



## Editorials

## Hepatology and the “new reality” ushered in by the COVID-19 pandemic



## Editorial

On March 11, 2020, the World Health Organization declared the SARS-CoV-2 infection (COVID-19), which originated in December 2019 in Wuhan, China, a global pandemic [1].

The role of COVID-19 in the pathogenesis of gastrointestinal symptoms associated with viral infections has been the subject of a number of publications, many reporting a high prevalence of nausea, vomiting, abdominal pain, diarrhea and anorexia [2–4]. More importantly, fecal viral shedding of SARS-CoV-2 is a potential transmission mechanism currently under investigation [5].

The precise ways in which SARS-COV-2 interacts with the gastrointestinal tract remain unknown. However, SARS-COV-19 is believed to use ACE2 as a viral receptor, and since ACE2 mRNA is highly expressed in the gastrointestinal system, this raises the possibility of COVID-19 fecal-oral transmission [6].

In a concise review published in the last issue of *Annals of Hepatology*, Ezequiel Ridruejo and Alejandro Soza [7] discussed current published data concerning COVID-19 and its effect on the liver. In the review, they highlighted the importance of maintaining a high degree of skepticism when evaluating the flood of publications regarding the COVID-19 pandemic. The impact of COVID-19 on a variety of fields in hepatology is currently unknown. These areas of interest include patients with pre-existing liver disease (e.g., hepatocellular carcinoma) and the risk of COVID-19-related complications, pharmacologic interactions, liver transplant candidates/donors, and immunosuppression in post-liver transplant patients. As many non-peer reviewed publications are constantly being cited, we must be cautious in evaluating the evidence to make the best possible decisions in clinical practice.

As the lung is the organ most affected by COVID-19, patients may develop acute respiratory distress syndrome (ARDS), ultimately leading to an increase in the mortality rate. A retrospective study in patients with ARDS reported greater 90-day mortality in cirrhotic than in non-cirrhotic patients, with an adjusted HR of 2.09 (95% IC 1.27–3.45,  $P=0.004$ ) [8]. The first results made public by two international reporting registries (COVID-Hep.net and COVID-Cirrhosis.org) were based on 153 submissions from 21 countries and four continents. According to these findings, of a total of 103 patients with cirrhosis, 23.3% were admitted to an intensive care unit, 17% required invasive ventilation and 39.8% died [9]; not surprisingly, this exceeded the mortality rate in populations not studied [10].

The population we treated at Medica Sur Clinic and Foundation from May 14th through June 5th, 2020, included 155 patients with a positive reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2, of whom 71.6% were men with a mean age of 51 years. Upon examination, at least one gastrointestinal symptom was reported in 36.1% of patients, with diarrhea being the most common at 25.8%. Up to 96.8% of patients had at least one abnormal liver function test result, the most frequent being lactate dehydrogenase at 96.8%. Only two patients had previous chronic liver disease, and the global mortality rate reached 7.1%. While there is no conclusive evidence thus far of a specific mechanism causing liver damage from COVID-19, at least five theories have been proposed: [1] direct cytopathic damage [2], systemic inflammatory response [3], liver hypoxia and ischemia [4], acute-on-chronic liver injury, and [5] drug-induced liver injury [11]. We are barely beginning to understand the dynamics of COVID-19, and therefore additional clinical and epidemiological data are needed in order to develop risk predictors, identify high-risk populations, and propose new public-health policies.

To help meet the challenge of unifying clinical criteria concerning the relationship between COVID-19 and liver disease, the Asian Pacific Association for the Study of the Liver (APASL) has organized a task force including key opinion leaders in hepatology from several countries. This group is responsible for analyzing data, sharing experiences, providing recommendations for the management of liver injury, liver transplants and autoimmune liver disease, and conducting clinical trials [12].

COVID-19 clearly constitutes a major health challenge around the world, as it affects virtually every organ in the human body. Because transmission occurs primarily through exposure to droplets and is a particular threat to the respiratory tract, authorities have recommended - and in many cases imposed - quarantine measures. The implementation of these measures has led to the rapid development of telemedicine technologies as a way of minimizing direct person-to-person contact and ensuring patient follow-up during confinement. Most gastrointestinal and liver societies have recommended the suspension of routine control visits and encouraged follow-up through video-assisted telemedicine or phone calls. This has launched a new era of remote healthcare management in most disciplines [13], especially in liver transplant clinics [14]. As regards education, remote technologies are also being used to maintain and in many areas adapt the medical curriculum [15], transforming telemedicine

technologies into a tool widely used by most universities worldwide.

Also in the last issue of *Annals of Hepatology*, Marco Arrese [16] shared the first results from a successful initiative conducted by the University of New Mexico Health Sciences Center through its Extension for Community Healthcare Outcomes (ECHO) project. This project is focused on patients in rural and underserved areas to help guide the treatment of hepatitis C virus infection. The article discussed the many pluses and minuses of telemedicine, as well as the future challenges that must be addressed in order to implement these technologies in light of the “new reality” ushered in by the COVID-19 pandemic.

Similarly, the Medica Sur Clinic and Foundation has launched a Digital Hospital project which facilitates the practice of telemedicine. These efforts include a digital file that is being created in collaboration with Amazon, Cisco and Endeavor [17].

Current and future generations of hepatologists and family physicians will undoubtedly need to be alert and acquire additional knowledge about tools for providing medical and hospital services. We are also using these tools in many centers as part of continuing research and teaching efforts designed to better serve patients, health services and medical residents as well.

## References

- [1] WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020 [Internet]. [cited 2020 Jul 2]. Available from: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-11-march-2020>.
- [2] Schmulson M, Dávalos MF, Berumen J. Beware: Gastrointestinal symptoms can be a manifestation of COVID-19. *Rev Gastroenterol Mex* 2020, <http://dx.doi.org/10.1016/j.rgmex.2020.04.001>.
- [3] Tariq R, Saha S, Furqan F, Hassett L, Pardi D, Khanna S. Prevalence and mortality of COVID-19 patients with gastrointestinal symptoms: a systematic review and meta-analysis. *Mayo Clin Proc* 2020, <http://dx.doi.org/10.1016/j.mayocp.2020.06.003>.
- [4] Mao R, Qiu Y, He JS, Tan JY, Li XH, Liang J, et al. Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2020;5(7):667–78, [http://dx.doi.org/10.1016/S2468-1253\(20\)30126-6](http://dx.doi.org/10.1016/S2468-1253(20)30126-6).
- [5] D'Amico F, Baumgart DC, Danese S, Peyrin-Biroulet L. Diarrhea during COVID-19 infection: pathogenesis, epidemiology, prevention and management. *Clin Gastroenterol Hepatol* 2020;(May):1–10, <http://dx.doi.org/10.1016/j.cgh.2020.04.001>.
- [6] Hindson J. COVID-19: faecal–oral transmission? *Nat Rev Gastroenterol Hepatol* 2020;17(5):259, <http://dx.doi.org/10.1038/s41575-020-0295-7>.
- [7] Ridruejo E, Soza A. The liver in times of COVID-19: What hepatologists should know. *Ann Hepatol* 2020;19(4):353–8, <http://dx.doi.org/10.1016/j.aohp.2020.05.001>.
- [8] Gaccouin A, Locuffier M, Uhel F, Letheulle J, Bouju P, Fillatre P, et al. Liver cirrhosis is independently associated with 90-day mortality in ARDS patients. *Shock* 2016;45(1):16–21, <http://dx.doi.org/10.1097/SHK.0000000000000487>.
- [9] Moon AM, Webb GJ, Aloman C, Armstrong MJ, Cargill T, Mrcep P, et al. High mortality rates for SARS-CoV-2 infection in patients with pre-existing chronic liver disease and cirrhosis: preliminary results from an international registry. *J Hepatol* 2020, <http://dx.doi.org/10.1016/j.jhep.2020.05.013>.
- [10] COVID-19 Map - Johns Hopkins Coronavirus Resource Center [Internet]. [cited 2020 Jul 2]. Available from: <https://coronavirus.jhu.edu/map.html>.
- [11] Méndez-Sánchez N, Valencia-Rodríguez A, Qi X, Yoshida EM, Romero-Gómez M, George J, et al. What Has the COVID-19 Pandemic Taught Us so Far? Addressing the Problem from a Hepatologist's Perspective. *J Clin Transl Hepatol* 2020;8(2):1–4, <http://dx.doi.org/10.14218/JCTH.2020.00024>.
- [12] Gregory C, Rino G, Richard G, Ghazinyan H, Dokmeci K, Tatsuo K, et al. Clinical practice guidance for hepatology and liver transplant providers during the COVID-19 pandemic: APASL expert panel consensus recommendations. *Hepatology* 2020;(0123456789), <http://dx.doi.org/10.1007/s12072-020-10054-w>.
- [13] Perkins S, Cohen JM, Nelson CA, Bunick CG. Telemedicine in the era of COVID-19: Experience of an academic department of dermatology. *J Am Acad Dermatol* 2020;83(1):e43, <http://dx.doi.org/10.1016/j.jaad.2020.04.048>.
- [14] Fix OK, Serper M. Telemedicine and Telehepatology During the COVID-19 Pandemic. *Clin Liver Dis (Hoboken)* 2020;15(5):187–90, <http://dx.doi.org/10.1002/cld.971>.
- [15] Wong RY. Medical education during COVID-19: lessons from a pandemic. *BCM J* 2020;62(5):170–1.
- [16] Arrese M. Telemedicine, COVID-19 and liver diseases: Revamping remote care initiatives in hepatology. *Ann Hepatol* 2020;19(4):339–40, <http://dx.doi.org/10.1016/j.aohp.2020.05.002>.
- [17] Serper M, Cubell AW, Deleener ME, Casher TK, Rosenberg DJ, Whitebloom D, et al. Telemedicine in Liver Disease and Beyond: Can the COVID-19 Crisis Lead to Action? *Hepatology* 2020, <http://dx.doi.org/10.1002/hep.31276>.

Misael Uribe<sup>a,b,\*</sup>

Jorge Aquino-Matus<sup>a,b</sup>

<sup>a</sup> Obesity and Digestive Diseases Unit, Medica Sur  
Clinic and Foundation, Mexico City

<sup>b</sup> National Autonomous University of Mexico, Mexico  
City

\* Corresponding author.

E-mail address: [muribe@medicasur.org.mx](mailto:muribe@medicasur.org.mx)  
(M. Uribe)

7 August 2020