Secondary Transmission of Coronavirus Disease from Presymptomatic Persons, China

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We explored the secondary attack rate in different types of contact with persons presymptomatic for coronavirus disease (COVID-19). Close contacts who lived with or had frequent contact with an index case-patient had a higher risk for COVID-19. Our findings provide population-based evidence for transmission from persons with presymptomatic COVID-19 infections.

Coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is rapidly spreading across the globe. Some case reports and modeling studies suggest asymptomatic carriage of SARS-CoV-2 plays a role in transmission (*1*–*3*). Studies have shown that 30%–59% of SARS-CoV-2 infections are asymptomatic (*3*,*4*), which poses tremendous infection control challenges. To control asymptomatic infections, China implemented active case surveillance and enhanced social distancing measures, which include contact tracing, quarantine for key populations, medical observation, and curtailed social activities (*5*). However, additional information on the characteristics of presymptomatic transmission is needed to develop targeted control and prevention guidance.

We analyzed contact-tracing surveillance data collected during January 28–March 15, 2020, to explore the secondary attack rate from different types of contact with persons presymptomatic for COVID-19 in Guangzhou, China. Asymptomatic COVID-19 cases were found mainly through close contact screening, clustered epidemic investigations, follow-up investigation of infection sources, and active surveillance of key populations with travel or residence history in areas with continuous transmission of COVID-19 in China and abroad. We developed a case definition for presymptomatic COVID-19, criteria for close contact, and contact investigation and management guidelines (Appendix, https://wwwnc.cdc.gov/EID/article/26/8/20-1142.pdf). We estimated secondary attack rate (SAR) and 95% CI based on the proportion of COVID-19 incidence among close contacts. We calculated the mean reproductive number (R_0) from the number of secondary infections observed among close contacts of each index case. The study was approved by the ethics committee of Guangzhou Center for Disease Control and Prevention, which granted a waiver for informed consent. Data collection was conducted under the authority of the China Center for Disease Control and Prevention.

As of March 15, a total of 359 COVID-19 cases were confirmed in Guangzhou. Among them, 83 (23%) persons were asymptomatic at diagnosis; 71 (86%) of whom later developed symptoms. Among presymptomatic cases, 38 had ≥1 (range 1–90, median 4) close contact. We identified and included 369 close contacts in this study. Median age of close contacts was 35 years (range 0–93 years), 23.8% were family members of an index case, and 12 were confirmed to be infected via nucleic acid testing. Among them, 8 close contacts developed symptoms, and 4 were asymptomatic at the time of this study (Appendix Table).

The overall SAR was 3.3% (95% CI 1.9%–5.6%). The SAR among household contacts was 16.1% and was 1.1% for social contacts, and 0 for workplace contacts. Older close contacts had the highest SAR compared with other age groups; 8.0% in persons ≥60 years of age compared with 1.4%–5.6% in persons <60 years of age. Close contacts of asymptomatic index case-patients had the lowest SAR, 0.8%, but the SAR was 3.5% for those with mild symptoms, 5.7% for those with moderate symptoms, and 4.5% for those with severe symptoms. Close contacts that lived with an index case-patient had 12 times the risk for infection and those who had frequent contact with an index case-patient, >5 contacts during 2 days before the index case was confirmed, had 29 times the risk for infection (Table).

Our findings substantiate previous reports from China and Germany (*1*,*2*,*6*) and show that SARS-CoV-2 can be transmitted during asymptomatic COVID-19 infection period. The probability of infection increased substantially among close contacts who shared living environments or had frequent contact with an index case-patient, which underlines the need for prompt contact-based surveillance and social distancing (*7*). Our results also showed most secondary infections occurred in confined familial clusters and that persons ≥60 years of age appear to be more vulnerable to being infected. These results are consistent with previous reports on epidemiologic

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Table. Characteristics of and secondary attack rates among 369 close contacts of persons with presymptomatic coronavirus disease 2019, China*

Variable	No. contacts	No. infected	Attack rate, % (95% CI)	Relative risk (95% CI)
Sex				
M	217	5	2.3 (0.1–5.2)	Referent
F	152	7	4.6 (2.2–8.9)	2.1 (0.6–6.6)
Age				
≤17	46	2	4.3 (1.2–14.5)	Referent
18–30	104	3	2.9 (1.0–8.1)	0.7 (0.1–4.1)
31–40	72	1	1.4 (0.2–7.4)	0.4 (0.03–3.5)
41–50	68	1	1.5 (0.3–7.9)	0.4 (0.03–3.7)
51–60	54	3	5.6 (1.9–15.1)	1.3 (0.2–8.1)
≥61	25	2	8.0 (1.4–27.5)	1.9 (0.3–14.5)
Index case-patient status*				
Asymptomatic	119	1	0.8 (0.2–5.6)	Referent
Mild symptoms	141	5	3.5 (1.5–8.0)	4.3 (0.5–37.7)
Moderate symptoms	87	5	5.7 (2.5–12.8)	7.2 (0.8–62.7)
Severe symptoms	22	1	4.5 (0.8–21.8)	5.6 (0.3–93.4)
Contact mode				
Social interaction with friends or relatives	66	1	1.5 (0.3–8.1)	Referent
Lived together	62	10	16.1 (9.0–27.2)	12.5 (1.6–100.8)
Worked together	119	0	0	0
Social interaction with strangers	122	1	0.8 (0.2–4.9)	0.5 (0.03–8.7)
Contact frequency†				
Rare	149	1	0.7 (0.1–3.7)	Referent
Moderate	159	1	0.6 (0.1–3.5)	0.9 (0.1–15.1)
Frequent	61	10	16.4 (9.2–27.6)	29.0 (3.6–232.3)

*Status as of March 30, 2020, based on the person's clinical course assessed by a physician. Moderate symptoms included fever, respiratory symptoms, and radiographic evidence of pneumonia. Severe symptoms included breathing rate ≥30/min; oxygen saturation level ≤93% at rest; oxygen concentration level PaO_2/FiO_2 ≤300 mmHg (1 mmHg = 0.133kPa); lung infiltrates >50% within the past 24–48 h; respiratory failure requiring mechanical ventilation; septic shock; or multiple organ dysfunction or failure. All other symptomatic cases were classified as mild.
†Rare contact was defined as contacted with index cases <2 times during 2 days preceding confirmation of infection. Moderate contact was defined as contacted with index cases 3–5 times during 2 days preceding confirmation of infection. Frequent contact was defined as contacted with index cases ≥5 times during 2 days preceding confirmation of infection.

characteristics of 72,314 COVID-19 cases in China (*8*) and suggest that household-based isolation should be cautiously implemented for persons with asymptomatic suspected cases. We also noted that persons with asymptomatic infections appeared to be less effective in transmitting the virus. However, this finding should not discourage isolation and surveillance efforts. The R_0 in this cohort was 0.3 (95% CI 0.2–0.5), which was far smaller than the overall R_0 of 2.2 reported previously (*9*). This low transmission level could be the result of active surveillance, centralized quarantine, and forceful social-distancing strategies in Guangzhou.

Interpretation of the findings should be taken with caution, and several limitations influence our estimation of the SAR. First, the number of close contacts was limited because we only included those who had been reached, and asymptomatic infections might have been missed. Second, we excluded close contacts who were exposed to ≥2 confirmed COVID-19 case-patients. Third, the presymptomatic transmission period is not well defined.

Despite these limitations, our analysis provides valuable information on secondary transmission of SARS-CoV-2 in different types of contact with presymptomatic COVID-19 case-patients. Further evidence is needed to define the population characteristics, communicable period, and the volume and duration of viral shedding from persons with asymptomatic infections.

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Abdominal Visceral Infarction in 3 Patients with COVID-19

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A high incidence of thrombotic events has been reported in patients with coronavirus disease (COVID-19), which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. We report 3 clinical cases of patients in Italy with COVID-19 who developed abdominal viscera infarction, demonstrated by computed tomography.

Frequent thrombotic events, mostly pulmonary embolisms, have been reported in patients with coronavirus disease (COVID-19) (*1*–*4*). We describe 3 cases of COVID-19 complicated by abdominal visceral infarction that occurred in inhabitants of the Emilia Romagna region in northern Italy.

Patient 1, a 54-year-old male former smoker with a history of asthma and quiescent ulcerative colitis not receiving any treatment, was admitted to the emergency department (ED) on February 28, 2020, for syncope. He was discharged after undergoing chest radiography and brain computed tomography (CT), the results of which were unremarkable. He returned to the ED after 5 days for treatment of dyspnea, fatigue, and fever. Blood tests revealed decreased oxygen saturation (94%), increased C-reactive protein (CRP) level (5.38 mg/dL; reference <0.5 mg/dL), and lymphopenia (0.69 × 10^3 cells/mm^3; reference range 0.8–4 × 10^3 cells/mm^3). Chest CT scan demonstrated bilateral viral pneumonia, and nasopharyngeal and oropharyngeal swab specimens were positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). He was hospitalized and treated with lopinavir/ritonavir (400/100 mg orally 2×/d), and hydroxychloroquine (200 mg orally 2×/d). He was discharged to home after 3 hospital days, on therapy; no anticoagulant prophylaxis was suggested. He was rehospitalized 6 days after discharge when he developed sharp right flank and lumbar pain, fever, and dysuria. Blood and urine tests revealed neutrophilia (9.9 × 10^3 cells/mm^3; reference range 1.6–7.5 × 10^3 cells/mm^3), increased lactate dehydrogenase (LDH) (1,507 U/L; reference range 28–378 U/L), increased CRP (1.43 mg/dL), and proteinuria (50 mg/dL). CT scan demonstrated a large right kidney arterial infarction (Figure, panel A). He was treated with low molecular weight

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Appendix

Presymptomatic Coronavirus Disease (COVID-19) Case Definition

We defined presymptomatic COVID-19 cases (index case) as the persons with positive nucleic acid tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, but without relevant clinical symptoms, such as fever, cough, sore throat, and other symptoms and signs that persons could self-perceive or that could be clinically identifiable. We included 2 types of presymptomatic COVID-19 cases. For one, the asymptomatic person has a positive nucleic acid test, but after the 14-day incubation period the person remains asymptomatic; no self-perceived or clinically recognized symptoms or signs ever manifest. For the other, the asymptomatic person has a positive nucleic acid test, and has no self-perceived or clinically recognizable symptoms and signs at the time of sampling, but the person later develops clinical manifestations during medical observation, i.e., a latent period of "asymptomatic infection." Asymptomatic COVID-19 cases were found mainly through screening of close contacts, clustered epidemic investigations, follow-up investigation of infection sources, and active surveillance of key populations with a history of travel to or residence in areas with continuous transmission of COVID-19. We only included secondary cases that met the presymptomatic COVID-19 case criteria because they could still have a third round of transmission, but this did not happen in our cases.

Close Contact Criteria

According to China Center for Disease Control (China CDC) guidelines for COVID-19 close contact investigation and management, close contact of asymptomatic COVID-19 case refers to a person who had contact with index case without using proper protection during 2 days before the index case was tested. Proper protection usually refers to wearing a surgical mask consistently while in contact with the index case. Contact investigation interviews were conducted by trained Guangzhou CDC epidemiologists to collect information on the number of close contacts, the mode and frequency of contact, and other factors. Close contacts include any of the following: family members living together in the same household; direct caregivers or those providing medical treatment and nursing services; medical staff carrying out care activities that might generate aerosols in the same space; people sharing a small place, such as an office, workshop, elevator, cafeteria, or classroom; persons sharing meals or visiting together, or those providing catering and entertainment services in a closed environment; medical personnel, family members, or other persons who have close contact with the case; sharing transportation, such as in vehicle, or on a flight or ship, and having close contact with an index case, which includes passengers, attendants, or companions, such as family members, colleagues, or friends.

After interviews, the on-site investigators assessed whether additional persons might meet the criteria for close contact. We excluded close contacts when there was shared exposure to $\geq$2 confirmed COVID-19 cases.

Contact Management

Close contacts were put in quarantine at a centralized facility, such as hotel, housed in separate rooms, and underwent medical observation for 14 days. All close contacts had nucleic acid testing at the beginning and end of the medical observation. Extra testing was provided for those who developed symptoms during quarantine.

Management Process

1. Informed consent. When carrying out medical observation, provide written or oral information to the contact on rationale, duration, legal basis, precautions, and disease-related reason for medical observation, and the medical and health institutions, contact persons, and contact information of entities responsible for medical observation.

2. Health monitoring. Each morning and evening, the staff of the designated medical and health institutions take temperature measurements of the close contacts, ask about their health status, and give necessary help and guidance.

3. Observation period. The medical observation period is 14 days after the last effective contact with the case without taking proper protection. If a close contact tests negative during medical observation, he or she still needs to continue observation until the 14-day period expires.

4. Treatment for abnormal symptoms. During medical observation, the close contact should immediately report any symptoms, such as fever, dry cough, or other respiratory symptoms; diarrhea; or conjunctival congestion, to the local health department. Then the contact will be sent to the designated medical institution for treatment and further testing. Additional close contacts of suspected, clinically diagnosed, and confirmed cases, will be traced and put in quarantine.

5. Lift medical observation. When the medical observation period expires, close contacts who remain asymptomatic will be released if they have 2 negative nucleic acid tests conducted >24 hours apart. Close contacts can be released prior to the 14-day observation period if the suspected index case is ruled out.

Appendix Table. Characteristics of 12 secondary cases of coronavirus disease (COVID-19) transmitted by asymptomatic persons, China

Index cases*		Secondary cases					
Sex	Symptoms	Age, y/ sex	Relationship to index case	Contact mode	Symptoms	Incubation period, d†	Serial interval‡
M	Mild	23/M	Brother-in-law	Lived together	Moderate	8	11
M	Mild	24/F	Girl friend	Lived together	Asymptomatic	–	–
M	Mild	3/M	Son	Lived together	Mild	6	1
F	Moderate	58/F	Friend	Social interaction	Moderate	6	8
M	Mild	54/F	Mother-in-law	Lived together	Mild	9	12
M	Severe	79/F	Wife	Lived together	Mild	7	7
F	Moderate	57/M	Husband	Lived together	Moderate	11	9
F	Mild	44/F	Mother	Lived together	Mild	6	1
F	Moderate	63/F	Mother-in-law	Lived together	Moderate	10	9
F	Moderate	36/F	Wife	Lived together	Asymptomatic	–	–
F	Moderate	3/M	Son	Lived together	Asymptomatic	–	–
M	Asymptomatic	30/M	Colleague	Social interaction	Asymptomatic	–	–

*Index cases were asymptomatic at time of contact. Symptom severity of index cases are reported at time of COVID-19 diagnosis.

†Incubation period was defined as the interval between last contact with asymptomatic persons later identified as COVID-19 index cases and the onset of clinical signs and symptoms. Incubation period was estimated only for cases that had onset of signs and symptoms.

‡Serial interval was defined as the interval between onset of signs and symptoms in index case and secondary case. We calculated serial intervals only for pairs in which the index and secondary cases both had clinical manifestations