

Do prolonged syndrome of COVID-19 and variants of SARS-CoV-2 cause hepatitis of unknown origin in Oaxaca?

¿Síndrome COVID-19 prolongada y las variantes de SARS-CoV-2 causa de la hepatitis de origen desconocido en Oaxaca?

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To the Editor,

I resume with great interest Rojo del Moral's article. Indeed, long COVID-19 represents a high percentage of current medical consultations and has high social importance¹. Faced with the increase in hepatitis of unknown origin, the possibility of post-COVID hepatopathy, or coronavirus 2-induced hepatitis due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) should be ruled out. Since SARS-CoV-2 can bind to heparan sulfate, apoE, and the angiotensin-converting enzyme 2 (ACE2) at the endothelial level, its internalization becomes possible by activating vascular endothelial growth factor and cathepsin E, even being stored in cells or tissues in syncytia².

This is the case of a 4-year-old girl, non-jaundiced. General urine examination revealed urobilinogenuria and positive urobilinogen. Elevated lactate dehydrogenase (LDH), gamma-glutamyl transpeptidase (GGT), and bilirubin levels were noted (Table 1). Ultrasound revealed decreased bile flow in the intrahepatic ducts. Viral hepatitis tests turned out negative (Table 1). As a relevant history, 4 months prior, she had a SARS-CoV-2 infection. Currently, only real-time quantitative polymerase chain reaction (qRT-PCR) for SARS-CoV-2 in stool has tested positive. She was put on ivermectin at a dose of 150 µg/kg every 24 hours for 3 days and OM-85 infant granules for 30 days.

Case #2 is a 3.7-year-old woman who presented with a fever of 38.9 °C, urobilinogenuria, and mild jaundice on her skin and conjunctiva. Pharyngeal enanthema was observed upon examination³. Elevated bilirubin and transaminases levels were noted, with negative viral hepatitis tests, qRT-PCR for SARS-CoV-2 in nasopharyngeal, oropharyngeal, and stool samples all turned out positive. As a relevant history, her parents had contracted the BA.1/BA.2 combined variant of Omicron in Los Angeles, CA, United States. She was treated with ivermectin at a dose of 150 µg/kg every 24 hours for 3 days, Vita Deyon® One Shot, and a single dose of pirfenidone LP® 50 mg, and OM-85 (Broncho-Vaxom®) infant granules for 30 days. Both patients improved 21 days into treatment (Table 1). Thus, case #1 was an intrahepatic cholestasis in the context of long COVID-19, and case #2 was a SARS-CoV-2-induced acute hepatitis.

For the management of COVID-19 related hepatopathy, early diagnosis is crucial to inhibit viral replication and reverse liver damage. In this regard, in rural areas, we have ivermectin and OM-85 as well as Vita Deyon® One Shot and pirfenidone LP® for their triple antiviral effect vs COVID-19, reducing the expression of ACE2, anti-cytokine storm, and antioxidants, attenuating the mitochondrial stress associated with COVID-19^{4,5}. In conclusion, we provide population-based evidence of COVID-19 related hepatopathy in Mexico, both in the acute phase and in the context of

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Table 1. Sociodemographic and clinical data of patients with COVID-19 related hepatitis

Socio-demographic data	Case #1	Case #2	21 days after admission	
Socio-demographic Data	At admission	21 days after admission		
Gender	Woman	Woman		
Age	4 years	3.7 years		
Social status	Middle class	Lower class		
Ancestry	Zapotec/Afro-Mexican	Zapotec		
City of origin	Miahuatlán de Porfirio Díaz	Putla de Guerrero		
Type of housing	Semi-urban	Rural without soil		
History of COVID-19	DeltaAY.4/OmicronBA.1	No		
Family history of COVID-19	Yes, variant unknown	Yes, BA.1/BA.2 variant		
SARS-CoV-2 tests				
Nasopharyngeal and oropharyngeal qRT-PCR	Negative	Negative	Positive	Negative
Stool qRT-PCR	Positive	Negative	Positive	Negative
Liver function tests				
AST	22 UI/L	25 UI/L	1234 UI/L	33 UI/L
ALT	47 UI/L	34 UI/L	634 UI/L	26 UI/L
LDH	916 UI/L	146 UI/L	803 UI/L	174 UI/L
GGT	435 UI/L	201 UI/L	286 UI/L	155 UI/L
Total bilirubin	1.4 mg/dL	0.9 mg/dL	1.5 mg/dL	1.1 mg/dL
Direct bilirubin	1.0 mg/dL	0.5 mg/dL	0.9 mg/dL	0.6 mg/dL
Indirect bilirubin	0.4 mg/dL	0.4 mg/dL	0.6 mg/dL	0.5 mg/dL
Viral hepatitis panel				
HAV qRT-PCR	Negative	Negative	Negative	Negative
HBV qRT-PCR	Negative	Negative	Negative	Negative
HCV qRT-PCR	Negative	Negative	Negative	Negative
HDV qRT-PCR	Negative	Negative	Negative	Negative
HEV qRT-PCR	Negative	Negative	Negative	Negative
Herpes simplex 1 and 2 qRT-PCR	Negative	Negative	Negative	Negative
Cytomegalovirus qRT-PCR	Negative	Negative	Negative	Negative
Autoimmunity markers				
Anti-TAPO antibodies	Negative	Negative	Positive	Negative
Anti-citrullinated peptide antibodies	Negative	Negative	Positive	Negative
Anti-ANA antibodies	Negative	Negative	Positive	Negative
Anti-SMA antibodies	Negative	Negative	Positive	Negative

ALT: alanine aminotransferase; ANA: antinuclear antibodies; AST: aspartate aminotransferase; HV: hepatitis virus; LDH: lactate dehydrogenase; GGT: gamma-glutamyl transpeptidase; qRT-PCR: real-time quantitative polymerase chain reaction; SMA: smooth muscle antibodies; TAPO: thyroperoxidase.

long COVID-19. We introduced a new test for COVID-19 monitoring—qRT-PCR in stool—which reinforces the theory of the GI transmission route through enterohaptic circulation, considering that we found SARS-CoV-2 in stool.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article.

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