

Clinical features and short-term outcomes of patients with **COVID-19 due to different exposure** history

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Abstract

An ongoing outbreak of Coronavirus Disease 2019 (COVID-19) has spread around the world. However, the clinical characteristics and outcomes of patients with COVID-19 related to different modes of exposure have not been well defined. We aimed to explore the clinical features and outcomes of COVID-19 related to one-time community exposure versus continuous household exposure.

Retrospective case–control study involving COVID-19 patients admitted to a tertiary designated center in China was performed. Patients were enrolled if they had known exposure history of one-time community exposure or continuous household exposure. Twenty patients were compared in terms of demographic characteristics, clinical presentation, chest CT images, laboratory results, treatments, and clinical outcomes at 1-month follow-up.

There were 10 patients in one-time community and continuous household exposure groups respectively. Males compromised 80% and 40% while the median ages were 37.5 and 51 years old in the 2 groups, respectively. Fever and cough were most common symptoms. Ground-glass opacities were presented on chest CT scan in 90% and 70% of the patients, and the median CT scores were 7 and 16 on admission, respectively. Three patients ranked severe in the community exposure group while 7 patients were severe or critical in household exposure group. On 1-month follow-up, all patients were improved clinically but COVID-19 IgG antibody detected positive. Median follow-up CT scores were 0 and 13 while pulmonary function test abnormalities were 0/9 and 2/7 in the 2 groups, respectively.

COVID-19 patients with one-time community exposure tended to be mild in severity and had better outcomes, comparing to those with continuous household exposure.

Abbreviations: ALT = almandine aminotransferase, AST = aspartate aminotransferase, COVID-19 = Coronavirus Disease 2019, GGO = ground-glass opacities, IQR = interquartile ranges, MERS = Middle East respiratory syndrome, RT-PCR = reverse transcription-polymerase chain-reaction, SARS = severe acute respiratory syndrome.

Keywords: clinical feature, Coronavirus Disease 2019 (COVID-19), exposure history, outcome, transmission

1. Introduction

In December 2019, a cluster of pneumonia cases of unknown etiology were initially reported in Wuhan, China and rapidly spread to the whole country.^[1] On February 2020, the World Health Organization (WHO) officially named this novel coronavirus pneumonia as Coronavirus Disease 2019

(COVID-19), whereas the virus has been named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). On March 11, 2020, the World Health Organization declared a pandemic in the world. As of June 6, 2020, there were 6,721,528 confirmed cases of COVID-19, with a mortality rate of almost 6%.^[2]

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The Ethics Committee of The First Affiliation Hospital of University of Science and Technology (Anhui Provincial Hospital) approved the collection of clinical data from the included patients with COVID-19 infections (No. 2020-XG (H)-007). Written informed consent was obtained from all the patients. To protect privacy of participants, all private information was kept anonymous. The results will be published in a peer-reviewed journal and will be disseminated electronically and in print regardless of results.

The authors do not have any financial or personal relationships with people or organizations that may have inappropriately influenced their work in the present article. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Huang et al first reported 41 patients of COVID-19 in which most patients had a history of exposure to Huanan Seafood Wholesale Market.^[3] The clinical manifestations included fever, nonproductive cough, dyspnea, normal or decreased leukocyte counts, and radiographic evidence of pneumonia. Organ dysfunction and death can occur in severe cases. Subsequently, Wang et al reported findings from 138 cases of COVID-19 from another hospital in Wuhan and the results suggested that the 2019-nCoV infection clustered within groups of humans in close contact. As with other coronavirus pneumonia SARS in 2003 and Middle East respiratory syndrome (MERS) in 2012, COVID-19 has been noted in family and hospital settings.^[4-7] In general, these 3 coronaviruses had similar high transmission index and presented differing mortality between 6% in COVID-19 and 30% in MERS. A recent Japanese study demonstrated almost 3/4 of 112 cases from the cruise ship "Diamond Princess" with COVID-19 were asymptomatic or mildly symptomatic.^[8] Better understanding of the pathogenesis of patients infected in different clinical settings can be important in managing patients optimally and controlling this ongoing pandemic. However, potential differences in clinical characteristics of COVID-19 patients caused by differing modes of exposure have not been well defined. The objective of our study was to summarize the characteristics and outcomes of patients with COVID-19 caused by one-time community exposure and continuous household exposure to SARS-COV2.

2. Methods

2.1. Study design

This was a single center, retrospective case–control study. All patients enrolled in this study were diagnosed according to World Health Organization interim guidance and the diagnosis of patients infected with COVID-19 was based on clinical features, imaging characteristics, and the presence of SARS-CoV-2 detected in specimens from the respiratory tract of the patients. The patients were all hospitalized at The First Affiliation Hospital of University of Science and Technology (Anhui Provincial Hospital) from January 22, 2020 to March 7, 2020. Researchers also directly communicated with patients or their families to ascertain exposure history. Outcomes were also compared between patients with continuous household exposure and those with one-time community exposure. The rerolling criteria was a clear history of single community exposure or continuous household exposures.

The Ethics Committee of The First Affiliation Hospital of University of Science and Technology (Anhui Provincial Hospital) approved the collection of clinical data from the included patients with COVID-19 infections. Written informed consent was obtained from each of the patients.

2.2. Data collection

Data were obtained with standardized data collection forms shared by the International Severe Acute Respiratory and Emerging Infection Consortium data collection forms from electronic medical records. Information recorded included demographic data, medical history, exposure history, underlying comorbidities, symptoms, signs, laboratory findings, chest computed tomographic (CT) scans, and treatment measures (i.e., antiviral therapy, corticosteroid therapy, Chinese traditional medicine therapy, respiratory support). Onset symptoms, laboratory values, chest CT scan, and treatment measures during the hospital stay were collected. The data of chest CT scan, coronavirus nucleic acid detection were collected 2 weeks and 1 month after discharge. Pulmonary function test was performed 1 month after discharge. All CT scores were AI assessed and blindly reassessed by a 20-year' experienced expert (Dr WW) according to the published method.^[8] In general, each lung was divided into 3 zones; each zone was evaluated for percentage of lung involvement on a scale of 0 to 4. Overall CT scores were the summation of scores from all 6 lung zones. The radiologist was blinded to the exposure history and clinical information on this cohort. A special follow-up team including physician (Dr XH) and several experienced nurses had multiple interviews with every patient by telephone. Pulmonary function tests were performed according to the ATS guidelines by a designated physician (Dr XC).

2.3. Statistical analysis

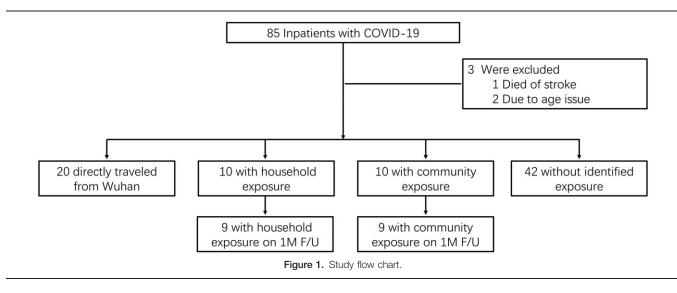
All the data were analyzed by Statistical Package for the Social Science Ver. 16.0 (SPSS, Inc, Chicago, IL) statistically. Categorical variables were summarized using frequencies and percentages, and continuous data were presented as the medians (interquartile ranges [IQRs]). The Mann–Whitney *U* test was used for continuous variables, and the χ^2 test or Fisher's exact test was used for categorical variables. All *P* values less than .05 were statistically significant. The analyses have not been adjusted for multiple comparisons and, given the potential for type I error, the findings should be interpreted as exploratory and descriptive.

3. Results

3.1. Presenting characteristics

Among the 85 hospitalized patients, 65 excluded as follows: a 4year-old child and a 93-year-old man were excluded due to age issue, a 55-year-old man died of fatal stroke within 24 hours on admission. The other 62 patients did not meet with the enrollment criteria: 20 patients had a directly travel in Wuhan and 42 patients had unidentifiable exposure history (Fig. 1). Finally, 10 patients with COVID-19 caused by one-time exposure to SARS-COV2 and 10 patients who had continuous household exposure were enrolled (Table 1). In the 10 patients with the onetime community exposure, 2 cases changed trains at Wuhan Railway Station for about 3 hours and the remaining 8 had participated in a group party (patient 1-4 with their classmate, an index patient), eating together or chatting face to face with patients in incubation period. The time was less than 5 hours in indoor spaces. All 10 patients in the household exposure group had continuous intimate contact with their family members who were identified with COVID-19 infection; 5 of these patients slept in the same bed with their spouses and the remaining lived together in a house.

The median age of COVID-19 patients caused by one-time community exposure to SARS-COV2 was younger (median, 37.5 years) than that of patients caused by continuous household exposure (median, 51 years) (P=.029). The most common onset symptom of 2 groups was fever (80% vs 80%). Other symptoms were cough, fatigue, and dyspnea. All 20 patients were hospitalized with no difference in duration of hospitalization between the 2 groups (20.5 days vs 18.0 days) (P=.315). There were alternately 3 and 4 patients, respectively, with underlying comorbidities



including essential hypertension in 1 and 3 patients, and diabetes in 1 and 2 patients.

In the community exposure group, most cases were mild (30%) and moderate (40%) in disease severity, while in the continuous household exposure group, more severe (50%) and critical cases (20%) were observed.

3.2. Laboratory examinations and chest CT

Between 2 groups, there were no significant differences of the numbers of white cell count, neutrophil count, lymphocyte count, procalcitonin, almandine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase, bilirubin, lactate dehydrogenase, creatine kinase, myoglobin, interleukin 6. Each group had patients with normal chest CT who were diagnosed by positive results of the nucleic acid of the coronavirus and close contact with the known COVID-19 patients.

The most common manifestation of chest CT of 2 groups was ground-glass opacities (90% vs 70%) and the median scores of CT were 7 and 16 retrospectively (Table 2). In most patients of our study, the distribution of disease was predominantly peripheral (subpleural) on the initial chest CT. As the disease advanced, follow-up CT images gradually presented more diffuse lung lesions (Figs. 2 and 3).

3.3. Treatment process and prognosis

All patients received antiviral drugs including lopinavir–ritonavir in 20 patients and α -interferon in 10 patients. Corticosteroids were prescribed in 8 patients including 6 patients in the household exposure group. In addition, tocilizumab, an anti-IL-6 receptor antibody, was used by 3 patients in each group. In total, 6 patients received traditional Chinese medicine therapies and no patients underwent mechanical ventilation. In the community exposure group, 2 patients received high-flow oxygen therapy along with 4 patients who needed supplemental oxygen therapy. In the household exposure group, 7 patients needed oxygen therapy including 4 who used high-flow oxygen therapy. The duration of viral shedding was 15 days and 13.5 days, respectively. All patients improved clinically and discharged within 5 weeks of symptom onset except for patient 14 who needed a continuing oxygen therapy.

3.4. Outcomes

We followed up 18 patients at 2 weeks and 1-month after hospital discharge; others were examined at local designated hospital. One month after discharge, 7 patients had almost normal chest CT and the CT scores of the other patients were significantly improved compared with those during hospitalization in the community exposure group. Although 3 patients had almost normal follow-up chest CT, the median CT scores were still high as 13 in the household exposure group. On 1-month follow-up visit, restrictive pulmonary function abnormalities were detected in 2 of 7 patients in household exposure group and all 9 patients were normal in community exposure group. 6-Minutes walk distances were 518 m and 455 m, respectively.

Overall, there were 4 patients who tested positive for SARS-CoV-2 nucleic acid (20%) 1-month after discharge without new symptoms and abnormalities in CT images. Patient 20 was detected to be positive of coronavirus nucleic acid by reverse transcription-polymerase chain-reaction (RT-PCR) on 32 days after discharge. The other 3 patients were detected positive at 2 weeks after discharge. On 1-month follow-up, 17 patients were detected to have circulating antibody to SARS-CoV-2, including 100% positive for IgG antibody and 53% positive for IgM antibody.

4. Discussion

This report, to our knowledge, is the first study to compare clinical characteristics and outcomes of patients with COVID-19 caused by one-time community exposure versus continuous household exposure to SARS-COV2. The median age of patients in community group was 37.5 years old, significantly younger than 51 years old in household group. Four patients received oxygen therapy in community exposure group while 7 patients needed oxygen therapy in household exposure group. At 1-month follow-up after discharge, both pulmonary function results and chest CT scores in household exposure group. Our results suggested the time length of exposure might be associated with the severity of patients with COVID-19 and the subsequent outcomes.

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Table 1

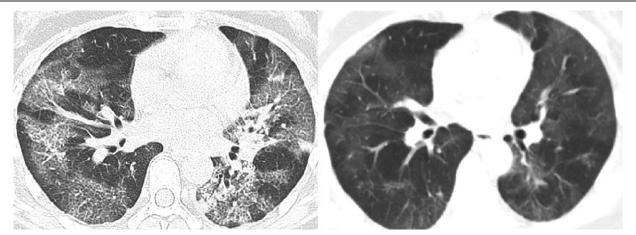


Figure 2. Chest CT images of patient 14 with COVID-19 caused by household exposure of her husband patient 9. (A) Chest CT images on day 6 after symptom onset showed the bilateral GGOs with mixed linear opacities. (B) Chest CT images showed the improvement in bilateral GGOs at 1-mo follow-up after discharge.

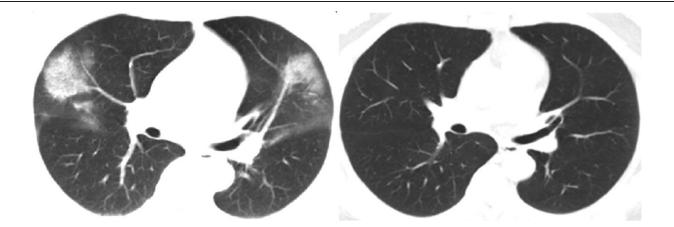


Figure 3. Chest CT images of patient 9 with COVID-19 caused by one-time community exposure. (A) Chest CT images showed the bilateral GGOs on day 12 after symptom onset. (B) Chest CT images showed the near-complete resolution of bilateral GGOs at 1-mo follow-up after discharge.

Table 2

Clinical features of patients with COVID-19 in community versus household exposure groups.

	Community group	Household group	Р
Male percentage	80% (8/10)	40% (4/10)	.17
Age (median, yr)	37.5	51	.029#
Severe percentage	30% (3/10)	70% (7/10) [*]	.179
Hospitalized time (median, d)	20.5	18	.315
WBC counts (median, 10 ⁹ /L)	5.37	4.84	.341
Lymphocyte counts (median, 109/L)	1.57	1.05	.085
CT scores on admission	7	16	.052
Oxygen therapy	4	7	.37
Corticosteroid use	2	6	.17
Liponavir-ritonavir use	10	10	
Alpha-interferon use	2	7	.07
CT scores on 1-mo follow-up	0	13	.023#
Pulmonary function abnormality	0/9	2/7 [†]	.471

CT = computed tomography.

* Including 2 critical patients.

⁺3 due to reactive infection.

[#] P < .05.

COVID-19 is caused by infection with severe acute coronavirus 2 (SARS-CoV-2).^[1] Although in the early January 2020, public reports showed that human-to-human transmission was limited or nonexistent, subsequent studies confirmed that such transmission did occur.^[9] Like other 2 kinds of coronavirus in SARS and MERS, person-to-person transmission of SARS-CoV-2 has been demonstrated in the household and healthcare settings.^[10–13] Moreover, rapid cluster transmission of pathogens has been shown in confined spaces as well as plane and cruise ship.^[14,15] A recent Japanese study demonstrated more than 40% of 1723 passengers in the cruise ship "Diamond Princess" to be positive carriers of SARS-CoV-2 after 2 weeks quarantine.^[16]

The transmission of SARS-CoV-2 in humans is thought to be via at least 3 sources: inhalation of liquid droplets produced by infected persons, close contact with infected persons, and contact with surfaces contaminated with SARS-CoV-2. The viral loads in throat swab and sputum samples peak at around 5 to 6 days after symptom onset while stool samples remain positive longer as shown on RT-PCR analysis.^[17] Data showed the SARS-CoV-2 could exist in some kinds of surfaces, even up to 48 hours on stainless steel.^[18]

In our study, the severity of COVID-19 caused by one-time community exposure was rather mild. The reason might be that the exposure quantities and length of airborne SARS-CoV-2 were rather low in social situation. On the contrast, family members might be continuously exposed to multiple sources and high burden of the virus. Therefore, the burden of exposure in household setting would be more severe, as shown in this study.

Fever, cough, and dyspnea were common symptoms of COVID-19 in this cohort as described in previous studies.^[3,19] Although fever duration was longer in patients due to household exposure history, there was no significant difference between the 2 groups. Therefore, it is important to distinguish from the common pneumonia. Some patients might contract influenza in the winter season. Peripheral lymphocytes counts were found to be decreased and significantly consistent with the inflammation status in COVID-19 patients.^[20] In this limited case series, the lymphocyte counts still decreased even in household exposure patients. This might be associated with viral production and secondary inflammatory storm by key cytokines of IL-6. Increasing IL-6 levels were recently reported to be associated with the severity of COVID-19 and poor prognosis.^[21,22] Due to limited cases, there was no significant increasing of IL-6 level on admission among these 2 groups.

As recent study on a cruise ship "Diamond Princess" showed some patients in this cohort did not present any symptoms such as cough and fever, but multiple peripheral ground-glass opacities (GGO) could be found on CT images.^[16] Chest CT has a high sensitivity for diagnosis of COVID-19 and be considered as a helpful tool for detection in epidemic areas. A study including more than one thousand suspected patients with COVID-19 in China showed almost 90% had positive chest CT scans on contrast to 60% positivity of RT-PCR method.^[23] When evaluated on confirmed patients with COVID-19, the dynamic changes in CT scans demonstrated the features at different stages.^[24] The predominant pattern of abnormalities was GGOs, associated with interlobular septal thickening and/or with consolidation at different times of disease evolution. Furthermore, CT scores and number of lung zone involved could be a good tool to indicate the temporal change of disease and guide the management.^[8] There were significant high CT scores in the household exposure group than those in community exposure group from hospital stay to 1-month follow-up. These were consistent with the clinical severity and the temporal evolution of inflammation with COVID-19.

According to a largest report of 44,415cases from the Chinese Center for Disease Control and Prevention, spectrum of disease was mild 81%, severe 14%, and critical 5%.^[10] In Italy, the severe and critical patients were accounted for 30% of 22,512 cases in a March data.^[25] Our results showed that 30% cases were severe in the community exposure group, which was consistent with the reported data. On contrast, 70% of patients in the household exposure group were severe or critical condition, which was significantly higher than national report and Italy data.^[10,25] This would be explained by longer exposure time in a confined space with high load of virus and recurrent contact with patients at incubation period. On the other hand, older people tend to stay at home and resulted in more exposure quantities to virus. Furthermore, older patients were more likely to have comorbid conditions such as hypertension and diabetes. These factors contributed to the higher percentage of severe cases in the household exposure group, we believe.^[10,26] In a retrospective study, multivariable regression showed increasing odds of inhospital death were associated with older age (odds ratio 1.10) among 191 patients in 2 designated hospital in Wuhan.^[27] While younger adults would like to go outside as well as join a party with friends, it might be associated with short exposure time with patients with COVID-19 and rather mild disorder.

The exposure style and relationship with the contagious patients with COVID-19 could also affect the severity of the disease. In the community exposure group, 5 of 7 patients (patients 1-5) who were infected in a party or a dinner at hotels presented as mild or moderate A 48-years patient was infected simply in a chat with a patient with COVID-19 about 30 minutes, and patient 8 was infected during a short transfer at the Wuhan station. In the household setting, 2 of 3 mild or moderate cases were infected by her cousin or brother in a same house. However, 4 of 7 severe or critical patients were infected by their spouses. Obviously, eating in a house in the daytime and sleeping on a same bed at night largely increased the exposure duration to spouses who carried SARS-CoV-2. Previous study on family clusters with MERS also demonstrated there was a high risk (RR 4.1, 95% CI 1.5–11.2) associated with sleeping in a room with index patient.^[28] Those results suggested that living with family members carried SARS-CoV-2 in the household settings together for more time led to a higher risk of infection of COVID-19 and potentially severe conditions.

In this study, all patients improved clinically, and the median hospitalization time was 2 weeks. Despite different severities, there were no significant differences in the duration of SARS-CoV-2 PCR positivity and hospitalization time between the 2 groups. After discharge, clinical symptoms and CT images abnormalities were improved among most patients. Pulmonary function test results were consistent with the improvement of CT abnormalities. Comparing with the follow-up studies of SARS, the pulmonary function and CT images improved more and faster in this cohort.^[29]

There are several limitations in this study. First, because of the retrospective nature, recall bias could not be avoided completely. Second, the number of study subjects was rather limited in both groups. Third, our hospital was one of the 4 designated tertiary centers in Anhui Province. Not all patients were followed up in our follow-up clinic after discharge. Despite these limitations, the strengths of this study are notable. We evaluated symptoms, blood tests, CT scan examinations, and pulmonary function tests in 18 participants after discharged and had access to multiple chest CT images in all 20 patients both in hospitalized time and follow-up period. Our special team also had multiple interviews by telephone with all patients and contacted the physicians at the local hospital every 2 weeks. Thus, longitudinal studies on a larger cohort would be helpful to understand the transmission, pathogenesis, and clinical features of this ongoing pandemic disease in different exposure history in different settings.

5. Conclusions

COVID-19 patients with one-time community exposure tended to be mild in severity and had better outcomes, comparing to those with continuous household exposure. Further studies with large number of patients were recommended to confirm the difference in human to human transmission in various setting and exposure history and explore the underlying mechanisms.

Acknowledgments

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Author contributions

Xianmeng Chen and Xiaowen Hu conceived the idea, designed, and supervised the study, drafted the manuscript, and had full access to all the data and took responsibility for the integrity of the data. Jie Cao analyzed data and performed statistical analysis. All the authors reviewed and approved the final version of the manuscript.

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