



## COVID-19 Liver Injury Whether due to Virus or Medication: A Case Report

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### ABSTRACT

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Mild cases of liver injury had been found on COVID-19 cases worldwide. However, the growing prevalence and severity of the cases indicated the dangerous spread of liver impairment to a considerable amount of the population. A 59-year-old COVID positive man come to the emergency room with fever, cough, and nausea. He was treated with favipiravir, azithromycin and other symptomatic drugs. On the seventh day of treatment, patient had a significant increased in liver enzymes, AST was 162 U/L dan ALT was 465 U/L. Patient was diagnosed with acute liver injury. Favipiravir was stopped and he was given hepatoprotection agents. On the tenth day patient had no complaint and was discharged. COVID-19 patients have high risk of impaired liver function, either because of the infection treatment drugs. Administration of hepatoprotective agents and discontinuation of suspected drugs suspected should benefits the patients.

### KEYWORDS:

Coronavirus disease 2019; liver impairment; drug induced liver injury; case report

### BACKGROUND

The beginning of the deadly global incident began in March 2020 with an unknown viral infection, which later branded as the Coronavirus disease 2019 (COVID-19).<sup>1</sup> The Severe Acute Respiratory Syndrome Coronavirus-2 as the causative agent destroy many internal organs that had angiotensin converting enzyme II (ACE2) receptor for its bonding, including the liver. Patients of the infection had been reported with abnormal liver function readings.<sup>2</sup> Despite its mild impairment, liver abnormalities in COVID-19 were apparent in a lot of patients, progressing along the disease.<sup>3</sup> Hereby, the following case illustrated how COVID-19 and its related liver impairment can be treated and well diagnosed in a limited facility governmental hospital.

### CASE ILLUSTRATION

A 59-year-old man came to our institution in June 2021 in Jakarta, Indonesia. He prompted with fever, cough, and nausea over the last six days. Previously, he had been diagnosed with hypertension, yet it was uncontrolled. He confessed to no other prior disease nor hepatotoxic items

ingestion. Physical examination was remarkable except for a 175/95 high blood pressure. Full blood count revealed borderline platelet ( $150,000/\text{mm}^3$ ) and normal leukocyte count, while liver function test showed 53 U/L and 47 U/L of aspartate transaminase (AST) and alanine transaminase (ALT), respectively. Subsequent blood analysis also portrayed high C-reactive protein (CRP, 35.3 mg/L) and D-dimer (977 ng/ml). The thorax x-ray depicted signs of pneumonia. We then did antigen and polymerase chain reaction COVID-19 test which both came back positive (cycle threshold value < 40).

The patient consequently diagnosed with confirmed COVID-19 case and first grade hypertension. He was hospitalized and treated with intravenous (IV) azithromycin 1 x 500 mg, IV omeprazole 2 x 40 mg, subcutaneous heparin 2 x 5000 unit, along with per oral medications of vitamin D 1 x 2000-unit, zinc 1 x 20 mg, paracetamol 3 x 500 mg, acetylcysteine 2 x 600mg, amlodipine 1 x 10mg, and favipiravir 2 x 1600 mg for the first day and 2 x 600 mg for another six days.

Transaminitis was observed in the seventh day of hospitalization. No apparent clinical changes nor new complaint from the patient; nevertheless, the AST and ALT elevated to 162 U/L and 465 U/L. Viral hepatitis etiologies of A, B, and C were negative. Diagnosis of acute liver injury was added, and the patient was given hepatoprotective agents composed of 3 x 1 tablet of curcumin and two days treatment with glycyrrhizin medication. Improvement was noted on the

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next two days amounting to a decrease of AST to 56 U/L and ALT to 305 U/L. The tenth day marked the patient released as he had no complaint, stable vital signs, normal lab values, and is clinically well.

### DISCUSSION

The current case illustrated how COVID-19 infections can injure the liver, which was noted via transaminitis with over five times levels increase. Liver enzymes was found as one of the progression predictors of COVID-19 with severer cases resulting in a more heightened ALT and AST.<sup>4,5</sup> The underlying mechanisms revolve around psychological stress, inflammation, cytokine responses, and disease progression. The stigma, emotional stress, and isolation negative impacts dig the liver through hormonal and poor lifestyle.<sup>1</sup> Superinflammatory conditions by COVID-19 bond to the ACE2 receptor also causes direct damage to cells and tissues by the abnormal secondary signaling and cytokine cascade.<sup>3</sup> Furthermore, the high amount and variance of drug for COVID-19 treatment also apply huge burden to the liver as it heavily metabolizes the active component and thus drug induced liver damage.<sup>3</sup> In particular, favipiravir can increase ALT, AST, and total bilirubin levels of COVID-19 patients, but the difference is non-significant toward the control group. Contrarily, the use of azithromycin has been associated with short-duration hepatocellular injury.<sup>6</sup>

Differential diagnosis of the current case would be typhoid fever and dengue fever or dengue hemorrhagic fever. The first was excluded due to no typhoidal characteristics presented in the patient (e.g., relative bradycardia, coated tongue, step ladder fever); while the latter since the patient's clinical and lab conditions do not correspond to the dengue case definitions (DF: fever and at least two of ocular pain, headache, muscle pain, rash, bleeding, leukopenia | DHF: fever, platelet  $\leq 100 \times 10^9/L$ , bleeding, and plasma leakage).<sup>7</sup> Management of this patient includes looking for other etiologies by testing for hepatitis A, B, and C, administration of hepatoprotective agents and discontinuation of antiviral drugs suspected of causing impaired liver function. Yu et al suggests the need to monitor liver function regularly and look for other etiologies such as viral (hepatitis A, B and C) and cardiac injury.<sup>2</sup> Patients with severe liver injury due to COVID-19 can be given hepatoprotectors, such as glycyrrhizinic which has an anti-inflammatory effect to protect liver function.<sup>3</sup>

The case bridged the COVID-19 disease to the possibility of both direct injury and indirect drug induced injury to the liver. However, there are some limitations including limited facility to perform extra examinations like ultrasonography and biopsy.

### CONCLUSION

COVID-19 patients have high risk of impaired liver function, either because of the infection treatment drugs. Administration of hepatoprotective agents and

discontinuation of suspected drugs suspected should benefits the patients.

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