

The transmission and diagnosis of 2019 novel coronavirus infection disease (COVID-19): A Chinese perspective

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Abstract

2019 novel coronavirus (SARS-CoV-2), which originated in Wuhan, China, has attracted the world's attention over the last month. The Chinese government has taken emergency measures to control the outbreak and has undertaken initial steps in the diagnosis and treatment of 2019 novel coronavirus infection disease (COVID-19). However, SARS-CoV-2 possesses powerful pathogenicity as well as transmissibility and still holds many mysteries that are yet to be solved, such as whether the virus can be transmitted by asymptomatic patients or by mothers to their infants. Our research presents selected available cases of COVID-19 in China to better understand the transmission and diagnosis regarding this infectious disease.

KEYWORDS

COVID-19, diagnosis, novel coronavirus, SARS-CoV-2, transmission

2019 novel coronavirus (SARS-CoV-2) originated in a wet market in Wuhan, China, though the market may not be the only source of the coronavirus.¹ SARS-CoV-2 is a betacoronavirus with a single-stranded, enveloped RNA, belonging to the sarbecovirus subgenus of the Coronaviridae family.² Its RNA genome is 29 891 nucleotides in size, encoding 9860 amino acids.³ Moreover, 26 countries have recorded infected cases, especially in Japan, which has a maximum of 705 cases (as of February 19). Most countries lack experience in the diagnosis and management of COVID-19. This article reviews various noteworthy cases of COVID-19 in China for reference, and all cases were verified by local health commissions or multiple media outlets.

1 | SARS-CoV-2 POSSESSES POWERFUL PATHOGENICITY AND TRANSMISSIBILITY

Patient 1, a 56-year-old male from Zhejiang, China, was diagnosed with COVID-19 on February 4. He had no history of exposure to outbreak areas or symptomatic people. According to a video from the District Public Security Department, on the morning of January 23, this patient and another confirmed patient were present at the same stall for 15 seconds at a vegetable market, where both of them did not wear masks.⁴

Patients 2 and 3, a husband and wife couple from Zhejiang, China, were also confirmed to have the disease on January 25 and 27. Similar to Patient 1, the couple had no history of epidemiological contact. According to a video from the District Public Security Department, on the afternoon of January 22, Patient 2 and a confirmed individual were at the same clinic for 50 seconds, where both of them did not wear masks.⁵

SARS-CoV-2 possesses powerful pathogenicity and transmissibility, being more infectious than SARS-CoV and MERS-CoV.⁶ Encountering a confirmed patient and being close for 15 or 50 seconds is not the only route of infection, though it is the most likely route in the above two cases. Moreover, being infected within a very short exposure time is possible in the absence of masks.⁷ The powerful infectivity of SARS-CoV-2 may be explained by the latest findings reported by Wrapp D et al,⁸ which showed that the SARS-CoV-2 S binds to angiotensin-converting enzyme 2 (ACE2) receptors with a higher affinity than SARS-CoV S. Another underlying reason was reported by Zou L et al⁹ in that the shedding pattern of viral nucleic acid in patients infected with SARS-CoV-2 is similar to that in patients with influenza and appears to be different from that in patients infected with SARS-CoV.

SARS-CoV-2 often causes cluster transmission, especially within family clusters. In some cities, cases involving cluster transmission accounted for 50% to 80% of all confirmed cases of COVID-19.¹⁰

Human-to-human transmission of SARS-CoV and MERS-CoV occurred mainly through nosocomial transmission, and transmission between family members only occurred in 13% to 21% of MERS cases and 22% to 39% of SARS cases.¹¹

SARS-CoV-2 can be transmitted by droplets and contact. A study in South Korea showed that many environmental surfaces of patients with MERS were contaminated by MERS-CoV, and virus RNA was detected from environmental surfaces within 5 days after the last positive PCR of patients' respiratory samples.¹² Guangzhou CDC also found SARS-CoV-2 in the house of a confirmed patient,¹³ which serves as evidence of contact transmission. Moreover, live viruses have been found in the feces of patients with COVID-19,¹⁴ however, the fecal-oral transmission of the virus has not been shown. Studies have shown that SARS-CoV may be detected in the feces of most SARS patients,¹⁵ and the virus within feces could survive at room temperature for at least 1 to 2 days.¹⁶ It is possible but infrequent for SARS-CoV to spread via the fecal-oral route.¹⁷ In patients with MERS, feces and urine samples also yielded viral RNA.¹⁸ Given the evidence of fecal contamination of SARS-CoV and MERS-CoV as well as their ability to survive in feces, it is possible that SARS-CoV-2 may also be transmitted through the fecal-oral route.¹⁹ Additionally, in regard to the expression of ACE2 in the intestine and kidney, SARS-CoV-2 may infect these tissues and enter the feces, allowing its potential spread via fecal-oral route.²⁰

The *Lancet* also reminded doctors not to ignore SARS-CoV-2 transmission via ocular surfaces as infected droplets and bodily fluids may easily contaminate the human conjunctival epithelium.²¹ Guangfa Wang, a member of the National Health Commission of the People's Republic of China (NHC) expert panel on pneumonia, was exposed to a fever clinic in Wuhan with only his eyes unprotected. He then demonstrated symptoms of conjunctivitis in his left lower eyelid 2 days before the onset of COVID-19.²²

On February 19, the NHC published the 6th edition of *Guideline on diagnosis and treatment of COVID-19 (the 6th Guideline for COVID-19)*.²³ This document asserted that the transmission of SARS-CoV-2 mainly occurs via large droplets and contact. Additionally, the virus may spread in an unventilated environment with high levels of viral aerosols.

In addition, researchers claimed the spread of SARS-CoV-2 could be characterized by super-spreading events.²⁴ However, there is no evidence of super-spreading events in any medical institution that treats patients suffering from COVID-19.⁶ And a study in South Korea showed that for transmission of MERS-CoV nonisolated in-hospital days was the only factor which tended to be higher in super-spreaders than usual-spreaders.²⁵ Therefore, whether there are super-spreaders or not, early isolation is necessary to reduce the size of the outbreak of SARS-CoV-2.

2 | SARS-CoV-2 MAY BE TRANSMITTED THROUGH ASYMPTOMATIC PATIENTS

Over the past few days, asymptomatic patients were found in many Chinese cities. Table 1 outlines its summary.

TABLE 1 Summary of asymptomatic patients

	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10
Gender	Male	Male	Female	Female	Female	Male	Male
Age (years old)	30	60	23	76	41	36	35
Location (province)	Hangzhou	Henan	Shandong	Shandong	Heilongjiang	Sichuan	Hunan
Epidemiological history	Yes (exposure to relevant environment)	Yes (contact with confirmed person)	Yes (contact with confirmed person)	Yes (contact with confirmed person)	Yes (exposure to relevant environment)	Yes (contact with confirmed person)	Yes (exposure to relevant environment)
Fever, cough, and other symptoms	No	No	No	No	No	No	No
Infect others	Colleagues	*	*	*	*	*	Relatives
Infected numbers	*	*	*	*	*	*	7
Confirmed time or onset time	2 d after back to Wuhan	5 d after index patient confirmed	1 d after index patient confirmed	1 d after index patient confirmed	4 d after index patient confirmed	Onset 2 d after confirmed	4 d after relatives confirmed

Note: *unknown information that cannot be obtained.

On January 24, *The Lancet* reported a familial cluster of SARS-CoV-2 infection. Five family members with a travel history to Wuhan were confirmed to have COVID-19 after returning to Shenzhen, with their asymptomatic child presenting with no fever, respiratory tract symptoms or diarrhoea but had ground-glass lung opacities seen on radiography.²⁶ Subsequently, asymptomatic patients were discovered in many Chinese cities with most of them having an epidemiological history.

Asymptomatic infections may occur due to weakened immune responses and subclinical manifestations, or because the virus is waiting for opportunities to reproduce and invade. To understand its mechanism requires additional investigation of asymptomatic patients as well as blood tests pointing to signs of an immune response, which can help detect asymptomatic or presymptomatic cases.²⁷ A study showed that during the outbreak of SARS-CoV, of all exposed health care workers, 7.5% were asymptomatic SARS-positive cases. Asymptomatic SARS was associated with lower SARS antibody titers and a higher use of masks compared to that of pneumonic SARS.²⁸ Another study showed that of 255 patients with laboratory-confirmed MERS-CoV, a total of 64 patients (25.1%) were reported to be asymptomatic. However, 33 (52%) of the 64 patients were interviewed with 26 (79%) of them having reported at least one respiratory symptom.²⁹ This phenomenon indicates whether asymptomatic patients were actually infected without showing symptoms.

Whether asymptomatic people can transmit SARS-CoV-2 to others is unclear. *The 6th Guide for COVID-19* noted that asymptomatic patients may serve as a source of infection. An article in *NEJM* first reported a German to be confirmed with COVID-19 after contact with an asymptomatic Chinese patient.³⁰ However, it turned out that the Chinese patient had a fever in Germany and took antipyretics. A recent study in *NEJM* reported that a viral load detected in an asymptomatic patient was similar to that detected in symptomatic patients, indicating the potential for transmission in asymptomatic patients.⁹ Table 1 indicates that these asymptomatic patients may infect others or develop symptoms later, but the number of patients involved is small. We remind readers to take this into account when interpreting the research results and conclusions as some of the above observations may be accidental.

Another uncertainty is whether those who are asymptomatic can cause large-scale infections. A study in South Korea showed that during the MERS outbreak in Korea, an asymptomatic patient with MERS was discovered, and none of the 82 persons exposed to that patient without protection was infected.³¹ Most of the asymptomatic patients had close contact with confirmed patients, hence, they may be isolated in a timely manner when tracking close contacts. Moreover, the number of asymptomatic patients was very small; according to epidemiological data in mainland China, only 1.2% of patients with COVID-19 are asymptomatic.⁶ Due to the above reasons, such patients will generally not cause large-scale transmissions of SARS-CoV-2.³²

3 | THERE IS NO CURRENT EVIDENCE THAT SARS-CoV-2 CAN BE TRANSMITTED IN THE UTERUS

Patient 11, an infant born at the Wuhan Children's Hospital on February 2, was delivered by a mother who was confirmed to have COVID-19. The cord blood and placental tissue were collected immediately and tested negative for SARS-CoV-2, but nasopharyngeal swab samples collected 36 hours after birth were positive.³³

SARS-CoV-2 is a novel virus and shares a 79.0% nucleotide identity with the sequence of SARS-CoV and a 51.8% identity with that of MERS-CoV.³⁴ Therefore, the risk of vertical transmission of COVID-19 may be similar to SARS-CoV and MERS-CoV. A study in Hong Kong investigated 12 pregnant women with SARS and showed that all five newborn infants were negative for SARS, especially three of which who were delivered in the acute stage of maternal SARS infection and faced serious risks of perinatal infection.³⁵ Another article reported a pregnant woman with MERS in which all laboratory results related to MERS-CoV in the newborn were negative, as well as that of the cord blood and placenta.³⁶

Infants may certainly be infected by COVID-19, however. The latest research in *JAMA* reported nine infants under 1 year of age suffering from COVID-19, the youngest of which is only 56 days old.³⁷ Currently, no evidence exists that shows SARS-CoV-2 may be transmitted in the uterus.³⁸ Here, the newborn infant was negative for the disease in both cord blood and placenta but lacked pharyngeal swab specimens at birth. The swabs positive for SARS-CoV-2 were collected 36 hours following the birth. Therefore, the possibility of transmission by droplets and contact cannot be ignored.

Recently, *The Lancet* reported nine pregnant women confirmed with COVID-19³⁹ who all delivered by cesarean section. Neonatal throat swabs, amniotic fluid, cord blood, and breastmilk samples from six of these patients were collected, and all samples tested negative for SARS-CoV-2. This indicates that the risk of vertical transmission of SARS-CoV-2 is limited as no presence of virus particles in the products of conception or in the infants existed. However, limited by a small sample size, more investigation and evidence is required to confirm this conclusion.

4 | PATIENTS WITH NEGATIVE SARS-CoV-2 SWABS MAY ALSO BE DIAGNOSED WITH COVID-19

Patient 12, a male from Wuhan, China, was admitted to the Beijing Sino-Japanese friendship hospital for "severe influenza A" on January 30. He had oropharyngeal swabs done with real-time RT-PCR three times before admission, where all tested negative for SARS-CoV-2 but positive for influenza A virus. After admission, he used an invasive ventilator to assist in his ventilation and was confirmed to be positive for SARS-CoV-2 via alveolar lavage test on February 5. A total of 23 staff were quarantined for 14 days as a result.⁴⁰

TABLE 2 Diagnostic criteria of 2019 COVID-19 (*the revised version of the 5th edition*)

Diagnostic criteria	Other cities except Hubei province	Hubei province
Suspected	Epidemiological history consistent with any two clinical features	Epidemiological history + fever and/or respiratory tract symptoms + LWC/NWC/LLC in the early period.
Clinically confirmed	-	Suspected + radiographic evidence
Confirmed	Suspected + RT-PCR or suspected + full genome sequences	Suspected/clinically confirmed + RT-PCR or suspected/clinically confirmed + full genome sequences

Abbreviations: LLC, low lymphocyte count; LWC, low white-cell count; NWC, normal white-cell count.

This case involves the diagnosis of COVID-19. In specific cases, the diagnostic criteria of infectious diseases should be extended to prevent epidemics. In the middle of January, when the NHC visited Wuhan, patients with COVID-19 had been defined by historical criteria: (a) a history of exposure to the Southern China seafood market; (b) symptoms of fever; and (c) the full genome of the virus from respiratory or serum specimens were identical to SARS-CoV-2 sequences.⁴¹ The diagnostic criteria were strict as only a few people are able to sequence the entire viral genome, which resulted in many patients having diseases unable to receive a diagnosis.⁴¹ Therefore, although primary hospitals noticed human-to-human virus transmissions, evidence was still unclear because only 41 cases were confirmed in Wuhan between January 5 and January 15,⁴² which directly led to the delay of epidemic control. Until January 17, experts analyzed the epidemiological data of infected pneumonia cases and found that some cases had no history of exposure to the seafood market. They adopted an optimized SARS-CoV-2 nucleic acid detection kit (RT-PCR) to test specimens of patients with unexplained pneumonia and confirmed 17 COVID-19 cases after reconsidering the diagnostic criteria.⁴³ Therefore, the number of confirmed cases began to increase dramatically each day, and the Chinese Government began to fight against SARS-CoV-2.

The 5th edition of *Guideline on diagnosis and treatment of COVID-19 (the 5th Guideline for COVID-19)* published by NHC⁴⁴ shows that patients satisfying the following criteria are considered to have COVID-19: (a) epidemiological history; and (b) clinical features of (i) fever and/or respiratory tract symptoms, (ii) radiographic evidence, (iii) low or normal white-cell count or low lymphocyte count in the early period. Patients possessing an epidemiological history, consistent with any two clinical features, are diagnosed as suspected cases. Suspected cases are confirmed using any of the following pathogenic detection criteria: (a) positive for SARS-CoV-2 via respiratory or serum specimens examined with real-time RT-PCR; or (b) the full genome sequences of the virus from respiratory or serum specimens were identical to SARS-CoV-2 sequences.

Nonetheless, the PCR results for SARS-CoV-2 are related to the quality of the examined kit as well as to the novel coronavirus's characteristics, sampling location, sampling volume, transportation, and storage, as well as laboratory test conditions and personnel operation. SARS-CoV-2 interacts with the ACE2 receptor, a cell-surface protein mainly found on lung alveolar epithelial cells.⁴⁵ The alveolar lavage test is the best way to confirm SARS-CoV-2, however, the detection of alveolar lavage fluid is mostly used in severe patients using an invasive ventilator. Sputum is considered the

second choice, though the coughs of many patients with COVID-19 are unproductive.⁴⁶ Therefore, pharyngeal swabs are the most common sampling method, however, they may occasionally cause missed diagnoses for smaller levels of SARS-CoV-2 residing in the pharynx. In addition, PCR detection takes up a lot of time, hampering the control of infectious diseases. Therefore, *the Revised Version of the 5th edition* added clinical confirmed standards for the Hubei Province.⁴⁷ Here, suspected cases are defined as patients having an epidemiological history with (i) and (iii) clinical features. Clinically confirmed cases are defined as suspected cases with (ii), as noted in Table 2.

After the revised diagnostic criteria was adopted, the number of COVID-19 cases in Hubei Province increased by 14840 on February 12 compared to February 11 (data taken from the NHC). After most patients were diagnosed, *the 6th Guideline for COVID-19*²³ published by the NHC on February 19 canceled the diagnostic differences between Hubei and other provinces. At the same time, patients without a clear epidemiological history were able to be diagnosed as suspected cases according to the three clinical characteristics mentioned above.

5 | CONCLUSIONS

SARS-CoV-2 possesses powerful pathogenicity and transmissibility and deserves attention from all countries across the world. It can be transmitted by asymptomatic patients, but vertical transmission from mother to child remains to be confirmed. Clinical features, epidemiological history and pathogen detection are important in the diagnosis of COVID-19, where making an accurate diagnosis in time is necessary to control the outbreak. To solve any uncertainties regarding SARS-CoV-2, additional investigations concerning asymptomatic and pregnant patients are required.

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