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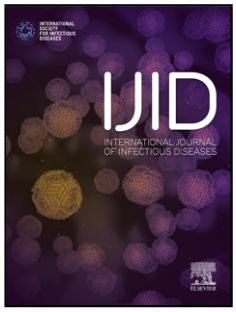

Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster

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Manuscript Title: Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster

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Highlights:

- We report a familial cluster of COVID-19 to evidence that a potential transmission of the disease during the incubation period.
- A familial cluster of 4 patients with COVID-19 in Zhoushan, China, had contact with an asymptomatic family member who was developed symptoms later.
- The infectivity during the incubation period for the SARS-CoV-2 is a big challenge for controlling the disease.

Transmission of COVID-19 in the terminal stage of incubation period: a familial cluster

Abstract: We report a familial cluster of 2019 novel coronavirus disease (COVID-19) to evidence that a potential transmission of the COVID-19 during the incubation period. The first patient in this familial cluster was identified in presymptomatic period, as a close contact of a confirmed patient. Five family members had close contact with the first patient during his incubation period, four of them were confirmed to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in the subsequent sampling test.

Keywords: SARS-CoV-2; incubation period; cluster; COVID-19

An emerging infectious disease, 2019 novel coronavirus disease (COVID-19), was identified to be associated with a novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which was initially reported in December 2019 in Wuhan City, China [1]. Family and hospital clusters with COVID-19 cases were previously reported and person-to-person transmission has been confirmed [2]. Until now, the infectious period of the disease has not been fully explained [3,4]. Here, we report a familial cluster of COVID-19 to evidence that a potential transmission of the disease during the incubation period.

On 8 February 2020, Zhoushan center for disease control and prevention (CDC) received a request from Wuxi CDC, Jiangsu province, China, for assistance in the management of the close contacts of a SARS-CoV-2 infection person (person A) who confirmed in Wuxi city. Zhoushan CDC responded immediately and put the person A's family members (person B, C, D, E, F in Zhoushan City) concentrated at an isolation site and collected their throat swab samples for SARS-CoV-2 testing. On 9 February 2020, Zhoushan CDC identified four laboratory confirmed SARS-CoV-2 infections among person A's family members, and one of whom remained asymptomatic throughout the isolation period. Detailed epidemiological investigations are reported below. Timeline of exposure to the asymptomatic carrier of the SARS-CoV-2 that causes COVID-19 in a familial cluster seen in figure.

Person A is a 51-year-old man who is the first reported SARS-CoV-2 infection in this familial cluster. On January 26, he drove back to Wuxi city alone from his hometown in Hunan province, and then lived with his relatives from January 26 to January 28. Since the person A returned from Hunan province, he was managed for quarantine 14 days at home by the community organization on January 29. However, residential segregation in the community was not mandatory at the time. On January 31, he drove back to his home in Zhoushan city alone and lived together with his families for 4 days. On February 3, he drove back to Wuxi city alone,

then he lived alone at home and did not go out. On February 4, his relative who had previously (January 26 to January 28) lived with him were detected to have SARS-CoV-2 infection. On February 5, as the close contact, he was transferred to the isolation site and his throat swab samples were collected for SARS-CoV-2 detection. On February 6, he was confirmed to have SARS-CoV-2 infection by RT-PCR (Ct values were not available), but he did not has any symptoms as described previously at the time [5]. Then, he was transported to local infectious diseases hospital for isolation. On February 7, he developed fever and chest CT showed slight ground glass changes.

From January 31 to February 3, Person A lived together with his father-in-law (Person B), mother-in-law (Person C), wife (Person F), wife's sister (Person D), daughter (Person E). On 9 February 2020, as the close contacts of Person A, the staff of Zhoushan CDC collected their throat swab samples for SARS-CoV-2 detection and four of them were positive (Person B, C, D, E) (Ct values shown in table). They had no contact with people who with fever or respiratory symptoms in Wuhan or other areas with persistent local COVID-19 transmission in the 14 days prior to the onset of the disease, and no history of contact with wild animals or poultry. Person B had no clinical symptoms, but chest CT showed mild ground glass changes in the both lungs at the time of confirmed. Person C and D had slight symptom with cough, and chest CT

showed mild ground glass changes in the lung at the time of confirmed. Person E is a 7-year-old girl who was asymptomatic during the whole medical observation period, and the chest CT showed normal.

A familial cluster of 4 patients with COVID-19 in Zhoushan, China, had close contact before their symptom onset with an asymptomatic family member who was developed symptoms later and diagnosed in Wuxi city. All persons' respiratory specimens were collected for SARS-CoV-2 detection by RT-PCR assay [5]. Person A's laboratory test and epidemiological investigation was conducted by Wuxi CDC. Unfortunately, SARS-CoV-2 detection as well as chest CT examination for person A had not been conducted before February 6th, so we do not know when he began to shed virus and have imaging changes in both lungs.

The present report suggests that the SARS-CoV-2 may have been transmitted in theterminal stage of incubation period. The infectivity during the incubation period for the SARS-CoV-2 is a big challenge for controlling the disease, especially with the new considerations for the potential infectious sources, the recognition of close contacts, and the isolation of close contacts.

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Ethical Approval

Approval was not required.

Conflict of Interest

No conflict of interest to declare.

Competing interests

The authors declare that they have no conflict of interest.

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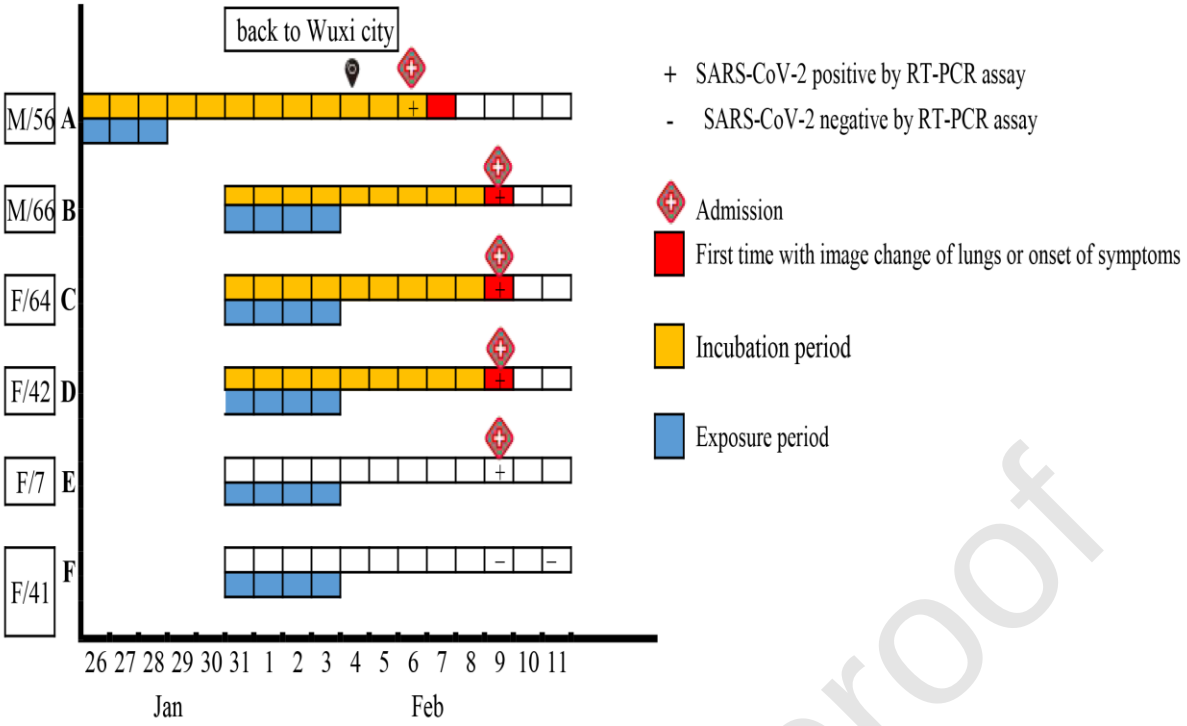

Figure. Epidemiologic linkage and timeline of severe acute respiratory syndrome coronavirus 2 infection within a familial cluster.

Table. Ct values for the RT-PCR results of four laboratory confirmed COVID-19 patients.

Cases	Gender	Age	Sample types	ORF1ab	Nucleoprotein gene	sampling data
Person B	Male	66	sputum	22.33	23.19	9 February 2020
Person C	Female	64	throat swab and sputum	19.66	22.40	9 February 2020
Person D	Female	42	throat swab and sputum	24.96	26.09	9 February 2020
Person E	Female	7	throat swab and sputum	25.13	26.16	9 February 2020