Metawea et al. in the *Digestive and Liver Disease* summarizes pathophysiological mechanisms about coronavirus disease 2019 (COVID-19) associated liver injury [1]. Despite a high incidence of liver injury in COVID-19 patients [2], acute liver failure (ALF) or subacute liver failure (SALF), which often manifests as jaundice, coagulopathy, hepatic encephalopathy (HE), and even progression to multiple organ failure [3], are rarely recognized. Considering that ALF is life-threatening with a high mortality [3], we attempted to analyze the characteristics and in-hospital outcomes of COVID-19 patients with ALF/SALF.

This study followed the Declaration of Helsinki and obtained the ethical approved of the Medical Ethical Committee of the General Hospital of Northern Theater Command. Written informed consent was waived by the Medical Ethical Committee of the General Hospital of Northern Theater Command [number Y (2021) 38]. This study reviewed the medical records of 3041 COVID-19 patients admitted to the Huoshenshan Hospital from February 2020 to April 2020. COVID-19 patients who were diagnosed with or developed ALF/SALF were further identified. Age, gender, underlying diseases, and malignancy were not limited. Exclusion criteria were as follows: 1) patients who were previously diagnosed with liver diseases, including chronic liver disease, cirrhosis, and liver cancer, etc.; and 2) patients who did not undergo liver biochemical examinations at admission and during hospitalization.

According to the Chinese guideline regarding management of liver failure [4], ALF is diagnosed, if a patient has developed HE grade II or above within two weeks and meets all of the following criteria: 1) fatigue accompanied by obvious anorexia, abdominal distension, nausea, vomiting, and other severe gastrointestinal symptoms; 2) rapid worsening of jaundice presenting with total bilirubin (TBIL) level of greater than or equal to 10 times the upper limit of normal (ULN) or a daily increase of TBIL level of $\geq$ 17.1μmol/L; 3) bleeding tendency presenting with prothrombin activity (PTA) of $\leq$ 40% or international normalized ratio (INR) of $\geq$ 1.5, with exclusion of other causes for bleeding tendency; and 4) progressive shrinking of the liver. SALF is diagnosed, if a patient meets all of the following criteria within 2 to 26 weeks: 1) fatigue accompanied by obvious gastrointestinal symptoms; 2) rapid worsening of jaundice presenting with TBIL level of $\geq$ 10 times the ULN or a daily increase of TBIL level of $\geq$ 17.1μmol/L; and 3) bleeding tendency presenting with PTA $\leq$ 40% or INR of $\geq$ 1.5, with exclusion of other causes for bleeding tendency.

A total of six patients were eligible, of whom two and four had ALF and SALF, respectively. The median age was 69 years old and four (66.67%) patients were male. Two patients had hypertension and one had diabetes. At admission, five, one, and four patients presented with fatigue, nausea, and poor appetite, respectively; and three and three patients had severe and critical COVID-19, respectively.

At admission, three patients had elevated serum transaminase levels, of whom two had elevated aspartate aminotransferase (AST) level (range: 127.7–191.9 U/L) and three elevated alanine aminotransferase (ALT) level (range: 81.2–90.6 U/L); two had elevated TBIL level (range: 26.9–123.9 μmol/L); and one had elevated INR (2.01).

During hospitalization, all patients developed elevated serum transaminase levels with the highest AST level exceeding 800 U/L and the highest ALT level exceeding 1000 U/L; all patients developed varying degrees of elevated TBIL level, of whom one developed elevated TBIL level of $\geq$ 10 times the ULN (exceeding 684 μmol/L), and the remaining five had a daily increase of TBIL level of $\geq$17.1 μmol/L; and all patients also developed elevated INR (range: 1.54–3.14) **(Fig. 1)**. All patients developed HE grade II or greater, mainly presenting with sleepiness and coma. HE developed in COVID-19 patients with ALF and SALF within a median duration of 4.5 (range: 4–5) days and 25.75 (range: 10–36) days after admission, respectively.

During hospitalization, all patients underwent invasive mechanical ventilation, of whom two underwent both extracorporeal membrane oxygenation and continuous renal replacement therapy (CRRT), and three underwent CRRT alone. All patients developed multiple complications, including acute myocardial injury in six patients, respiratory failure in six patients, shock in six patients, acute respiratory distress syndrome in three patients, and acute renal injury in three patients.

All patients were admitted or transferred to the intensive care unit. All six patients finally died. One patients died on the day of onset of liver failure, four within 10 days since the onset of liver failure, and one on 25 days since the onset of liver failure.

ALF/SALF is infrequent, but fatal in COVID-19 patients. In patients with severe and critical COVID-19, it should be necessary to alert the risk of ALF/SALF and consider the prophylactic strategy of hepatic protection in a timely fashion.

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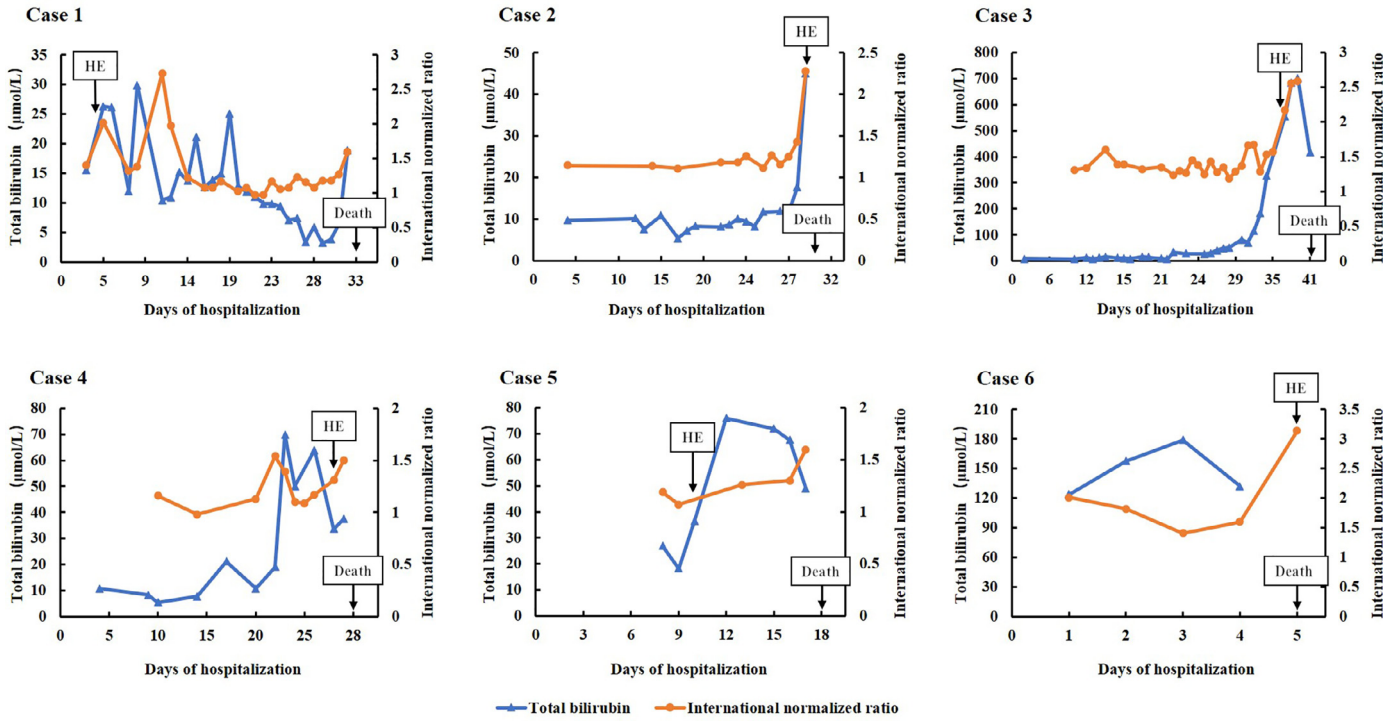

Fig. 1. Dynamic changes of total bilirubin level and international normalized ratio during hospitalization.

Availability of data and material

The datasets generated and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declaration of Competing Interest

The authors declare that there is no conflict of interest in this study.

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