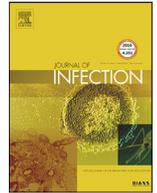




Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Household transmission of SARS-CoV-2[☆]

Zhongliang Wang^a, Wanli Ma^b, Xin Zheng^c, Gang Wu^a, Ruiguang Zhang^{a,*}

^a Cancer Center, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Jiefang Avenue 1277#, Wuhan 430022, China

^b Department of Respiratory and Critical Care Medicine, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China

^c Department of Infectious Diseases, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430022, China

ARTICLE INFO

Article history:

Accepted 21 March 2020

Available online xxx

Keywords:

SARS-CoV-2

Transmission

Household

Wuhan

SUMMARY

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused an epidemic in China and many other countries. Many infected clusters have been found within familial households, but the data about secondary transmission among household contacts is limited.

Methods: In this retrospective case series, we enrolled 85 patients infected with SARS-CoV-2 and their household members in Wuhan. Patients were confirmed infected with SARS-CoV-2 by real-time reverse transcription polymerase chain reaction (RT-PCR) assays on throat swabs. Epidemiological, clinical and laboratory data of the household members were collected.

Results: There were 155 close contacts in total. 104 contacts received RT-PCR assays, with 47 (30%) positive cases and 57 (37%) negative cases. 51 (33%) cases did not received RT-PCR tests for they showed no symptoms of pneumonia during the 2 weeks of quarantine. The infection rate of close contacts was 38% for households with 1 contact, 50% for households with 2 contacts, and 31% for households with 3 contacts.

Conclusions: The rate of secondary transmission among household contacts of patients with SARS-CoV-2 infection was 30%. Our data provide insight into the rate of secondary transmission of SARS-CoV-2 in home.

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Introduction

In December 2019, a series of cases with respiratory symptoms and typical chest CT features were reported in Wuhan, Hubei, China.¹ A previously unknown betacoronavirus was then discovered through the use of full-genome sequencing in samples from these patients, and was believed to be the pathogen of coronavirus disease 2019 (COVID-19).^{2,3} This novel coronavirus was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has caused an epidemic in China and many other countries with the number of suspected cases and deaths increasing daily.⁴⁻⁶

Abbreviations: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; RT-PCR, real-time reverse transcription polymerase chain reaction; ORF1ab, open reading frame1ab; Ct value, cycle threshold value; CT, computed X-ray tomography; MERS-CoV, Middle East respiratory syndrome coronavirus; SARS-CoV, severe acute respiratory syndrome coronavirus; CFR, overall case-fatality rate.

[☆] The rate of secondary transmission among household contacts of patients with SARS-CoV-2 infection was 30% in Wuhan, China.

* Corresponding author

E-mail address: zrg27@163.com (R. Zhang).

From January 23, Wuhan city was blocked with all traffic strictly restricted and closely monitored.⁷ Citizens were restricted in home to control the human to human transmission of the SARS-CoV-2. People who had been in contact with COVID-19 patients were asked to quarantine themselves at home or were taken to special quarantine facilities. Numerous social workers and medical staff were arranged to monitor the close contacts for onset of symptoms. Transmission inside households became an important part of SARS-CoV-2 transmission. Many confirmed case clusters from family households were found.^{8,9} But up to now, the information about transmission in households is still limited. In this study, we describe the epidemiological, clinical and laboratory characteristics of 85 households with SARS-CoV-2 infected members in Wuhan to determine the transmission rate of SARS-CoV-2 among household members.

Methods

Patients

We enrolled 85 hospitalized patients in Union Hospital in Wuhan City, Hubei Province, China. All patients were confirmed infected with SARS-CoV-2 with real-time reverse transcription

<https://doi.org/10.1016/j.jinf.2020.03.040>

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Please cite this article as: Z. Wang, W. Ma and X. Zheng et al., Household transmission of SARS-CoV-2, Journal of Infection, <https://doi.org/10.1016/j.jinf.2020.03.040>

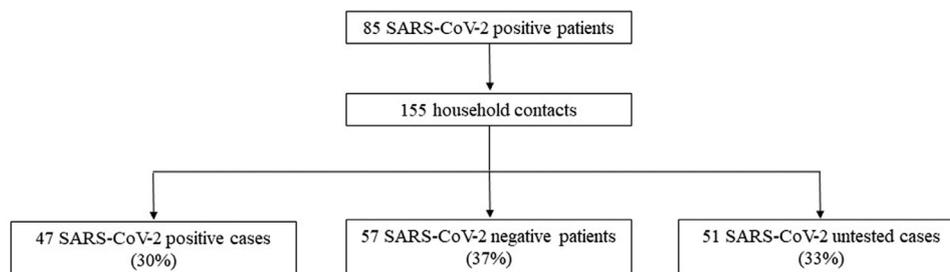


Fig. 1. The procedure of this study.

Legend: 85 confirmed patients of coronavirus disease 2019 (COVID-19) were enrolled. Related to these cases, 85 households were enrolled as one household per index patient, with a total of 155 household contacts. 104 cases received real-time reverse transcription polymerase chain reaction (RT-PCR) assays on throat swabs. 47 cases were positive, and 57 cases were negative. 51 cases did not receive RT-PCR tests for they had no symptoms of pneumonia during quarantine of at least two weeks.

polymerase chain reaction (RT-PCR) assays on throat swabs. The admission date were February 13 and February 14, 2020. Related to these cases, 85 households were enrolled with one household per index patient. The RT-PCR and clinical data of household members were obtained with review of clinical charts and laboratory records. The epidemiological, demographic and symptom data was collected with directly communicating with index patients or their families. The epidemiological, clinical, and laboratory characteristics were obtained with standardized data collection forms. All data was collected up to February 28, 2020. To ensure the accuracy of data, two independent researchers were arranged to review and check the data form. This study was approved by the medical ethics committee of Union Hospital affiliated to Tongji Medical college, Huazhong University of Science and Technology. The need for informed consent was waived by the institutional review board.

RT-PCR assays

The confirmation of SARS-CoV-2 infection is achieved by RT-PCR detection of throat swabs. The tests of hospitalized patients in Union hospital followed the recommendation of China National Center for Disease Control. Two target genes were set as described previously,³ including open reading frame1ab (ORF1ab) and nucleocapsid protein (N), and simultaneously amplified and tested during the real-time RT-PCR assay. Target 1 (ORF1ab): forward primer CCCTGTGGTTTACACTTAA; reverse primer ACGATTGTGCATCAGCTGA; and the probe 5'-FAM-CCGTCTGCGGTATGTGAAAGGTTATGG-BHQ1-3'. Target 2 (N): forward primer GGGGAAGTTCTCTGCTAGAAT; reverse primer CAGACATTTTGTCTCAAGCTG; and the probe 5'-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3'. A cycle threshold value (Ct value) less than 37 was defined as a positive record, and a Ct-value exceeds 40 was defined as a negative test. RT-PCR tests of household contacts were performed in authoritative laboratories designated by local centres for disease control and prevention.

Statistical analysis

Continuous variables were reported as mean with or without standard error. Categorical variables were reported as number and percentages. Statistical analysis was performed with SPSS software (version 26.0).

Results

A total of 85 index patients and 155 household contacts were enrolled, with 47 (30%) of 155 contacts been confirmed infected with SARS-CoV-2 by RT-PCR assays of throat swabs. 57 (37%) cases of the 155 household contacts showed negative results in RT-PCR tests of SARS-CoV-2. 51 (33%) household contacts were not

tested with SARS-CoV-2 for they were asymptomatic during quarantine for at least two weeks, and 16 of them received chest computed X-ray tomography (CT) and showed no signs of viral pneumonia (Fig. 1). No cases but 2 had passed the Huanan seafood market within 1 month from February 13, which was the place where the initial clustering cases of the epidemic were all related to.

The composition of these 85 households were 107 (45%) male adults, 115 (48%) female adults and 18 (7%) children (Table 1). 64 (60%) of 107 male adults and 66 (58%) of 115 female adults were confirmed infected with SARS-CoV-2. By contrast, only 2 (11%) of 18 children were validated as SARS-CoV-2 infections. As a whole, there were totally 240 cases in these 85 households, with 132 (55%) of them were confirmed with SARS-CoV-2 infection and 57 (24%) cases were negative in RT-PCR assays.

When we analyze the epidemic distribution of households, the index patients were considered as part of the households. Most cases showed symptoms of pneumonia or abnormal chest CT characteristics between January 21 and February 8 (Fig. 2). There were more than 10 new cases on 3 days, 13 cases on January 24, 11 cases on January 31 and 12 cases on February 1, respectively. There was 1 household with 4 infected cases, and the fourth case showed ground glass density enhancement in chest CT graph on February 17 and a positive RT-PCR result later. The mean time from onset of illness to admission was 14.2 ± 0.6 days.

As shown in Table 2, 37 (47%) households showed 1 SARS-CoV-2 infected contact, and 9 (12%) households showed 2 infected contacts. 1 (1%) household showed 3 infected contacts. Inside households, the mean time interval from the onset of first infection to the second infection was 5.5 ± 0.7 days. The mean time interval from the onset of second infection to the third infection was 3.0 ± 1.1 days. In the household containing 4 SARS-CoV-2 infections, case 4 showed abnormal chest CT characteristics 11 days after case 3 showed signs of infection. The most common clinical features at the onset of illness were fever, cough, and fatigue. Less common symptoms were sputum production, diarrhea, and headache, et al.

As 7 index patients live alone and did not have close contacts, 155 close contacts were distributed in 78 households. The number of close contacts in a household ranged from 1 to 6, and no household has 5 close contacts. The infection rate was 38% for households with 1 contact, 50% for households with 2 contacts, and 31% for households with 3 contacts. There was 1 household consisted of 6 contacts, involving 1 positive contact and 2 negative contacts. It appears that the infection rate inside households declined with increase of family members (Table 3).

Discussion

We report the epidemic data of 85 households with confirmed SARS-CoV-2 infected members in Wuhan City, showing a sec-

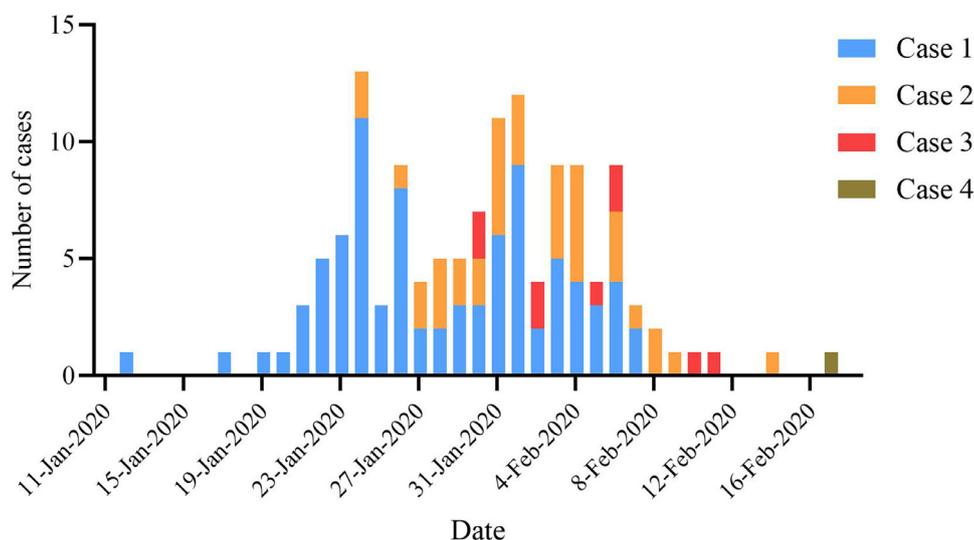


Fig. 2. Epidemic distribution of the confirmed cases with coronavirus disease 2019 by onset of illness.

Legend: Daily numbers of confirmed cases with coronavirus disease 2019 are plotted by date of onset of symptoms ($n=132$). Case 1 refers to the first infected case in a household, and the rest cases could be interpreted in the same manner.

Table 1
Detection of SARS-CoV-2 among all household members.

Household members	Total	Positive cases	Negative cases	Untested cases
Male adults	107/240(45%)	64/107(60%)	22/107(21%)	21/107(19%)
Female adults	115/240(48%)	66/115(58%)	27/115(23%)	22/115(19%)
Children	18/240(7%)	2/18(11%)	8/18(44%)	8/18(44%)
Total	240(100%)	132/240(55%)	57/240(24%)	51/240(21%)

Legend: Data are n/N (%), where N is the total number of cases with available data. SARS-CoV-2, 2019 severe acute respiratory syndrome coronavirus 2.

Table 2
Onset symptoms and time interval of patients with coronavirus disease 2019 in households.

	Case 1 ($n=85$)	Case 2 ($n=37$)	Case 3 ($n=9$)	Case 4 ($n=1$)
Time interval from the previous case (days)	..	5.5 ± 0.7	3.0 ± 1.1	11
Symptoms at the onset				
Fever	55(65%)	26(70%)	4(44%)	0
Cough	11(13%)	5(14%)	3(33%)	0
Fatigue	8(9%)	4(11%)	0	0
Myalgia	4(5%)	0	0	0
Dyspnea	2(2%)	0	0	0
Other symptoms	5(6%)	1(3%)	0	0
Asymptomatic	0	1(3%)	2(22%)	1(100%)

Legend: Case 1 refers to the first infected case with coronavirus disease 2019 in a household, and the rest cases could be interpreted in the same manner. Time interval from the previous cases was expressed as mean with standard error. Symptom data are n/N (%), where N is the total number of cases with available data.

secondary transmission rate of 30% among household members. The infection rate of close contacts was 38% for households with 1 contact, 50% for households with 2 contacts, and 31% for households with 3 contacts.

Now SARS-CoV-2 is spreading around the world. As a simple and effective method, people in the epidemic areas were asked to stay at home and reduce outgoing. But unless all suspected patients and close contacts of confirmed infections were quarantined, transmission among household members will still be an import route of transmission, especially in the areas with more family members. Data about transmission of SARS-CoV-2 in household contacts is now limited. In the report of Zunyou Wu,¹⁰ 20 provinces outside of Hubei in China found 1183 case clusters, 64% of the clusters have been within familial households. In another research on SARS-CoV-2 infected cases in Zhejiang province, China, 21 of 62 patients (34%) were associated with familial clusters. And previous works on other two coronavirus caused pneumonia

epidemics reported secondary transmission rate among household contacts of 5% for Middle East respiratory syndrome coronavirus (MERS-CoV) and 10.2% for severe acute respiratory syndrome coronavirus (SARS-CoV).^{11,12} Our work showed a secondary transmission rate of 30% among household contacts with SARS-CoV-2 infection in Wuhan city, which was similar with the data of Zhejiang province and much more severe than MERS-CoV and SARS-CoV did. This is in accordance with the fact that SARS-CoV-2 has caused infected cases in ever greater quantities and is spreading in a much higher speed than MERS-CoV and SARS-CoV.¹³⁻¹⁶ Based on the imported cases from Wuhan into other cities, the basic reproductive number for SARS-CoV-2 was 2.68. The epidemic doubling time was estimated to be 6.4 days.¹⁷ In this work, as there were only 3.0 ± 1.1 days between the onset of second infection and onset of third infection in households, we prefer to consider the second and third infections in households all as second-generation infections.

Table 3
Detection of SARS-CoV-2 among close contacts in households.

Number of contacts in household	Number of households	Positive contacts	Negative contacts	Untested contacts
1	39/78(50%)	15/39(38%)	12/39(31%)	12/39(31%)
2	15/78(19%)	15/30(50%)	6/30(20%)	9/30(30%)
3	12/78(15%)	11/36(31%)	13/36(36%)	12/36(33%)
4	11/78(14%)	5/44(11%)	24/44(55%)	15/44(34%)
5	0	0	0	0
6	1/78(1%)	1/6(17%)	2/6(33%)	3/6(50%)

Legend: 85 households were enrolled and 7 households with no close contacts were not excluded from analysis in this table. Data are n/N (%), where N is the total number of households or close contacts with available data. SARS-CoV-2, 2019 severe acute respiratory syndrome coronavirus 2.

The outbreak of COVID-19 on Cruise Ship Princess Diamond off the Japanese coast is an ideal model for analysis of transmission among limited population in a restricted place. On 3 February, 2020, 10 persons were initially confirmed to be infected with SARS-CoV-2. From 5 February, people were quarantined in their own rooms on the ship for 2 weeks. By 29 February, 705 of 3,700 passengers and crew (19%) were tested positive with SARS-CoV-2.^{18,19} Notably, this infection rate was achieved after an isolation of 14 days, even though the effect of isolation was partly hindered by the limited space on ship. It confirms that SARS-CoV-2 could spread rapidly among close contacts, which indicates that asking people stay in home is not enough to control the epidemic, and quarantine of suspected cases and close contacts is urgently needed.

People of all ages seem to be susceptible to SARS-CoV-2. The infection rate of children is much lower when compared with adults in most reports.^{3,10,20} In our work, the infection rate of children was 7%, whereas the infection rate of male adults was 45%. Based on the available evidence, without the results of serological studies, it is hard to tell if children are not susceptible. From the report of Zunyou Wu, the overall case-fatality rate (CFR) of 44 672 confirmed cases in China was 2.3%. Cases in those aged 70 to 79 years had an 8.0% CFR and cases in those aged 80 years and older had a 14.8% CFR,¹⁰ indicating elder patients with COVID-19 are more likely to die. Compared with community transmission, the transmission among household members is more dangerous for elder people for they tend to stay at home. If they were infected, the mortality rate would increase significantly with age. So, much more attention should be given to the elder family members when deal with SARS-CoV-2.

Our work has several limitations. Firstly, 51 cases did not receive RT-PCR tests and some of them may be positive. By the final date of follow up, all these 51 cases had passed at least 14 days away from close contact with positive patients and showed no symptoms of pneumonia. As the current estimate of the mean incubation period for COVID-19 was 6.4 days and only 1% of positive cases showed no symptom,^{10,20} it is likely that there is less possibility of positive patients in the 51 untested cases. Secondly, only 85 households were enrolled, and a larger scale of survey is needed to further illustrate this issue. Thirdly, only patients from Union Hospital were reviewed. Because of the possible biases, this sample may not be able to represent the integral population of Wuhan.

In conclusion, SARS-CoV-2 induced a secondary transmission among household contacts of 30%, which is much higher than SARS-CoV and MERS-CoV did. Timely quarantine of all confirmed patients, suspected cases and close contacts is urgently needed to prevent COVID-19 from a wider spread.

Declaration of Competing Interest

We declare no competing interests.

Acknowledgments

Not applicable.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

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