# Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper

Tobias Boettler, Philip N Newsome, Mario U. Mondelli, Mojca Maticic, Elisa Cordero, Markus Cornberg, Thomas Berg

## General recommendations for the prevention of SARS-CoV-2 infection

Even though our understanding of the epidemiology of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection remains limited, three methods of virus transmission have been reported: person-to-person transmission through respiratory droplets, contact transmission by touching contaminated surfaces followed by touching mouths, nose or eyes, and aerosol transmission by inhaling high concentrations of foaming aerosols in a relatively closed environment, which happens on specific occasions [1, 2]. In addition, the digestive system has been indicated as a possible route of viral transmission, as discussed above. The transmission of SARS-CoV-2 is often unpredictable and difficult to prevent. Therefore, understanding the viral, host, environmental, and behavioural characteristics may help in creating strategies for prevention and control of viral transmission.

Studies have shown that SARS-CoV-2 has a high level of transmissibility. The estimated initial median of the basic reproduction ($R_0$) was shown to be 2.79, meaning that one infected person will – on average – infect 2.79 other people, however $R_0$ differs among various regions [3]. Besides, even asymptomatically infected persons or those presenting with minimal symptoms were found to be contagious [4]. Reports have already shown that the incubation period can be extended beyond 14 days, however, the vast majority of cases becomes symptomatic within 14 days [5]. The signs and

symptoms of coronavirus disease 2019 (COVID-19) are not specific and are therefore difficult to distinguish from those of other respiratory virus infections. The 70% sensitivity of a single nasopharyngeal swab performed early in the course of disease represents an additional obstacle in making an accurate diagnosis [6]. Delayed diagnoses were reported to be one of the leading reasons for nosocomial transmissions.

Thus, effective prevention and control measures that are rapidly implemented and highly targeted within the community and healthcare settings are of critical importance to prevent transmission of SARS-CoV-2. For the general population, behavioural recommendations such as washing hands, covering coughs, and social distance are needed, whereas for healthcare workers extremely rigorous infection control has to be implemented [7]. Prompt identification of infected persons, their isolation and contact tracing might be sufficient to reduce viral transmission allowing control of a cluster of infected individuals. However, delays in isolation of patients from the onset of symptoms will markedly reduce such control [8].

Healthcare settings represent one of the most critical environments for prevention and control of SARS-CoV-2 transmission. Universal infection control procedures are necessary to be performed in all areas of all settings. Besides, precise triage protocols, special behavioural protocols and patterns for staff, patients, and visitors, rapid diagnosis and strict isolation such as isolation rooms, partitions to protect against respiratory droplets and ventilation systems must be implemented immediately [9, 10]. Measures are targeted to enable rapid detection and isolation of all potentially contagious patients and those with high suspicion of being infected, and to prevent the further spread of infection.

Special attention must be paid to infection control during certain procedures which enable aerosolization of virus-containing droplets, producing a much more effectively and widely disseminated infection. Such procedures include bronchoscopy, intubation, suctioning, sputum induction, nebulizer therapies, as well as esophagogastroduodenoscopy [11]. They should be performed under strict infection control procedures and, if possible, take place in units with airborne infection isolation. Although the virus has so far not been detected in liver tissue, the expression of its receptor on cholangiocytes and shedding of the virus in the faeces [12] suggest that the virus might be present in the liver as well. Thus, liver biopsy and certainly colonoscopy may also represent a risk for viral transmission if strict infection control measures are not implemented. Basically, ensuring cleanliness of toilets and other potentially contaminated surfaces is of extreme importance. Effective decontamination and strict environmental hygiene are crucial in elimination of respiratory droplets and faecal shedding from a contaminated healthcare environment [13]. Finally, in case of nosocomial transmission, possible modes of spread have to be carefully analysed, to improve strategies for further prevention of viral transmission.

It has recently been suggested that several drugs could increase susceptibility for SARS-CoV-2 infection and/or result in a more severe course of COVID-19. Most prominently, Ibuprofen and angiotensin-converting enzyme (ACE)-inhibitors (ACE-I) have been discussed. While for Ibuprofen no actual or theoretical explanation has been proposed, ACE-I have been suggested to upregulate ACE2, which could increase susceptibility for SARS-CoV-2. Based on this hypothesis, discontinuation of ACE-I usage in patients with hypertension and chronic heart disease has been discussed. However, based on the sparse evidence that is currently available, ACE-I should not be withdrawn in patients on stable medication until further evidence emerges [14, 15].

## References


[1] van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. New England Journal of Medicine 2020.

[2] Ghinai I, McPherson TD, Hunter JC, Kirking HL, Christiansen D, Joshi K, et al. First known person-to-person transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the USA. The Lancet 2020.

[3] Liu Y, Gayle AA, Wilder-Smith A, Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. Journal of Travel Medicine 2020;27.

[4] Wang W, Tang J, Wei F. Updated understanding of the outbreak of 2019 novel coronavirus (2019-nCoV) in Wuhan, China. Journal of Medical Virology 2020;92:441-447.

[5] Backer JA, Klinkenberg D, Wallinga J. Incubation period of 2019 novel coronavirus (2019-nCoV) infections among travellers from Wuhan, China, 20–28 January 2020. Eurosurveillance 2020;25:2000062.

[6] Fang Y, Zhang H, Xie J, Lin M, Ying L, Pang P, et al. Sensitivity of Chest CT for COVID-19: Comparison to RT-PCR. Radiology;0:200432.

[7] Adhikari SP, Meng S, Wu Y-J, Mao Y-P, Ye R-X, Wang Q-Z, et al. Epidemiology, causes, clinical manifestation and diagnosis, prevention and control of coronavirus disease (COVID-19) during the early outbreak period: a scoping review. Infectious Diseases of Poverty 2020;9:29.

[8] Hellewell J, Abbott S, Gimma A, Bosse NI, Jarvis CI, Russell TW, et al. Feasibility of controlling COVID-19 outbreaks by isolation of cases and contacts. The Lancet Global Health 2020;8:e488-e496.

[9] Park GE, Ko J-H, Peck KR, Lee JY, Lee JY, Cho SY, et al. Control of an Outbreak of Middle East Respiratory Syndrome in a Tertiary Hospital in Korea. Annals of Internal Medicine 2016;165:87-93.

[10] Klompas M. Coronavirus Disease 2019 (COVID-19): Protecting Hospitals From the Invisible. Annals of Internal Medicine 2020.

[11] Thomas RF, Christopher TL. Identifying and Interrupting Superspreading Events—Implications for Control of Severe Acute Respiratory Syndrome Coronavirus 2. Emerging Infectious Disease journal 2020;26.

[12] Gu J, Han B, Wang J. COVID-19: Gastrointestinal manifestations and potential fecal-oral transmission. Gastroenterology 2020.

[13] Ong SWX, Tan YK, Chia PY, Lee TH, Ng OT, Wong MSY, et al. Air, Surface Environmental, and Personal Protective Equipment Contamination by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) From a Symptomatic Patient. JAMA 2020.

[14] Kuster GM, Pfister O, Burkard T, Zhou Q, Twerenbold R, Haaf P, et al. SARS-CoV2: should inhibitors of the renin–angiotensin system be withdrawn in patients with COVID-19? European Heart Journal 2020.

[15] Position Statement of the ESC Council on Hypertension on ACE-Inhibitors and Angiotensin Receptor Blockers. 2020 [cited March 30th, 2020]; Available from: https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang