Am J Transl Res 2020;12(10):6434-6444
www.ajtr.org /ISSN:1943-8141/AJTR0118466

Original Article

The epidemiological characteristics of cluster transmission of coronavirus disease 2019 (COVID-19): a multi-center study in Jiangsu Province

Tao Han[1*], Lei Hua[2*], Shu He[2*], Yaqing Zhou[2], Can Hou[2], Jiaxin Chen[2], Jinxia Yuan[2], Yi Guo[2], Sheng Zhang[2], Qiaowei Jia[2], Chenhui Zhao[2], Jing Zhang[2], Quan Cao[1], Enzhi Jia[2]

Departments of [1]Critical Care Medicine, [2]Cardiovascular Medicine, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, Jiangsu Province, China. [*]Equal contributors.

Received June 26, 2020; Accepted August 20, 2020; Epub October 15, 2020; Published October 30, 2020

Abstract: Coronavirus Disease 2019 (COVID-19) pandemic has rapidly spread across the globe while little multi-center research about the epidemiological characteristics of cluster transmission is conducted. To provide a more comprehensive description of the epidemiological characteristics of cluster transmission and the virulence of SARS-CoV-2 carried by asymptomatic carriers, we studied the epidemiological characteristics of 70 clusters. 70 clusters including 311 consecutive subjects from January 20, 2020, to March 10, 2020, were enrolled. Of 70 clusters, 5 were infected by asymptomatic or presymptomatic carriers. We gathered and analyzed information about their demographic, epidemiological, clinical, diagnostic classification, and cluster characteristics. Among the 66 asymptomatic carriers in Jiangsu Province, 49 asymptomatic were observed in 311 subjects distributed in 70 clusters. We demonstrated that there is a significance between the severity of cases infected by asymptomatic carriers and cases infected by symptomatic patients (P=0.033) and the former usually presented with milder symptoms. A significant difference was shown regarding the level distribution of age (P=0.006) and the frequency distribution of gender (P=0.014) and disease severity of COVID-19 (P=0.008) among the seven groups classified by the relationship with the index cases. The average age of infected medical staff was the youngest and the majority of infected medical are females while the infected patients were generally oldest and usually accompanied by severest symptoms. We concluded that asymptomatic carriers are mainly screened out of clusters and the patients infected by asymptomatic carriers present with milder symptoms than those infected by symptomatic patients, which indicated that the SARS-CoV-2 shares decreased virulence among asymptomatic carriers. Effective measures should be taken to prevent transmission in hospitals to protect doctors, nurses, and patients.

Keywords: COVID-19, asymptomatic carrier, clusters, nosocomial infection

Introduction

According to the Situation Report - 100 about coronavirus disease 2019 (COVID-19) released by World Health Organization (WHO), by 10:00 CEST, 01 June 2020, 6,057,853 confirmed cases, including 3018681 (122,917 new) and 371166 deaths (4,000 new) have been reported globally [1]. With an increasing number of infections and deaths, COVID-19 poses a significant threat to public health.

Cluster transmission plays an important role in COVID-19 spreading. Three clusters of COVID-19, containing 28 locally transmitted cases have been reported in Singapore [2]. Another study also reveals the epidemiology features of clusters, including age, gender, and incubation period [3]. Although clusters transmission has been reported before, few pieces of research have been conducted to explain whether the epidemiological characteristics of cluster transmission of COVID-19 presented in the same way in different situations.

With the development of COVID-19 research, it is notable that the asymptomatic carriers are potential sources of COVID-19 infection. Researchers in Germany have reported that the transmission of COVID-19 infection caused by the asymptomatic carrier. Moreover, a 2-family cluster of subjects with COVID-19 infected by having contact with infected but potentially pre-symptomatic subjects has been demonstrated

[4]. Besides, the familial cluster of COVID-19 infection from an asymptomatic case has been reported [5]. According to the recent study, 5% of COVID-19 infection resulted from the asymptomatic case [6]. However, the difference of virulence of SARS-CoV-2 carried by asymptomatic carriers and symptomatic patients and the features of asymptomatic carriers among clusters has not been fully explored.

The purpose of this study was to investigate whether the epidemiological characteristics of cluster transmission of COVID-19 do present the same in different situations and whether the virulence of SARS-CoV-2 between asymptomatic carriers and symptomatic patients is the same. We also aimed to study the features of asymptomatic carriers among clusters. Therefore, we carried out a multi-center study observing 70 clusters across 13 cities in Jiangsu Province, China.

Materials and methods

Subjects and methods

Study participants: From January 20, 2020 to March 10, 2020, 70 cluster outbreaks including 311 consecutive subjects (148 males and 163 females) aged from 1 to 97 years who were laboratory-confirmed asymptomatic carriers, mild cases, ordinary cases, severe and critical cases of Covid-19 from 13 cities across Jiangsu Province, China were enrolled in this study. Of the 311 subjects, 49 (15.8%), 97 (31.2%), 160 (51.4%), and 5 (1.6%) subjects were categorized into asymptomatic carriers, mild cases, ordinary cases, severe and critical cases of Covid-19 respectively. The demographic, epidemiological, clinical, diagnostic classification and cluster characteristics were collected and analyzed.

Study definitions: Asymptomatic carriers who present with no clinical symptoms but with a positive result of the pathogen tests of 2019-nCoV in respiratory tract specimens and so on were found mainly through the investigation of cluster outbreak and tracing of the infectious source. A cluster outbreak means that more than two confirmed cases or asymptomatic carriers are found within 14 days in a small area (such as a family, a building site, a work unit, etc.), and there is a possibility of human-to-human transmission caused by close contact or by exposure to infectious source altogether. The definitions about classifications of COVID-19 of the present study were based on the 6th edition guidance for COVID-19: prevention, control, diagnosis, and management issued by China's National Health Commission [7].

The incubation period means the time starting from the moment of exposure to severe acute respiratory syndrome-corona virus-2 (SARS-CoV-2) until signs and symptoms of COVID-19 appear. Epidemiological data were collected to speculate the latent period of COVID-19. For each subject, the time of exposure to SARS-CoV-2 and appearance of the earliest symptom was recorded as accurately as possible. We would use the time of events when it is precise; otherwise, the upper and lower limits of each event were given according to the case history. When the time of exposure to SARS-CoV-2 is an interval which means uncertain, the median of it was used as the onset of exposure to SARS-CoV-2 [8]. When the time interval of exposure to SARS-CoV-2 could not be determined, we defined it as 7 days according to the previous report [9].

Statistical analyses

Data were analyzed using Statistics Package for Social Sciences (ver. 16.0; SPSS Incorporated, Chicago, IL, USA). Subjects were categorized into two, seven, and ten groups according to the characteristics of the index case, the close contacts' relationships with the index cases, and manners of being infected respectively. Normally distributed variable of age was presented as mean ± standard deviation (SD), and the comparisons were analyzed using the independent-samples t-test and one-way ANOVA. Variable of incubation period with a skewed distribution were presented as median and quartile ranges, and the comparisons were made using the Mann-Whitney U test and Kruskal-Wallis H test. Categorical variables were compared using chi-square analyses. Statistical significance was considered if the two-tailed p-value was <0.05.

Results

The epidemiological characteristics of cluster transmission of COVID-19

The data source of the cluster transmission of COVID-19 in the present study was shown in Tables S1 and S2. The epidemiological characteristics of index cases and infected patients among 70 clusters were exhibited in **Table 1**.

Table 1. The epidemiological characteristics of index cases and infected patients among 70 clusters

Cluster	Index case			Infected cases from the index case			
	Age (years)	Gender	Incubation period (days)	Males	Females	Age (years, mean ± SD)	The incubation period (days, median (interquartile range))
1	52	Male	10	0	2	35.5±16.26	3.0
2	49	Male	10	2	1	29.0±17.35	5.0
3	32	Female	8	1	0	36.0	-
4	48	Male	4	6	4	38.9±16.02	8.5 (5.0-11.0)
5	25	Female	13	5	4	49.78±18.44	11.5 (7.0-14.0)
6	57	Male	4	5	1	49.1±7.46	14.0 (4.0-14.0)
7	80	Female	16	0	1	73.0	14
8	48	Male	7	11	2	43.0±15.92	9.0 (6.0-11.0)
9	2	Female	7	1	0	60.0	7.0
10	32	Male	5	1	1	47.0±22.63	6.0
11				2	2	44.75±27.5	6.0
12	51	Male	8	1	1	36.0±16.97	8.0
13	58	Male	7	1	0	32.0	5.0
14	57	Male	4	3	16	55.11±9.81	4.0 (4.0-10.0)
15	52	Male	13	2	5	41.57±8.48	8.0 (4.0-14.0)
16	46	Male	7	0	2	31.5±17.68	13.5 (13.0-14.0)
17	58	Male	5	2	0	45.0±16.97	6.0 (5.0-7.0)
18	42	Male	5	2	2	37.5±9.0	1.5 (1.0-2.75)
19	50	Female	7	1	3	17.75±10.01	2.0 (1.0-5.0)
20	75	Female	7	1	2	39.0±13.89	5.0 (2.0-6.0)
21	45	Female	7	2	4	65.83±15.01	6.0 (4.5-6.5)
22	36	Female	2	3	1	42.5±26.90	6.0 (5.0-10.0)
23	58	Female	4	2	1	67.33±5.03	7.0 (4.0-7.0)
24 (A)	68	Male		1	1	49.5±20.51	7.5 (6.0-9.0)
25	34	Male	4	0	2	20.0±19.80	1.0
26	68	Female	7	0	2	80.5±23.33	8.0
27	39	Male	7	0	1	33.0	-
28	52	Male	7	1	0	62.0	7.0
29	58	Female	10	0	1	53.0	10.0
30	50	Male	14	2	4	28.83±12.27	9.0 (6.75-11.25)
31	57	Male	7	2	3	49.8±16.81	15.0 (10.0-16.0)
32	73	Male	16	0	1	72.0	-
33	27	Male	1	1	1	13.5±17.68	6.5 (5.0-8.0)
34	30	Male	13	0	1	30.0	9.0
35				1	1	74.0±2.83	7.0
36	42	Female	18	2	2	33.75±27.16	21.0 (20.0-21.0)
37 (B)	6	Male		0	1	33.0	7.0
38	25	Female	7	0	1	25.0	7.0
39 (C)	57	Male		1	1	40.0±18.38	7.0
40	57	Female	7	1	1	42.5±21.92	7.0
41	32	Male	8	0	2	48.5±21.92	-
42	52	Female	7	1	1	52.0±1.41	14.5 (12.0-17.0)
43	67	Male	5	0	1	66.0	9.0
44	63	Female	4	0	1	12.0	12.0
45	30	Male	7	1	1	16.5±17.68	7.0

46	9	Female	7	1	1	64.0	4.5 (1.0-8.0)
47	48	Male	7	0	2	34.5±17.68	7.0
48	50	Male	22	0	3	25.33±23.54	24.5 (24.0-25.0)
49	56	Female	16	1	0	55.0	17.0
50	36	Female	1	1	0	32.0	3.0
51	36	Male	7	5	3	52.88±7.61	6.6 (3.0-7.5)
52	27	Female	7	1	1	77.0±2.83	2.5 (2.0-3.0)
53	49	Male	7	0	2	25.5±21.92	3.0 (1.0-5.0)
54	35	Male	7	0	1	63.0	-
55	54	Male	10	0	1	52.0	8.0
56 (D)	21	Male		5	4	37.22±21.21	11.0 (7.0-14.0)
57	26	Male	4	0	1	23.0	4.0
58	56	Male	5	2	4	47.0±18.53	9.5 (7.5-11.5)
59	23	Male	4	5	14	41.95±20.32	10.0 (8.0-12.0)
60	26	Male	7	0	2	51.0±35.36	5.5 (4.0-7.0)
61	60	Male	4	1	2	54.67±1.15	9.0 (5.0-12.0)
62	59	Female	7	0	1	62.0	6.0
63	27	Male	7	2	0	51.5±48.79	-
64	29	Male	7	5	0	39.4±24.72	7.0
65	73	Male	7	2	1	29.67±15.31	7.0
66	70	Male	7	1	1	25.0±25.46	3.0
67	7	Female	7	0	1	32.0	7.0
68	45	Male	5	3	5	42.38±15.46	11.0 (8.0-12.5)
69	50	Male	7	1	1	48.5±2.12	16.0 (12.0-20.0)
70 (E)	36	Male		1	2	47.0±9.54	7.0

Clusters A to cluster E illustrated the 5 clusters resulted from asymptomatic carriers, which can be found in **Table 1**. Cluster A corresponds with the 24th cluster in **Table 1**. Cluster B can be connected with the 37th cluster in **Table 1**. Cluster C equals the 39th cluster in **Table 1**. Cluster D can be linked with the 56th cluster in **Table 1**. Cluster E corresponds with the 70th cluster in **Table 1**.

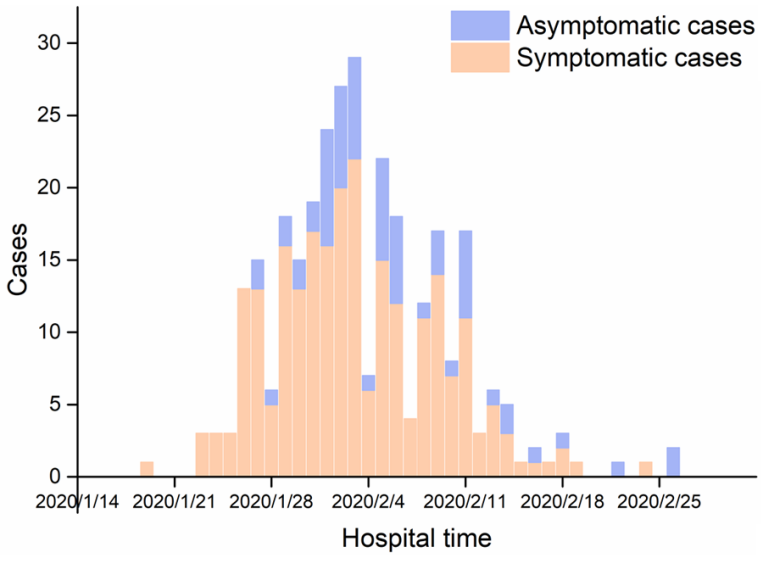

Figure 1. Cases admitted in hospital from January 19, 2020, to March 10, 2020, in Jiangsu Province.

Among the 70 cluster outbreaks in the present study, clear index cases can be found in 68 cluster outbreaks, and of the 68 cluster outbreaks, 5 clusters were transmitted by asymptomatic infected patients. 66 asymptomatic carriers were found from major hospitals in Jiangsu Province.

The epidemiological curve (**Figure 1**) shows the characteristics of persistent cluster transmission from January 19, 2020, to March 10, 2020, in Jiangsu Province. The earliest onset time of the cases that can be traced back is

Table 2. The epidemiological characteristics of cluster transmission of COVID-19 grouped by the characteristics of the index case

Index case	Infected cases from the index case						
	Age (years, mean ± SD)	The incubation period (days, median (interquartile range))	Males	Females	Asymptomatic carrier	Mile case	Ordinary case, severe case, critical case
Asymptomatic cases	40.47±4.28	7 (7-9.50)	8	9	4	10	3
Symptomatic cases	44.41±1.31	7 (5-11)	97	129	40	74	112
Statistical parameter	-0.799	-0.365	0.11			6.810	
P value	0.425	0.715	0.740			0.033	

Table 3. The epidemiological characteristics of cluster transmission of COVID-19 grouped by the close contacts' relationships with the index cases

Close contacts	Infected cases from the index case						
	Age (years, mean ± SD)	The incubation period (days, median (interquartile range))	Males	Females	Asymptomatic carrier	Mile case	Ordinary case, severe case, critical case
Family members	42.36±20.86	7 (5-10)	41	65	19	37	50
Relatives	42.11±23.19	8 (7-11)	11	17	7	8	13
Friends	45.17±11.07	5 (1.5-7.50)	4	2	0	4	2
Colleagues/Classmates	49.88±16.24	8 (4-11)	22	29	10	27	14
Medical staff	26.82±4.67	8 (4.5-11.5)	1	10	2	2	7
Patients	53.71±17.38	8.5 (4.75-11.75)	7	7	2	0	12
Others	44.19±17.40	9 (6-12)	19	8	6	4	17
Statistical parameter	6724.035	7.289	16.006			26.992	
P value	0.006	0.295	0.014			0.008	

January 19, and there is a peak in the area, which appears on February 3. Also, the epidemic curve suggested that the onset of symptomatic infection is earlier than that of asymptomatic infection.

The epidemiological characteristics of cluster transmission of COVID-19 grouped by the characteristics of the index case

The independent samples t-test, Mann-Whitney U test, and chi-square test were used to analyze the epidemiological characteristics of cluster transmission of COVID-19 grouped by the characteristics of the index case, and the results were shown in **Table 2**. The results showed no significant difference was found among the frequency distribution of gender, level distribution of age, and incubation period between the two groups categorized by the characteristics of the index case. However, the frequency distribution of disease severity of COVID-19 significantly differed between the two groups (P=0.033), cases infected by asymptomatic carriers are mainly asymptomaticly infected persons and mildly infected patients, and cases infected by symptomatic infected persons are mainly ordinary cases, severe cases, and critical cases.

The epidemiological characteristics of cluster transmission of COVID-19 grouped by the close contacts' relationships with the index cases

The One-Way ANOVA test, Kruskal-Wallis H test, and chi-square test were used to analyze the epidemiological characteristics of cluster transmission of COVID-19 grouped by the close contacts' relationships with index cases, and the results were shown in **Table 3**. The significant difference was not found among the seven groups giving the level distribution latent period. However, the significant difference was found regarding the level distribution of age (P=0.006) and the frequency distribution of gender (P=0.014) and disease severity of COVID-19 (P=0.008) among the seven groups respectively. Among the close contacts of COVID-19 cases, the infected medical staff is the youngest group and is mainly composed of females, and the infected patients group is the oldest one, the majority of which are ordinary cases, severe cases, critical cases.

Table 4. The epidemiological characteristics of cluster transmission of COVID-19 grouped by manners of being infected

Close contact style	Infected cases from the index case						
	Age (years, mean ± SD)	The incubation period (days, median (interquartile range))	Males	Females	Asymptomatic carrier	Mile case	Ordinary case, severe case, critical case
Living with the case	42.98±20.88	7 (5-10)	30	60	17	35	38
Dining together	48.71±18.15	7 (4-10)	39	34	15	28	30
Working/Studying together	44.29±16.90	10 (2-14)	3	4	0	2	5
Taking the same transportation	43.17±22.36	6 (3.75-6.75)	3	3	2	2	2
Providing medical service	31.45±14.10	8.5 (4.75-11.25)	2	9	1	2	8
Same ward	48.0	12 (7.50-14)	0	1	0	0	1
Same diagnosis and treatment environment	54.5±17.57	12 (7.5-14)	9	5	4	2	8
Short conversation	38.67±11.15	8 (3.75-10.25)	2	4	0	3	3
Same building	32.63±13.07	9 (7.5-12)	3	5	3	1	4
Same activity environment	40.04±21.10	7 (6-9)	14	13	2	9	16
Statistical parameter	6636.211	12.745	14.064			18.972	
P value	0.041	0.175	0.120			0.394	

The epidemiological characteristics of cluster transmission of COVID-19 grouped by manners of being infected

Table 4 presented the epidemiological characteristics of cluster transmission of COVID-19 grouped by manners of being infected analyzed via the One-Way ANOVA test, Kruskal-Wallis H test, and chi-square test. The difference in age among the 10 groups of close contacts was statistically significant (*P*=0.041), providing medical service infected with the youngest. And, no significant difference was found concerning the level distribution of the latent period (*P*=0.175) and the frequency distribution of gender (*P*=0.120) and disease severity of COVID-19 (*P*=0.394).

The epidemiological characteristics of cluster transmission of coronavirus disease 2019 (COVID-19) from asymptomatic cases

*Cluster A (Cluster 24 in **Table 1**):* Patient-Index is a 68-year-old otherwise-healthy man and was tested positive by nucleic acid test on January 03, 2020. He went to Wuxue, Hubei province to apply for a medical insurance card on January 19, 2020, and returned to Nanjing the following day. He suggested that he was totally asymptomatic and well since he came from Hubei. Patient 1 is the son of the patient index and reported that the first symptom that appeared on him was dizziness and tiredness with a fever of 38.4°C on January 16, 2020, after which he received clinical treatment in a local hospital. The confirmation test of the SARS-CoV-2 infection was positive on February 02, 2020. His mother was tested positive by RT-PCR assays on February 03, 2020. Patient 2 is the wife of the index patient and cohabited with the index patient since he came back from Wuxue, Hubei province on January 19, 2020. She had a fever of 38.7°C accompanied by tiredness and vomiting since January 31, 2020. She was then treated in a local clinic and the RT-PCR assays were identified as positive. The chronology of the symptom onset of Cluster A is shown in **Figure 2**.

*Cluster B (Cluster 37 in **Table 1**):* The index patient is a 7-year-old boy visiting Wuhan relatives with his parents before the Spring Festival and returning to Nanjing on January 21, 2020. He showed no symptoms of infection but was tested positive on the qRT-PCR assay. Patient 1 is the index patient's mother and went to Wuhan with her husband and son. She developed a sore throat on January 18, 2020, but still returned to Nanjing on January 21, 2020. She received treatment on January 26, 2020, in a local hospital and was tested positive on nucleic acid testing on February 5, 2020. Her husband, son, and parents were also tested positive on the qRT-PCR assay. The chronology of the symptom onset of Cluster B is revealed in **Figure 3**.

*Cluster C (Cluster 39 in **Table 1**):* The index patient is a 57-year-old Nanjing resident working in Wuhan who drove back to Nanjing together with his son and a colleague on January 22, 2020, and was reported being asymptom-

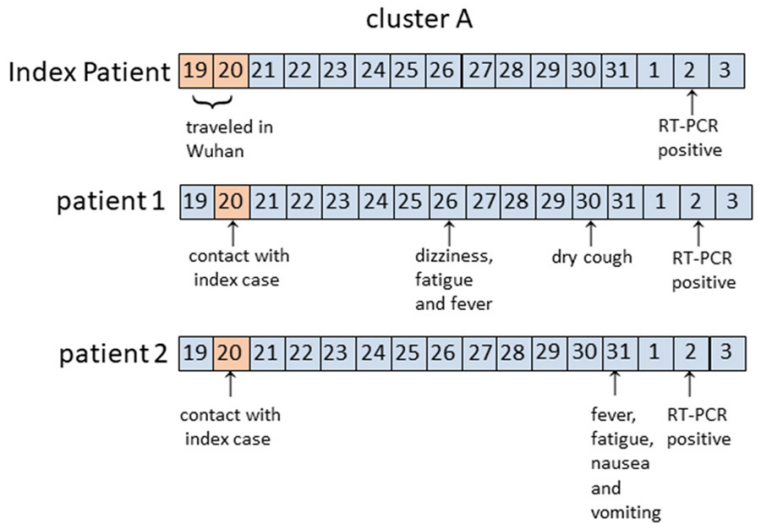

Figure 2. Timeline of Exposure to Index case with Asymptomatic COVID-19 Infection of the cluster A in the present study. Boxes filled in red are the dates on which patients traveled in Wuhan or had close contacts with the index case. The blue boxes mean the dates on which patients separated from the index case. The arrows point to the date of symptom onset or the date of RT-PCR Positive.

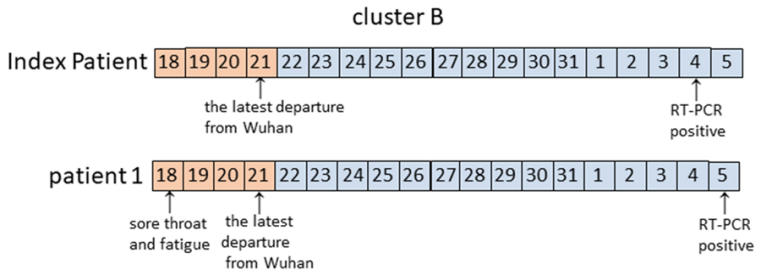

Figure 3. Timeline of Exposure to Index case with Asymptomatic COVID-19 Infection of cluster B in the present study. Boxes painted with red are the dates on which patients traveled in Wuhan or had close contacts with the index case. The blue boxes mean the dates on which patients separated from the index case. The arrows point to the date of symptom onset or the date of RT-PCR Positive.

atic but was nonetheless tested positive for SARS-CoV-2 on January 22, 2020. Patient 1 is the index patient's wife living and working in Nanjing. She had close contact with her husband and son after their arrival. He presented with no symptoms but was tested positive on RT-PCR assays on January 28, 2020. A short conversation was conducted with his parents and mother-in-law but none of them showed any symptoms. Patient 2 is the index patient's 27-year-old son living in Wuhan with his father. His father drove back to Nanjing together with him and his father's colleague on January 22, 2020. He developed a fever of 37.5°C on January 25, 2020, and tested positive by RT-PCR assays on January 27, 2020. None of the families he had contacted showed COVID-19-relevant symptoms. The chronology of symptom onset of Cluster C is presented in **Figure 4**.

*Cluster D (Cluster 56 in **Table 1**):* All patients of cluster D went to Hubei province to visit relatives but on different dates, including index patient, patient 2, patient 3, patient 4 on January 13, 2020, patient 1 on January 7, 2020, patient 5, patient 6, patient 7 on January 16, 2020, after which they all came back to Wuxi on January 7, 2020, in two separate cars. They were all found to be positive on qRT-PCR assays but not on the same day, patient 5, patient 6 and patient 7 on February 5, 2020, and the rest of patients on February 6, 2020. Patient 3 got a headache on February 2, 2020 while patient 4 presented with headache on January 31, 2020, and dry cough on February 2, 2020. The symptom of dry cough appeared in patient 6 on January 28, 2020. Patient 7 showed the symptom of snuffle on February 3, 2020, and patient 9 developed a fever on February 1, 2020. Among the cluster, index patient, patient 1, patient 2, and patient 8 presented no symptoms of infection except having laboratory-confirmed SARS-CoV-2-infection. **Figure 5A** and **5B** show the chronology of the symptom onset of Cluster D.

*Cluster E (Cluster 70 in **Table 1**):* From Wuhan to Nanjing with four other friends on January 21, 2020. He was placed under home quarantine upon his return. He developed no symptoms while testing positive on laboratory confirmation of SARS-CoV-2-infection on February 1, 2020. Patient 1 is a 53-year-old male who drove from Wuhan to Nanjing with Index pa-

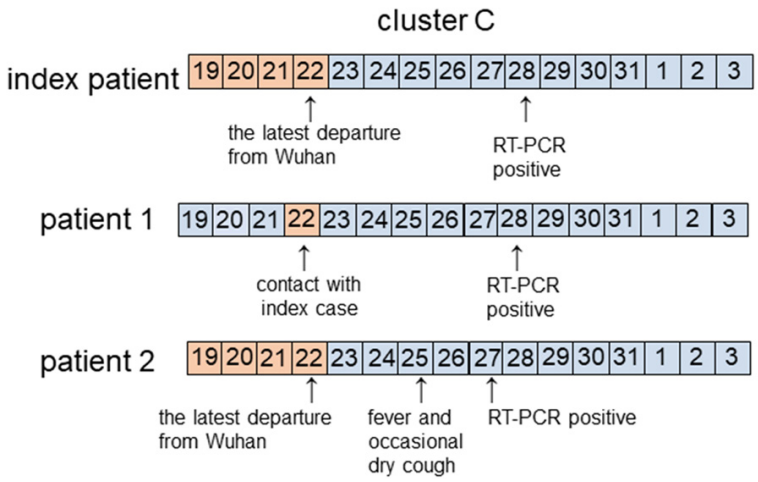

Figure 4. Timeline of Exposure to Index case with Asymptomatic COVID-19 Infection of cluster C in the present study. Boxes filled in red are the dates on which patients traveled in Wuhan or had close contacts with the index case. The blue boxes mean the dates on which patients separated from the index case. The arrows point to the date of symptom onset or the date of RT-PCR Positive.

tient on January 21, 2020, and then developed a fever on January 23, 2020. Patient 2 is a Yangzhou resident living in Wuhan. She took the car back to Yangzhou with the index patient on January 21, 2020, and was under home quarantine after her arrival. She presented with symptoms of fever and cough on January 27, 2020. The laboratory confirmation of SARS-CoV-2-infection is on February 3, 2020. Patient 3 is a Yangzhou resident working in Wuhan. The date of departure with the other three friends from Wuhan was January 21, 2020. The symptom of cough was shown on January 27, 2020, accompanied by tiredness. Timeline of Exposure to Index case with Asymptomatic COVID-19 Infection of the cluster E was shown in **Figure 6**.

Discussion

In China, cases of COVID-19 were initially found in Wuhan, Hubei Province, in December 2019 and January 2020. From the report, the evidence of human-to-human transmission among close contacts has been confirmed since mid-December 2019 [10]. Subsequently, on Jan 2, 2020, and Jan 10, 2020, one family cluster of COVID-19 was found in Wuhan, China [11], and a family of six patients who traveled to Wuhan from Shenzhen [12] respectively. Subsequent studies suggested that cluster transmission of COVID-19 had occurred in China [13] and outside of China [14]. However, to date, the studies that focused on the cluster transmission of COVID-19 are mostly single-center studies, and the large sample multi-center study has not been reported.

The epidemiological characteristics of cluster transmission of COVID-19 from asymptomatic cases in Jiangsu Province have been reported in our study. The main findings from our study are as follows: the persistent cluster transmission was found from January 19, 2020, to March 10, 2020, in Jiangsu Province; among the 70 cluster outbreaks in our study, 5 clusters were transmitted by asymptomatic infected patients; the frequency distribution of disease severity of COVID-19 significantly differed between the two groups according to the characteristics of the index case (P=0.033); cases infected by asymptomatic carrier are mainly asymptomatic infected carriers and mildly infected patients, and cases infected by symptomatic infected persons are the mainly ordinary cases, severe cases, and critical cases.

In our study, the epidemiological characteristics of 70 cluster outbreaks of COVID-19 from 13 cities across Jiangsu Province, China have been reported. According to our research, 49 (15.8%) patients are asymptomatic carriers which is much higher than the results from the previous study [6]. And the number of all the asymptomatic carriers collected from major hospitals in Jiangsu Province is 66, 49 (74.2%) of which distributed among the 70 clusters. This difference suggests that asymptomatic carriers are mainly screened out of clusters, which is similar to the findings in Jinan, China [15]. Our study also demonstrated that the symptoms of patients infected by asymptomatic carriers are usually milder than those infected by symptomatic patients. This reinforces the work of others who have shown that asymptomatic carriers share a lower reproduction potential than symptomatically infected hosts [16]. And, the results from our study confirmed that the infected medical staff tend to be

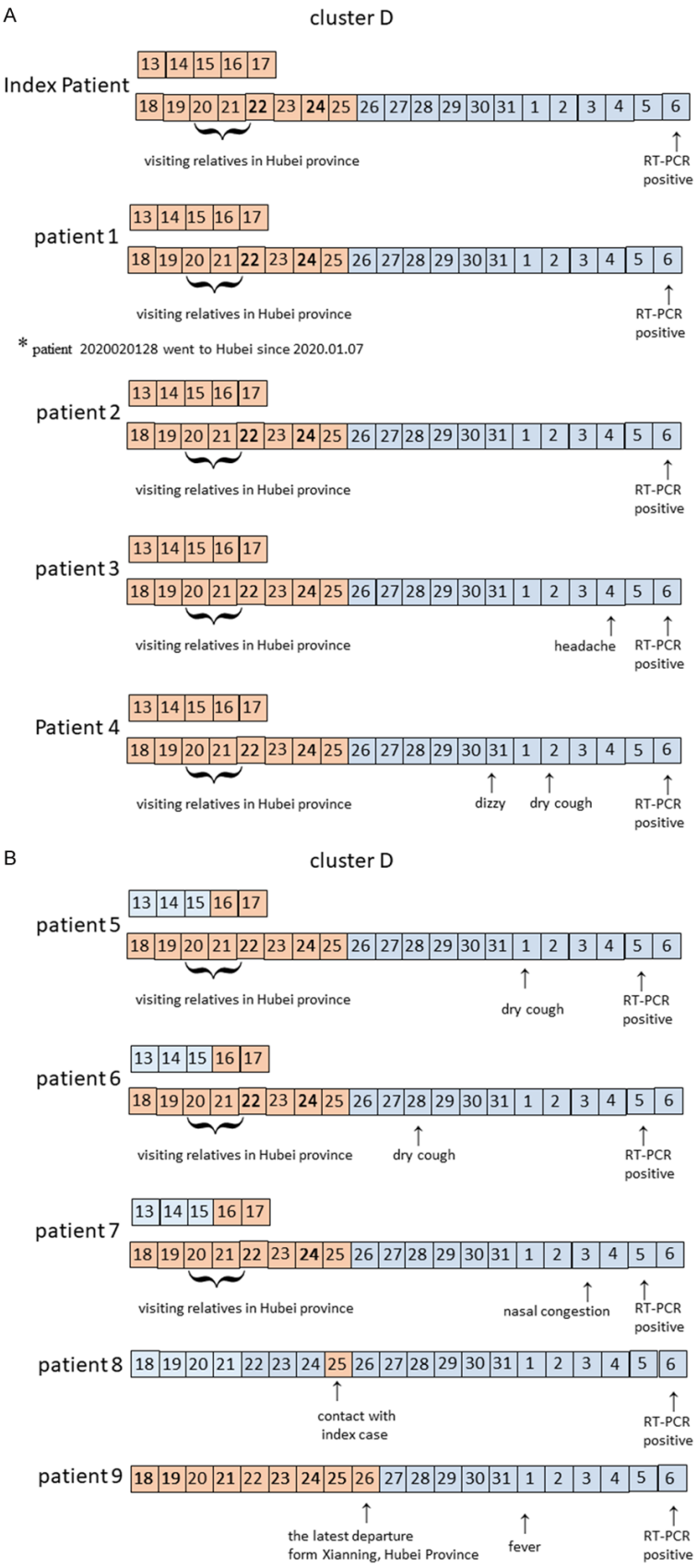

Figure 5. A. Timeline of Exposure to Index case with Asymptomatic COVID-19 Infection of the cluster D in the present study. Boxes filled in red are the dates on which patients traveled in Wuhan or had close contacts with the index case. The blue boxes mean the dates on which patients separated from the index case. The arrows point to the date of symptom onset or the date of RT-PCR Positive. B. Timeline of Exposure to Index case with Asymptomatic COVID-19 Infection of the cluster D in the present study. Boxes filled in red are the dates on which patients traveled in Wuhan or had close contacts with the index case. The blue boxes mean the dates on which patients separated from the index case. The arrows point to the date of symptom onset or the date of RT-PCR Positive.

younger than other infected population and the majority of them are females and the oldest population are patients among which ordinary cases, severe cases, critical cases account for more than that in other groups. The findings of the present study are consistent with cluster transmission of COVID-19 in hospital settings, the reports of infected medical staff (mostly are nurse) and patients in other studies [17]. Therefore, a comprehensive and objective identification strategy of nosocomial infection is necessary to be designed to prevent and control the epidemic effectively.

Our study suffers from some limitations although it is multicenter research. The results are concluded from 13 cities in Jiangsu Province. Thus, our results must be interpreted with some caution when applied in other cities or other countries. Moreover, the data

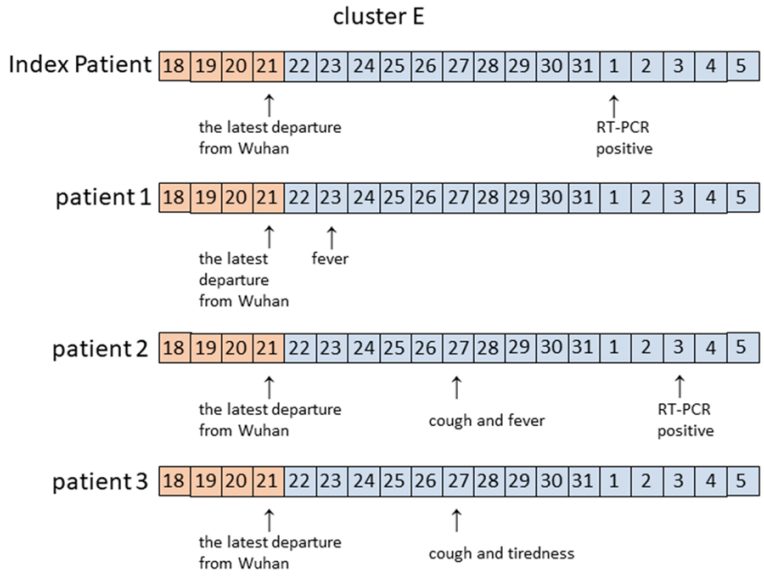

Figure 6. Timeline of Exposure to Index case with Asymptomatic COVID-19 Infection of the cluster E in the present study. Boxes filled in red are the dates on which patients traveled in Wuhan or had close contacts with the index case. The blue boxes mean the dates on which patients separated from the index case. The arrows point to the date of symptom onset or the date of RT-PCR Positive.

collected from the website is incomplete and there are still 2 index patients we could not find despite all of our might. Once these presymptomatic carriers developed any symptoms, we would classify them into the symptomatic group. However, we still could not ensure that all the asymptomatic or presymptomatic carriers will not present any discomfort in the next following days. From the data presented in this investigation, we only enrolled the patients who were involved in clusters and their epidemiological characteristics may be inconsistent with those not in clusters. Therefore, we cannot completely exclude the possibility that these results are biased.

Overall, our study has demonstrated the epidemiological characteristics of cluster transmission of coronavirus disease 2019 (COVID-19) from asymptomatic cases by conducting multicenter research in Jiangsu Province, China. We reveal that cases infected with SARS-CoV-2 by asymptomatic patients would present with milder symptoms in comparison with those infected by symptomatic patients. Medical staff suffering from COVID-19 were observed to be the youngest groups while patients tend to be the oldest infected group and once patients got infected with SARS-CoV-2 they developed more severe syndromes than average ones. As the COVID-19 pandemic challenges the world, here we do our best to show its characteristic more comprehensively.

Conclusion

In this study, we showed the characteristics of cluster transmission among 70 clusters across Jiangsu Province. These findings suggest that we screened the asymptomatic carriers mainly out of clusters and patients infected by symptomatic patients showed more severe symptoms than those infected by asymptomatic patients. We also found that in the infected groups, the medical staff is the youngest one and mainly composed of females. Infected patients tend to be older than other close contacts and most of them were ordinary cases, severe cases, critical cases. The results demonstrate that effective measures should be taken to prevent cluster transmission in hospitals to protect the medical staff and patients.

Acknowledgements

This study was supported by the National Natural Science Foundation of China (No. 81170180, 30400173, 30971257, and 81970302). A project funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions. We would like to acknowledge colleagues for helpful comments.

Disclosure of conflict of interest

None.

Address correspondence to: Dr. Quan Cao, Department of Critical Care Medicine, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, Jiangsu Province, China. Tel: +86-13851992695; E-mail: 2004caoquan@163.com; Dr. Enzhi Jia, Department of Cardiovascular Medicine, The First Affiliated Hospital of Nanjing Medical University, Guangzhou Road 300, Nanjing

210029, Jiangsu Province, China. Tel: +86-13951623205; E-mail: enzhijia@njmu.edu.cn

References

[1] Coronavirus disease (COVID-19) Situation Report. Coronavirus disease (COVID-19) Situation Report - 133 2020.

[2] Yong SEF, Anderson DE, Wei WE, Pang J, Chia WN, Tan CW, Teoh YL, Rajendram P, Toh MPHS, Poh C, Koh VTJ, Lum J, Suhaimi NM, Chia PY, Chen MI, Vasoo S, Ong B, Leo YS, Wang L and Lee VJM. Connecting clusters of COVID-19: an epidemiological and serological investigation. Lancet Infect Dis 2020; 20: 809-815.

[3] Song R, Han B, Song M, Wang L, Conlon CP, Dong T, Tian D, Zhang W, Chen Z, Zhang F, Shi M and Li X. Clinical and epidemiological features of COVID-19 family clusters in Beijing, China. J Infect 2020; 81: e26-e30.

[4] Tong ZD, Tang A, Li KF, Li P, Wang HL, Yi JP, Zhang YL and Yan JB. Potential presymptomatic transmission of SARS-CoV-2, Zhejiang Province, China, 2020. Emerg Infect Dis 2020; 26: 1052-1054.

[5] Zhang J, Tian S, Lou J and Chen Y. Familial cluster of COVID-19 infection from an asymptomatic. Crit Care 2020; 24: 119.

[6] Tian S, Hu N, Lou J, Chen K, Kang X, Xiang Z, Chen H, Wang D, Liu N, Liu D, Chen G, Zhang Y, Li D, Li J, Lian H, Niu S, Zhang L and Zhang J. Characteristics of COVID-19 infection in Beijing. J Infect 2020; 80: 401-406.

[7] Guidance for Corona Virus Disease 2019: Prevention, Control, Diagnosis and Management. Published in People's Medical Publishing House, Beijing, 2020.

[8] Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, Azman AS, Reich NG and Lessler J. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. Ann Intern Med 2020; 172: 577-582.

[9] Sun L, Shen L, Fan J, Gu F, Hu M, An Y, Zhou Q, Fan H and Bi J. Clinical features of patients with coronavirus disease 2019 (COVID-19) from a designated hospital in Beijing, China. J Med Virol 2020; 5: 10.

[10] Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY, Xing X, Xiang N, Wu Y, Li C, Chen Q, Li D, Liu T, Zhao J, Liu M, Tu W, Chen C, Jin L, Yang R, Wang Q, Zhou S, Wang R, Liu H, Luo Y, Liu Y, Shao G, Li H, Tao Z, Yang Y, Deng Z, Liu B, Ma Z, Zhang Y, Shi G, Lam TTY, Wu JT, Gao GF, Cowling BJ, Yang B, Leung GM and Feng Z. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N Engl J Med 2020; 382: 1199-1207.

[11] Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z, Yu T, Xia J, Wei Y, Wu W, Xie X, Yin W, Li H, Liu M, Xiao Y, Gao H, Guo L, Xie J, Wang G, Jiang R, Gao Z, Jin Q, Wang J and Cao B. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; 395: 497-506.

[12] Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, Xing F, Liu J, Yip CC, Poon RW, Tsoi HW, Lo SK, Chan KH, Poon VK, Chan WM, Ip JD, Cai JP, Cheng VC, Chen H, Hui CK and Yuen KY. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020; 395: 514-523.

[13] Cai J, Sun W, Huang J, Gamber M, Wu J and He G. Indirect virus transmission in cluster of COVID-19 cases, Wenzhou, China, 2020. Emerg Infect Dis 2020; 26: 1343-1345.

[14] Pung R, Chiew CJ, Young BE, Chin S, Chen MI, Clapham HE, Cook AR, Maurer-Stroh S, Toh MPHS, Poh C, Low M, Lum J, Koh VTJ, Mak TM, Cui L, Lin RVTP, Heng D, Leo YS, Lye DC and Lee VJM; Singapore 2019 Novel Coronavirus Outbreak Research Team. Investigation of three clusters of COVID-19 in Singapore: implications for surveillance and response measures. Lancet 2020; 395: 1039-1046.

[15] Ma Y, Xu QN, Wang FL, Ma XM, Wang XY, Zhang XG and Zhang ZF. Characteristics of asymptomatic patients with SARS-CoV-2 infection in Jinan, China. Microbes Infect 2020; 22: 212-217.

[16] Chisholm RH, Campbell PT, Wu Y, Tong SYC, McVernon J and Geard N. Implications of asymptomatic carriers for infectious disease transmission and control. R Soc Open Sci 2018; 5: 172341.

[17] Epidemiology Working Group for NCIP Epidemic Response, Chinese Center for Disease Control and Prevention. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. Zhonghua Liu Xing Bing Xue Za Zhi 2020; 41: 145-151.

Table S1. The data source of the cluster transmission of COVID-19 in the present study

Cluster	Data source	Cluster	Data source
1	http://m.cz.bendibao.com/news/47285_7.shtm	36	https://mp.weixin.qq.com/s/Qre3frEzlIOY5L18UXCNSA
2	http://m.cz.bendibao.com/news/47285_7.shtm	37	https://mp.weixin.qq.com/s/eRfZkbt3pjH17zmNKpQlpw
3	http://m.cz.bendibao.com/news/47285_7.shtm	38	http://jiangsu.sina.com.cn/news/general/2020-02-11/detail-iimxyqvz1998527.shtml
4	http://m.cz.bendibao.com/news/47285_7.shtm	39	http://jiangsu.sina.com.cn/news/general/2020-02-11/detail-iimxyqvz1998527.shtml
5	http://m.cz.bendibao.com/news/47285_7.shtm	40	http://m.nt.bendibao.com/live/41116.shtm
6	http://m.nt.bendibao.com/live/41110.shtm	41	http://m.zj.bendibao.com/cyfw/1387.shtm
7	http://m.nt.bendibao.com/live/41110.shtm	42	http://m.nt.bendibao.com/live/41116.shtm
8	http://m.ha.bendibao.com/news/1562.shtm	43	http://m.suzhou.bendibao.com/news/72018.shtm
9	http://m.xz.bendibao.com/news/44242.shtm	44	http://m.suzhou.bendibao.com/news/72018.shtm
10	http://m.ha.bendibao.com/news/1562.shtm	45	http://m.suzhou.bendibao.com/news/72018.shtm
11	http://m.taizhou.bendibao.com/news/1716.shtm	46	http://m.suzhou.bendibao.com/news/72018.shtm
12	http://m.taizhou.bendibao.com/news/1716.shtm	47	http://m.suzhou.bendibao.com/news/72018.shtm
13	http://m.taizhou.bendibao.com/news/1716.shtm	48	http://m.suzhou.bendibao.com/news/72018.shtm
14	http://nj.bendibao.com/news/2020210/79448.shtm	49	http://m.taizhou.bendibao.com/news/1716.shtm
15	http://www.lyg.gov.cn/zglygzfmhwz/zxtg2020/content/228ee20c-48a2-408f-bb13-36b255f3b252.html	50	http://m.taizhou.bendibao.com/news/1716.shtm
16	http://nj.bendibao.com/news/2020210/79448.shtm	51	http://m.wx.bendibao.com/news/46509.shtm
17	http://nj.bendibao.com/news/2020210/79448.shtm	52	http://m.wx.bendibao.com/news/46509.shtm
18	https://mp.weixin.qq.com/s/oeyPSZYc5rHR68dQOeM82w	53	http://m.wx.bendibao.com/news/46509.shtm
19	https://mp.weixin.qq.com/s/n5rfbi-RoI7s91_ltvNikA https://mp.weixin.qq.com/s/kfx4YyrHyLywdBfUEEYHEw	54	http://m.wx.bendibao.com/news/46509.shtm
20	https://mp.weixin.qq.com/s/-87DQ2B-CG8TTaRv5DjJKQ	55	http://m.zj.bendibao.com/cyfw/1387.shtm
21	http://js.people.com.cn/n2/2020/0206/c360303-33770563.html	56	http://m.wx.bendibao.com/news/46509.shtm
22	https://mp.weixin.qq.com/s/oeyPSZYc5rHR68dQOeM82w	57	http://m.wx.bendibao.com/news/46509.shtm
23	https://mp.weixin.qq.com/s/-iOtgUO6nAlzI0fY95Rihw	58	http://m.xz.bendibao.com/news/44242.shtm
24	https://mp.weixin.qq.com/s/6I4i8gve7u8DosuIPwptmQ	59	http://m.xz.bendibao.com/news/44242.shtm
25	https://mp.weixin.qq.com/s/gxlkNp--m-u-97I3Kd0fPg	60	http://m.zj.bendibao.com/cyfw/1387.shtm
26	https://mp.weixin.qq.com/s/lwbnXZQhFbYQ64PnuLQzCA	61	http://m.yancheng.bendibao.com/live/1987.shtm
27	https://mp.weixin.qq.com/s/lwbnXZQhFbYQ64PnuLQzCA	62	http://m.yancheng.bendibao.com/live/1987.shtm
28	https://mp.weixin.qq.com/s/gxlkNp--m-u-97I3Kd0fPg	63	http://m.yancheng.bendibao.com/live/1987.shtm
29	https://mp.weixin.qq.com/s/uk_fWtAAW24F9iHiAqHwuQ	64	http://m.yancheng.bendibao.com/live/1987.shtm
30	https://mp.weixin.qq.com/s/eRfZkbt3pjH17zmNKpQlpw https://mp.weixin.qq.com/s/Qre3frEzlIOY5L18UXCNSA	65	http://js.people.com.cn/n2/2020/0131/c360306-33752486.html
31	https://mp.weixin.qq.com/s/uk_fWtAAW24F9iHiAqHwuQ	66	http://www.yc123.com/thread-714751-1-1.htm
32	https://mp.weixin.qq.com/s/5zu8xv_LqpR_zRDkIJ5XDQ	67	http://m.yz.bendibao.com/mip/5685.shtm
33	https://mp.weixin.qq.com/s/eP3Wwfq4U8hVfRJMYtiMlQ	68	http://m.yz.bendibao.com/mip/5685.shtm
34	https://mp.weixin.qq.com/s/eP3Wwfq4U8hVfRJMYtiMlQ	69	http://m.yz.bendibao.com/mip/5685.shtm
35	https://mp.weixin.qq.com/s/eP3Wwfq4U8hVfRJMYtiMlQ	70	http://m.yz.bendibao.com/mip/5685.shtm

Table S2. The data source of the medical records where cluster transmission of COVID-19 was found in the present study

Cluster	Data source	Cluster	Data source
1	Department of Critical Care Medicine, Changzhou Third People's Hospital, Changzhou 213001, Jiangsu Province, China.	36	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.
2	Department of Critical Care Medicine, Changzhou Third People's Hospital, Changzhou 213001, Jiangsu Province, China.	37	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.
3	Department of Critical Care Medicine, Changzhou Third People's Hospital, Changzhou 213001, Jiangsu Province, China.	38	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.
4	Department of Critical Care Medicine, Changzhou Third People's Hospital, Changzhou 213001, Jiangsu Province, China.	39	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.
5	Department of Critical Care Medicine, Changzhou Third People's Hospital, Changzhou 213001, Jiangsu Province, China.	40	Department of Critical Care Medicine, the Third People's Hospital of Nantong City, Affiliated to Nantong University, Nantong 226006, Jiangsu Province, China.
6	Department of Critical Care Medicine, Haimen People's Hospital, Haimen 226100, Jiangsu Province, China. Department of Critical Care Medicine, The Third People's Hospital of Nantong City, Affiliated to Nantong University, Nantong 226006, Jiangsu Province, China.	41	Department of Critical Care Medicine, The Third People's Hospital of Zhenjiang, Zhenjiang 212003, Jiangsu Province, China.
7	Department of Critical Care Medicine, Haimen People's Hospital, Haimen 226100, Jiangsu Province, China.	42	Department of Critical Care Medicine, the Third People's Hospital of Nantong City, Affiliated to Nantong University, Nantong 226006, Jiangsu Province, China.
8	Department of Critical Care Medicine, Huai'an No. 4 People's Hospital, Huai'an 223300, Jiangsu Province, China.	43	Department of Critical Care Medicine, Suzhou No. 5 People's Hospital of Soochow University, Suzhou 215000, Jiangsu Province, China.
9	Department of Critical Care Medicine, Xuzhou Infectious Disease Hospital, Xuzhou 221004, Jiangsu Province, China.	44	Department of Critical Care Medicine, Suzhou No. 5 People's Hospital of Soochow University, Suzhou 215000, Jiangsu Province, China.
10	Department of Critical Care Medicine, Huai'an No. 4 People's Hospital, Huai'an 223300, Jiangsu Province, China.	45	Department of Critical Care Medicine, Suzhou No 5 People's Hospital of Soochow University, Suzhou 215000, Jiangsu Province, China.
11	Department of Critical Care Medicine, Jingjiang People's Hospital, Jingjiang 214500, Jiangsu Province, China.	46	Department of Critical Care Medicine, Suzhou No. 5 People's Hospital of Soochow University, Suzhou 215000, Jiangsu Province, China.
12	Department of Critical Care Medicine, Jingjiang People's Hospital, Jingjiang 214500, Jiangsu Province, China.	47	Department of Critical Care Medicine, Suzhou No. 5 People's Hospital of Soochow University, Suzhou 215000, Jiangsu Province, China.
13	Department of Critical Care Medicine, Jingjiang people's Hospital, Jingjiang 214500, Jiangsu Province, China.	48	Department of Critical Care Medicine, Suzhou No. 5 People's Hospital of Soochow University, Suzhou 215000, Jiangsu Province, China.
14	Department of Critical Care Medicine, The Fourth People's Hospital of Lianyungang, Lianyungang 222000, Jiangsu Province, China. Department of Critical Care Medicine, Lianyungang First People's Hospital, Lianyungang 222002, Jiangsu Province, China.	49	Department of Critical Care Medicine, Taixing People's Hospital, Taixing 225400, Jiangsu Province, China.
15	Department of Critical Care Medicine, The Fourth People's Hospital of Lianyungang, Lianyungang 222000, Jiangsu Province, China. Department of Critical Care Medicine, Lianyungang First People's Hospital, Lianyungang 222002, Jiangsu Province, China.	50	Department of Critical Care Medicine, Taizhou Second People's Hospital, Taizhou 223002, Jiangsu Province, China.
16	Department of Critical Care Medicine, The Fourth People's Hospital of Lianyungang, Lianyungang 222000, Jiangsu Province, China. Department of Critical Care Medicine, Lianyungang First People's Hospital, Lianyungang 222002, Jiangsu Province, China.	51	Department of Critical Care Medicine, Wuxi No. 5 People's Hospital, Wuxi 475004, Jiangsu Province, China.
17	Department of Critical Care Medicine, Lianyungang First People's Hospital, Lianyungang 222002, Jiangsu Province, China.	52	Department of Critical Care Medicine, Wuxi No. 5 People's Hospital, Wuxi 475004, Jiangsu Province, China.
18	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	53	Department of Critical Care Medicine, Wuxi No. 5 People's Hospital, Wuxi 475004, Jiangsu Province, China.

19	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	54	Department of Critical Care Medicine, Wuxi No. 5 People's Hospital, Wuxi 475004, Jiangsu Province, China.
20	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	55	Department of Critical Care Medicine, The Third People's Hospital of Zhenjiang, Zhenjiang 212003, Jiangsu Province, China.
21	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	56	Department of Critical Care Medicine, Wuxi No. 5 People's Hospital, Wuxi 475004, Jiangsu Province, China.
22	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	57	Department of Critical Care Medicine, Wuxi No. 5 People's Hospital, Wuxi 475004, Jiangsu Province, China.
23	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	58	Department of Critical Care Medicine, Xuzhou Infectious Disease Hospital, Xuzhou 221004, Jiangsu Province, China. Department of Critical Care Medicine, the Affiliated Hospital of Xuzhou Medical University, Xuzhou 221006, Jiangsu Province, China.
24	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	59	Department of Critical Care Medicine, Xuzhou Infectious Disease Hospital, Xuzhou 221004, Jiangsu Province, China. Department of Critical Care Medicine, the Affiliated Hospital of Xuzhou Medical University, Xuzhou 221006, Jiangsu Province, China.
25	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	60	Department of Critical Care Medicine, The Third People's Hospital of Zhenjiang, Zhenjiang 212003, Jiangsu Province, China.
26	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	61	Department of Critical Care Medicine, Yancheng Second People's Hospital, Yancheng 224003, Jiangsu Province, China.
27	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	62	Department of Critical Care Medicine, Yancheng Second People's Hospital, Yancheng 224003, Jiangsu Province, China.
28	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	63	Department of Critical Care Medicine, Yancheng Second People's Hospital, Yancheng 224003, Jiangsu Province, China.
29	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	64	Department of Critical Care Medicine, Yancheng Third People's Hospital, Yancheng 224001, Jiangsu Province, China.
30	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	65	Department of Critical Care Medicine, Yancheng First People's Hospital, Yancheng 224006, Jiangsu Province, China.
31	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	66	Department of Critical Care Medicine, Yancheng First People's Hospital, Yancheng 224006, Jiangsu Province, China.
32	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	67	Department of Critical Care Medicine, Yancheng First People's Hospital, Yancheng 224006, Jiangsu Province, China.
33	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	68	Department of Critical Care Medicine, Yangzhou Third People's Hospital, Yangzhou 225001, Jiangsu Province, China.
34	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	69	Department of Critical Care Medicine, Yangzhou Third People's Hospital, Yangzhou 225001, Jiangsu Province, China.
35	Department of Critical Care Medicine, Nanjing No. 2 Hospital, Nanjing 210003, Jiangsu Province, China.	70	Department of Critical Care Medicine, Yangzhou Third People's Hospital, Yangzhou 225001, Jiangsu Province, China.