

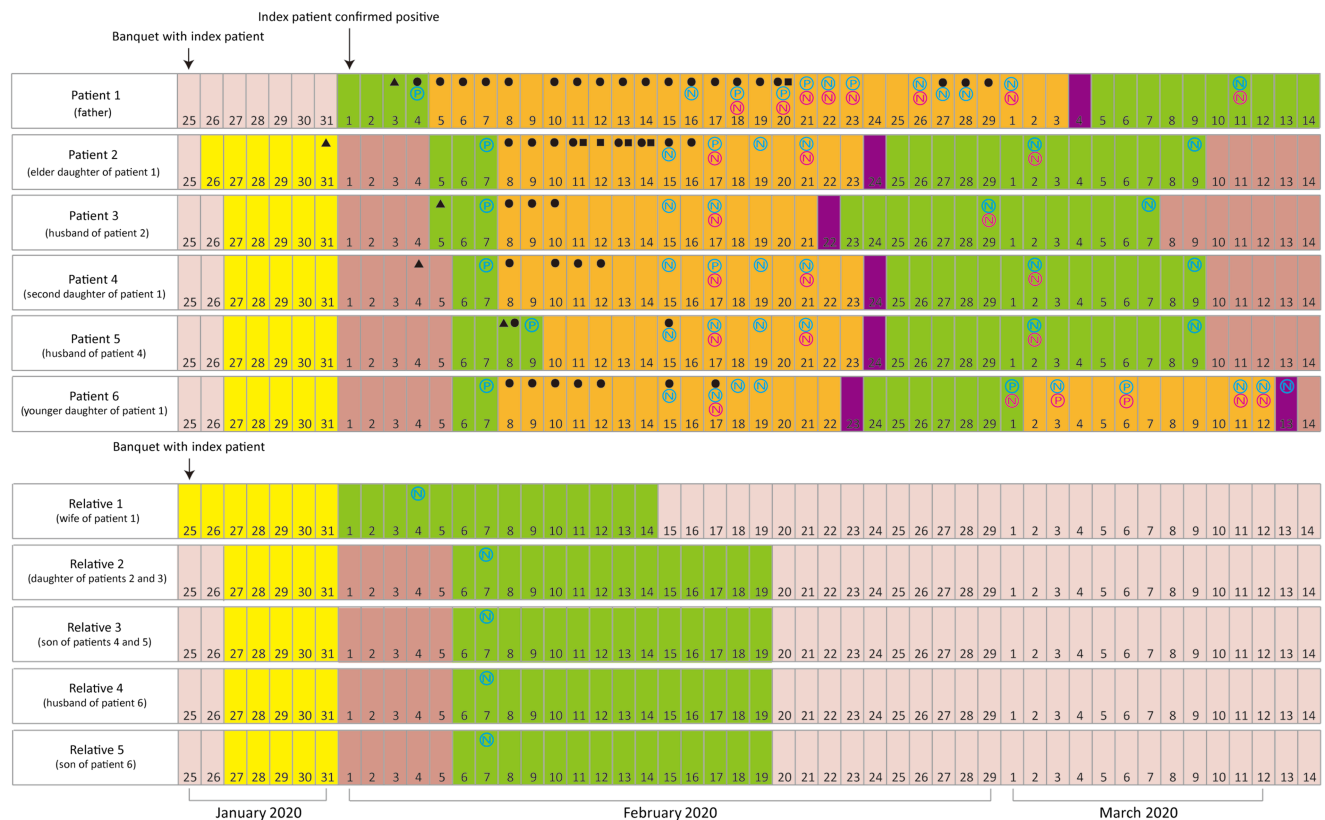
LETTER TO THE EDITOR

# RNA conversion of COVID-19 in respiratory and alimentary specimens during asymptomatic convalescence

To the Editor,

Few studies concerning novel coronavirus disease 2019 (COVID-19) have focused on the follow-up of recovered patients, especially subclinical infected individuals, which may lead to a serious threat to public health if neglected. Here, we report a recovered COVID-19 patient with both nasopharyngeal and anal swabs converting to be positive among an infected family cluster.

On February 8, 2020, a 46-year-old woman (patient 6) was admitted to Wuxi Fifth Affiliated Hospital of Jiangnan University due to positive COVID-19 reverse transcriptase-polymerase chain reaction (RT-PCR) result for nasopharyngeal swab after dining with family members (patients 1–5, relatives 1–5) for consecutive 5 days since January 27, including her father (patient 1) who attended a banquet with a later confirmed imported case (index



**FIGURE 1** Timeline of epidemiological and clinical characteristics of COVID-19 patients in a family cluster. The figure shows the epidemic investigation of patients 1–6 and relatives 1–5, including clinical symptoms, detections of COVID-19, contact histories, and hospitalization information. Grids in different colors represent the contact histories with patient 1, the status of quarantine, or hospitalization. Home quarantine; centralized quarantine; hospitalized; contact with patient 1; discharged; out of quarantine. Beginning of symptoms indicates the onset of COVID-19-related symptoms such as runny nose, cough, and muscle ache. Typical symptoms, including fever and diarrhea, are emphasized by symbols. If the examination of swabs is positive, the “P” in the circle is used; otherwise, the “N” in the circle is used. ●, Fever; ▲, beginning of symptoms; ■, diarrhea; ⊕/⊖, positive/negative nasopharyngeal swab; ⊕/⊖, positive/negative anal swab.

patient) of COVID-19 infection from Japan on January 25. Patients 1–5 were all confirmed positive before or after patient 6 and admitted to the same hospital while relatives 1–5 were exempted from infection (Fig. 1 and Table 1). She experienced a transient fever of peak value of 37.8 °C during admission, which normalized on February 13. Routine blood test manifested no decrease in white blood cell count or lymphocyte count. Meanwhile, chest computed tomography (CT) images did not present with typical abnormalities such as ground-glass opacities or consolidation. Antiviral regimens containing inhaled interferon, oral lopinavir/ritonavir tablets, and arbidol were given depending on the patient's condition. From February 15, RT-PCR results were negative for four nasopharyngeal swabs and one anal swab, and she was discharged on February 23.

Patient 6 was required to continue centralized quarantine for another 14 days. Unfortunately, the RT-PCR test of nasopharyngeal swab sample demonstrated recurrent positive 1 week after discharge (March 1) while anal swab test kept negative, so she was readmitted asymptotically. It was noteworthy that the subsequent anal swab tests turned positive (March 3 and March 6) after readmission while the synchronous nasopharyngeal swabs were negative and positive, respectively. Chest CT scan

performed on March 9 displayed no positive findings. On March 11 and 12, both nasopharyngeal and anal swabs RT-PCR results were negative. After three consecutive negative nasopharyngeal RT-PCR tests, she was prescribed home quarantine since March 13, with subsequent two negative nasopharyngeal RNA tests after 2 and 4 weeks. Meanwhile, the other infected family members were all discharged, and none of them got re-infection like patient 6.

Much of the research emphasis on infection control for COVID-19 seems to be overestimated on respiratory droplet transmission and critically ill cases. However, there is still little evidence summarizing the alternative transmission route, and the role of asymptomatic carriers or subclinical patients. COVID-19 was primarily discovered in respiratory specimens, and afterwards, the viral nucleic acids were identified in patients' urine, stool, gastrointestinal mucosa, and serum.<sup>1,2</sup> As far as patient 6 was concerned, she received four nasopharyngeal but only one anal swab test during hospitalization, which was likely to be false negative and led to the neglect of gastrointestinal tract monitoring. Xie *et al.*<sup>3</sup> mentioned that nearly 14% “re-positive” patients of all discharged patients in Guangzhou were detected by increasing the nasal swab tests. Another research also raised that enhancing




**Table 1** Characteristics, clinical outcomes, and treatment of patients 1–6

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	
Number of hospitalization	—	—	—	—	—	1st	2nd
Sex	Male	Female	Male	Female	Male	Female	
Age (years)	74	50	54	49	49	46	
Occupation	Retired	Worker	Employee	Employee	Employee	Jobless	
Comorbidities	Hypertension Diabetes	Hypertension	Hypertension	Hypertension	No	No	
Smokers	Yes	No	No	No	No	No	
History of residence in Wuhan	No	No	No	No	No	No	
Fever	Yes	Yes	Yes	Yes	Yes	Yes	No
Peak of temperature (°C)	39.5	38.2	38.0	38.3	37.8	37.8	36.9
Duration of fever (days)	26	9	3	5	2	7	—
Dry cough	Yes	Yes	No	Yes	Yes	No	No
Dyspnea	Yes	No	No	No	No	No	No
Diarrhea	Yes	Yes	No	No	No	No	No
Nausea and vomiting	No	No	No	No	No	No	No
Dizziness and headache	Yes	No	No	No	No	No	No
Myalgia and abdominal pain	No	Yes	Yes	No	No	No	No
Fatigue and anorexia	Yes	No	No	No	No	No	No
Nasopharyngeal swab	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Anal swab	Negative	Negative	Negative	Negative	Negative	Negative	Positive
Chest CT images	Bilateral pneumonia	Normal	Normal	Normal	Normal	Normal	Normal
Onset of symptom or positive RT-PCR to hospital admission (days)	2	8	3	4	2	1	1
Hospitalization time (days)	29	17	15	17	15	16	> 11
Complications	No	No	Abnormal liver function	No	No	No	No
Oxygen therapy	Yes	No	No	No	No	No	No
Antibiotic treatment	Yes	No	No	No	No	No	No
Antiviral treatment	Yes	Yes	Yes	Yes	Yes	Yes	No
Atomization treatment of $\alpha$ -interferon	Yes	Yes	Yes	Yes	Yes	Yes	No
Glucocorticoids	Yes	No	No	No	No	No	No
Traditional Chinese medicine treatment	Yes	Yes	Yes	Yes	Yes	Yes	No

CT, computed tomography; RT-PCR, reverse transcriptase-polymerase chain reaction.

nasal swab tests could eliminate the false negative rate since higher viral loads were detected in the upper respiratory tract.<sup>4</sup> On the other hand, some researchers advocated that diarrhea should be regarded as a vital symptom of COVID-19 infection.<sup>5,6</sup> Others mentioned that fecal–oral transmission may be a potential route of COVID-19 outbreak.<sup>7,8</sup> Therefore, a reassessment of latent and asymptomatic patients as sources of infection for the current prevention and control measures is warranted to eventually eliminate the disease.

With the increasing recovered COVID-19 cases, some recurrent positive tests of viral nucleic acids were reported in either nasopharyngeal or anal swab after discharge,<sup>8–10</sup> whereas our study for the first time described recurrent COVID-19 in both respiratory and alimentary specimens at the same time during asymptomatic convalescence. Positive results in both nasopharyngeal and anal swabs after recovery demonstrated the low possibility of false positives. Moreover, whether positive samples of two or more sites is indicative of the existence of active virus, as well as its potential possibility of transmission, remains unknown. A recent study declared that the positive ratio of nucleic acid tests was only 47.4% in the presumptive patients for COVID-19.<sup>11</sup> The asymptomatic infected patients may have been overlooked by nucleic acid tests only, which may be retrieved by applying antibody detection.<sup>12</sup> It is not clear whether the current discharge criteria were too lax and incomplete, or a secondary infection did occur. Taken together, centralized quarantine instead of home quarantine after discharge, appropriate extension of quarantine period, and increasing the frequency of nucleic acid tests at multiple sites accompanied with chest CT scanning during hospitalization as well as convalescent phase should be considered.

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