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Prolonged presence of SARS-CoV-2 viral RNA in faecal samples

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For the Chinese translation see Online for appendix 1

We present severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) real-time RT-PCR results of all respiratory and faecal samples from patients with coronavirus disease 2019 (COVID-19) at the Fifth Affiliated Hospital of Sun Yat-sen University, Zhuhai, China, throughout the course of their illness and obligated quarantine period. Real-time RT-PCR was used to detect COVID-19 following the recommended protocol (appendix 2, p 1). Patients with suspected SARS-CoV-2 were confirmed after two sequential positive respiratory tract sample results. Respiratory and faecal samples were collected every 1–2 days (depending on the availability of faecal samples) until two sequential negative results were obtained. We reviewed patients' demographic information, underlying diseases, clinical indices, and treatments from their official medical records. The study was approved by the Medical Ethical Committee of The Fifth Affiliated Hospital of Sun Yat-sen University (approval number K162-1) and informed consent was obtained from participants. Notably, patients who met discharge criteria were allowed to stay in hospital for extended observation and health care.

See Online for appendix 2

Between Jan 16 and March 15, 2020, we enrolled 98 patients. Both respiratory and faecal samples were collected from 74 (76%) patients. Faecal samples from 33 (45%) of 74 patients were negative for SARS CoV-2 RNA, while their respiratory swabs remained positive for a mean of 15·4 days (SD 6·7) from first symptom onset. Of the 41 (55%) of 74 patients with faecal samples that were positive for SARS-CoV-2 RNA, respiratory samples remained positive for SARS-CoV-2 RNA for a mean of 16·7 days (SD 6·7) and faecal samples remained positive for a mean of 27·9 days (10·7) after first symptom onset (ie, for a mean of 11·2 days [9·2] longer than for respiratory samples). The full disease course of the 41 patients with faecal samples that were positive for SARS-CoV-2 RNA is shown in the figure. Notably, patient 1 had positive faecal samples for 33 days continuously after the respiratory samples became negative, and patient 4 tested positive for SARS-CoV-2 RNA in their faecal sample for 47 days after first symptom onset (appendix 2, pp 4–5).

A summary of clinical symptoms and medical treatments is shown in the appendix 2 (pp 2–3, 6–8). The presence of gastrointestinal symptoms was not associated with faecal sample viral RNA positivity (p=0·45); disease severity was not associated with extended duration of faecal sample viral RNA positivity (p=0·60); however, antiviral treatment was positively associated with the presence of viral RNA in faecal samples (p=0·025; appendix 2, pp 2–3). These associations should be interpreted with caution because of the possibility of confounding. Additionally, the *Ct* values of all three targeted genes (*RdRp*, *N*, *E*) in the first faecal sample that was positive for viral RNA were negatively associated with the duration of faecal viral RNA positivity (*RdRp* gene $r = -0{\cdot}34$; *N* gene

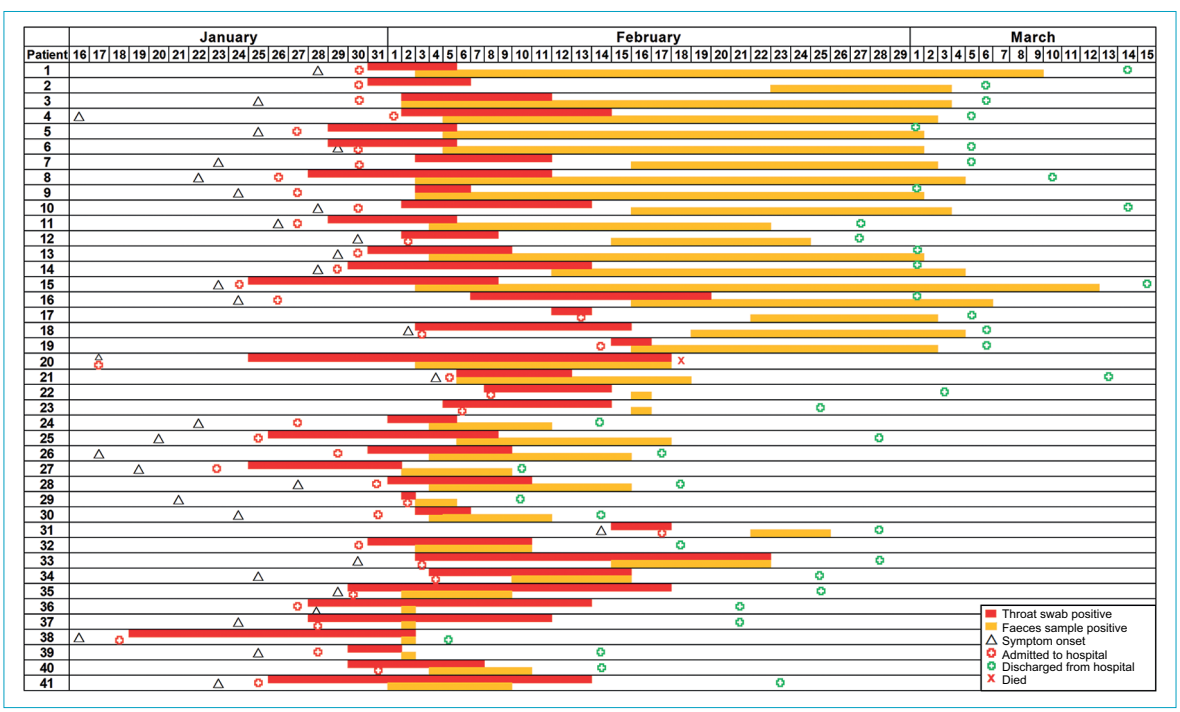

Figure: **Timeline of results from throat swabs and faecal samples through the course of disease for 41 patients with SARS-CoV-2 RNA positive faecal samples, January to March, 2020**

r = –0·02; and *E* gene *r* = –0·16), whereas the correlation of the *Ct* values with duration of faecal sample positivity was only significant for *RdRp* (p=0·033; *N* gene p=0·91; *E* gene p=0·33).

Our data suggest the possibility of extended duration of viral shedding in faeces, for nearly 5 weeks after the patients' respiratory samples tested negative for SARS-CoV-2 RNA. Although knowledge about the viability of SARS-CoV-2 is limited,[1] the virus could remain viable in the environment for days, which could lead to faecal–oral transmission, as seen with severe acute respiratory virus CoV and Middle East respiratory syndrome CoV.[2] Therefore, routine stool sample testing with real-time RT-PCR is highly recommended after the clearance of viral RNA in a patient's respiratory samples. Strict precautions to prevent transmission should be taken for patients who are in hospital or self-quarantined if their faecal samples test positive.

As with any new infectious disease, case definition evolves rapidly as knowledge of the disease accrues. Our data suggest that faecal sample positivity for SARS-CoV-2 RNA normally lags behind that of respiratory tract samples; therefore, we do not suggest the addition of testing of faecal samples to the existing diagnostic procedures for COVID-19. However, the decision on when to discontinue precautions to prevent transmission in patients who have recovered from COVID-19 is crucial for management of medical resources. We would suggest the addition of faecal testing for SARS-CoV-2.[3] Presently, the decision to discharge a patient is made if they show no relevant symptoms and at least two sequential negative results by real-time RT-PCR of sputum or respiratory tract samples collected more than 24 h apart. Here, we observed that for over half of patients, their faecal samples remained positive for SARS-CoV-2 RNA for a mean of 11·2 days after respiratory tract samples became negative for SARS-CoV-2 RNA, implying that the virus is actively replicating in the patient's gastrointestinal tract and that faecal–oral transmission could occur after viral clearance in the respiratory tract.

Determining whether a virus is viable using nucleic acid detection is difficult; further research using fresh stool samples at later timepoints in patients with extended duration of faecal sample positivity is required to define transmission potential. Additionally, we found patients normally had no or very mild symptoms after respiratory tract sample results became negative (data not shown); however, asymptomatic transmission has been reported.[4] No cases of transmission via the faecal–oral route have yet been reported for SARS-CoV-2, which might suggest that infection via this route is unlikely in quarantine facilities, in hospital, or while under self-isolation. However, potential faecal–oral transmission might pose an increased risk in contained living premises such as hostels, dormitories, trains, buses, and cruise ships.

Respiratory transmission is still the primary route for SARS-CoV-2 and evidence is not yet sufficient to develop practical measures for the group of patients with negative respiratory tract sample results but positive faecal samples. Further research into the viability and infectivity of SARS-CoV-2 in faeces is required.

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