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Original Article

Epidemiologic characteristics and differential management strategies of seven case series with COVID-19 outbreaks caused by asymptomatic carriers from June 2020 to May 2021 in China

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Abstract: With the COVID-19 epidemic quickly under control in China in the early stage of 2020, global cooperation/communications may pose great challenges to epidemic control and prevention in the country. Large-scale spread by asymptomatic carriers was a concern. We obtained data on new cluster outbreak regions with COVID-19 caused by asymptomatic carriers from June 2020 to May 2021 in China, and reported the epidemiological characteristics, the possible routes of viral transmission and infection, and different control strategies. These results show the importance of regular screening for high-risk populations and differential management strategies for epidemic control, which provide an objective basis for suppressing the spread of the SARS-CoV-2 virus. These experiences can be used as a reference to minimize the subsequent spread of virus mutants in various places.

Keywords: COVID-19 disease, asymptomatic carrier, severe acute respiratory syndrome coronavirus 2, scientific protective strategy

Introduction

Since December 2019, a new type of coronavirus pneumonia (coronavirus disease 2019, COVID-19) has developed into a global epidemic, which was declared a pandemic by the World Health Organization (WHO) on March 11, 2020. By the end of January 2021, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the new coronavirus behind the disease COVID-19, had infected over 100 million people around the world and caused about more than 2 million deaths. Facing the biggest global pandemic COVID-19 of this century, the governments and scientific community in various countries have been working hard to uncover the public health strategy for effective solutions [1-5].

It is well-known there are typically three transmission routes of infectious respiratory viruses, including droplet-borne route transmitted by appropriate droplets [6], suitable fomite route through contacts with contaminated object surface [7, 8], and airborne route through aerosols that can remain suspended over a longer time [9, 10]. The transmission of SARS-CoV-2 through fomite and droplet-borne routes used to be considered as the main pathways, but more recent studies have revealed the possibility of airborne transmission [11-19], particularly in crowded and inadequately ventilated indoor

spaces [20-22]. Fennelly [23] measured particle size distribution of infectious aerosols and observed that pathogens were more commonly found in small particles (<5 μm). Some studies have identified airborne transmission as a likely major pathway for asymptomatic transmission of SARS-CoV-2 [24, 25] and the superspreading events [26].

With the epidemic COVID-19 quickly under control in China at the early stage of 2020, Chinese public strategy and related health research have advanced the understandings of sporadic COVID-19 outbreaks and also empowered the strength to combat the COVID-19 disease all over the world. With the most recent mutants of omicron, it is still very important to know these strategies, which should be of significant clinical relevance and provide a reference for physicians. We collected and analyzed data the geographical and epidemiological characteristics of series cases with COVID-19 outbreaks caused by asymptomatic carrier from June 2020 to May 2021 in China.

Methods

At the beginning of June 1, 2020, we prospectively focus on the COVID-19 epidemic data from the Chinese Center for Disease Control and Prevention every day. Once having the new report of confirmed or asymptomatic case in China, we will track this epidemic and collect its epidemiological characteristics from announcements by the local Health Commission, and present a narrative research for geographical and epidemiological characteristics of series cases with COVID-19 outbreaks caused by asymptomatic carriers from June 2020 to May 2021 in China.

We searched epidemiologic data published on the website of WHO, the China Center for Disease Control and Prevention, National Health Commission, the Health Commission of Beijing and Tianjin city, Jilin, Shandong, and Heilongjiang Province from June 2020 to January 2021. Using the keywords “asymptomatic”, “COVID-19”, “SARS-CoV-2”, “2019-nCoV”, and we periodically searched the published medical literature using the PubMed service maintained by the U.S. National Library of Medicine of NIH. Confirmed COVID-19 cases are defined as persons who tested positive for SARS-CoV-2 and had clinical symptoms. Asymptomatic carrier refers to persons without clinical symptoms who tested positive for SARS-CoV-2.

Results

Geographic distribution of 7 series cases with COVID-19 outbreaks

From June 2020 to January 2021, the geographic distribution of 5 series cases in local sporadic outbreak regions with COVID-19 is shown in **Figure 1**. Qingdao, Tianjin and Dalian are coastal cities whereas Beijing and Jilin are inland cities. Data from 5 cities in China showed asymptomatic carrier-induced local sporadic outbreaks with SARS-CoV-2 (**Table 1**) by regular screening for high-risk groups, which was a key part of the COVID-19 surveillance. Furthermore, patient zero (asymptomatic case) in 4 cities (Qingdao, Tianjin, Shenzhen and Dalian) belonged to the environment-to-human transmission route of SARS-CoV-2, whereas that in other 3 cities (Beijing, Yingkou and Jilin) was the human-to-human route.

Epidemiologic characteristics of 7 series cases with COVID-19 outbreaks

Occupational distribution of 5 series cases in local sporadic outbreak regions with COVID-19 is shown in **Figures 1** and **2**, **Tables 1** and **2**. From September 2020 to May 2021, five cities in China had reported over 11 “patient zero” (11 asymptomatic cases). The gender of these asymptomatic carriers were men and their age was adult.

Among them, imported businessman (1), cold-chain transportation workers (9), and an individual marketer (1) were diagnosed. For the outbreak in Qingdao, Tianjin and Dalian, the source of the epidemic was from cold-chain transportation workers. In Beijing, the source of the epidemic was from imported businessman. In Jilin, the source of the epidemic was from an individual marketer.

The route of infection mainly included the droplet-borne route, the fomite route through contacts, and the airborne route through aerosols. Susceptible populations were involved in patients and accompanying staffs, people in the same building, people in shopping malls and workplaces, people in family gatherings, market-training halls, and the same community.

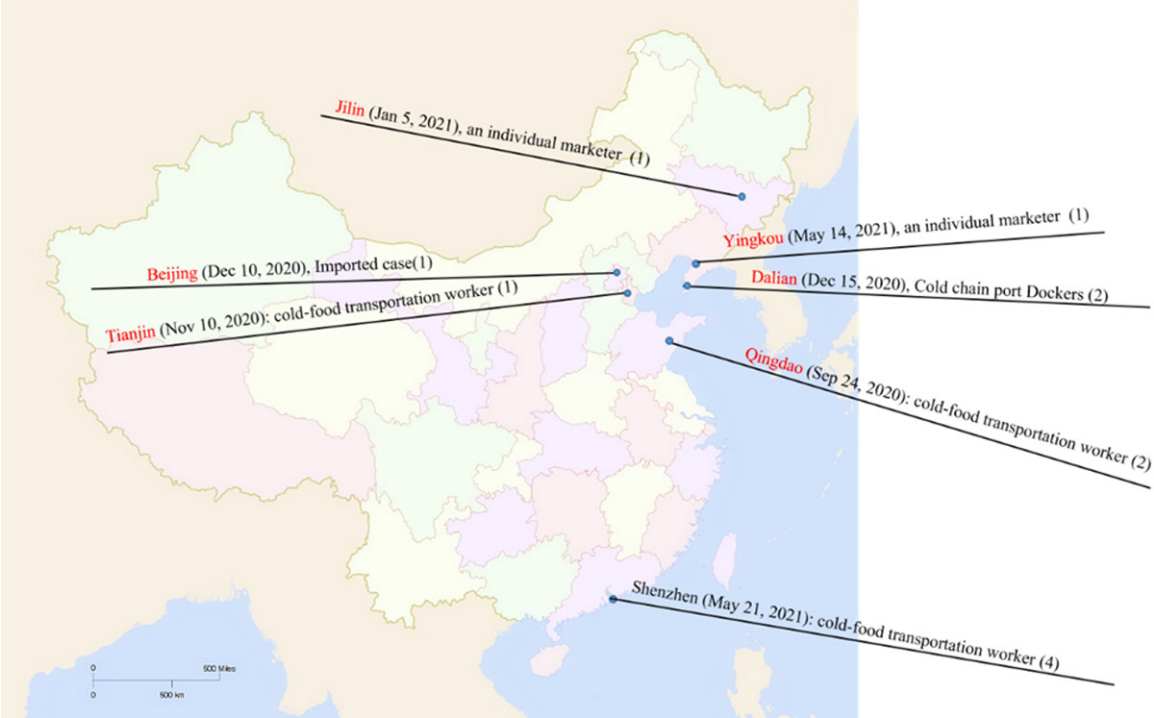

Figure 1. Geographical and occupational distribution of series cases in local sporadic outbreak regions with COVID-19 from June 2020 to January 2021.

In three transmission chains (Cases C, D, and E), there existed a superspreading phenomenon, which stands for a person who transmits COVID-19 to an unexpectedly or unusually large number of other people.

Differential management strategies of 5 series cases with COVID-19 outbreaks

Data of differential control strategies in new sporadic outbreak regions are presented in **Table 3**. In 5 series caseswith COVID-19 outbreaks, the same control measures to cut off the route of transmission mainly included individual methods of protection on science, quarantine of close contacts of people with asymptomatic and confirmed cases, and aggressive contact tracing. The different strategies of five cities were as follows: (1) in Jilin and Dalian, launching mass COVID-19 testing in the SARS-CoV-2-positive areas, designating a new high- or medium-risk area, locking down the corresponding community in response to new COVID-19 cases; (2) in Qingdao, Beijing and Tianjin, launching COVID-19 testing in local SARS-CoV-2-positive areas, designating a low-risk area, or locking down the corresponding local community.

The dynamic profile of "How to discover the source of infection" during the local sporadic COVID-19 outbreak is reported in **Figure 2**. In Cases A, B and D, the method of discovering asymptomatic carrier came from regular screening for high-risk groups. In Case C, the path of looking for the source of infection was "the first reported confirmed case of this epidemic → aggressive contact tracing → launching COVID-19 testing → discovering asymptomatic carrier (patient zero of this epidemic)". In Case E, the method of looking for asymptomatic carrier was "regular screening for people from high- or medium-risk areas → identifying for the case with positive nucleic acid test → aggressive contact tracing → launching COVID-19 testing → discovering asymptomatic carrier (patient zero of this epidemic)".

Transmission chain analysis of Case A (Qingdao city)

Cases 1 and 2 were quarantined in the hospital when they tested positive for SARS-CoV-2 nucleic acid on September 24, 2020, who were determined to have asymptomatic infection (**Figure 3**) [27]. During further investigation and treatment, they underwent chest computed

Table 1. Data of asymptomatic carrier in 5 series cases with new sporadic COVID-19 outbreak

City	Date	Number of patient zero	Occupation distribution	Geographical distribution	Age	Gender	Transmission route
Case A (Qingdao)	Sep. 24	2	transportation worker	Coastal city	Adult	Man	environment-to-human
Case B (Tianjin)	Nov. 10	1	transportation worker	Coastal city	Adult	Man	environment-to-human
Case C (Beijing)	Dec. 10	1	imported businessman	Inland city	29	Man	human-to-human
Case D (Dalian)	Dec. 15	5	cold-chain transportation workers	Coastal city	Adult	Man	environment-to-human
Case E (Jilin)	Jan. 5	1	individual marketer	Inland city	38	Man	human-to-human
Case F (Yingkou)	May 14	1	individual marketer	Coastal city	Adult	Woman	human-to-human
Case G (Shenzhen)	May 21	4	cold-chain transportation workers	Coastal city	Adult	Man	environment-to-human

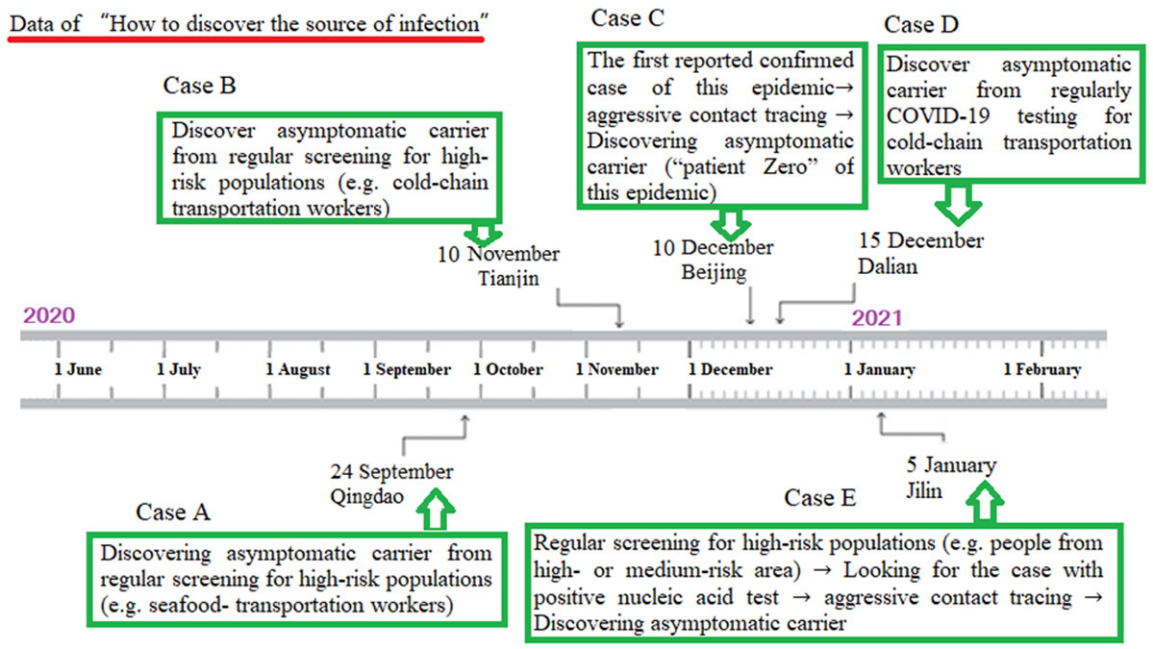

Figure 2. The graph's left-right axis (dates from September 2020 to January 2021) is used as a timeline of the key events and dynamic profile of "How to discover the source of infection" during the local sporadic COVID-19 outbreak. In Cases A, B and D, the method of discovering asymptomatic carrier came from regular screening for high-risk groups. In Case C, the path of looking for the source of infection was "the first reported confirmed case of this epidemic → aggressive contact tracing → launching COVID-19 testing → discovering asymptomatic carrier (patient zero of this epidemic)". In Case E, the method of looking for an asymptomatic carrier was "regular screening for people from high- or medium-risk areas → identifying for the case with positive nucleic acid test → aggressive contact tracing → launching COVID-19 testing → discovering asymptomatic carrier (patient zero of this epidemic)".

tomography (CT) scans in the CT suite visited by Case 3 (a hospitalized patient) and Case 4 (a nursing assistant). Case 1 later developed symptoms on October 14, 2020.

All persons associated with Cases 3 and 4, including those who lived in the same Ward Area and had close contact with SARS-CoV-2-positive patients, were tested for SARS-CoV-2 nucleic acids. Contact tracing results indicated that 9 cases were infected with SARSCoV-2, including 4 infirmed cases (Cases 3-6) and 5 asymptomatic cases (Cases 7-11) on October 12, 2020.

In addition, the Chinese Center for Disease Control and Prevention sequenced the entire genomes of 11 samples from this cluster. Viral genomes were identical in 11 cases, indicating that SARS-CoV-2 came from the same point of origin.

By October 16, 2020, Qingdao city had reported 13 confirmed cases since the asymptomatic

Table 2. Characteristics of 7 transmission chains with new sporadic COVID-19 outbreak

City	Source of infection	Main route of transmission	Susceptible population	Superspreading phenomenon	Number of COVID-19 infection patient
Case A in Qingdao	transportation worker	the fomite route through contacts	Patients and accompanying staffs	No	11
Case B in Tianjin	transportation worker	droplet-borne route	People in same building	No	8
Case C in Beijing	imported businessman	droplet-borne route	People in shopping malls and workplaces	Yes	16
Case D in Dalian	cold-chain transportation workers	the fomite route through contacts	People in family gathering and same community	Yes	109
Case E in Jilin	individual marketer	airborne route through aerosols	People in market-training hall and same community	Yes	103
Case F in Yingkou	individual marketer	airborne route through aerosols	People in family gathering and same community	No	3
Case G in Shenzhen	cold-chain transportation workers	the fomite route through contacts	People in family gathering and same community	No	4

Main source of COVID-19 infection stands for a person who transmits COVID-19 to an unexpectedly or unusually large number of other people.

Table 3. Management strategies in 5 series cases with new sporadic COVID-19 outbreak

City	Date	How to discover the source of infection	The same control measures to cut off the route of transmission	The different control measures to cut off the route of transmission
Case A in Qingdao	Sep. 24 2020	Discovering asymptomatic carrier from regular screening for high-risk groups (e.g. seafood-transportation workers)	1. individual methods of protection on science 2. quarantine of close contacts of people with asymptomatic and confirmed cases 3. aggressive contact tracing	launching COVID-19 testing in local SARS-CoV-2-positive areas, designating a low-risk area.
Case B in Tianjin	Nov. 10 2020	Discovering asymptomatic carrier from regular screening for high-risk populations (e.g. cold-chain transportation workers)		launching COVID-19 testing in local SARS-CoV-2-positive areas, designating a low-risk area.
Case C in Beijing	Dec. 10 2020	The first reported confirmed case of this epidemic → aggressive contact tracing → launching COVID-19 testing → Discovering asymptomatic carrier ("patient Zero" of this epidemic)		launching COVID-19 testing in local SARS-CoV-2-positive areas, designating a low-risk area, locking down the corresponding local community.
Case D in Dalian	Dec. 15 2020	Discovering asymptomatic carrier from regularly COVID-19 testing for cold-chain transportation workers		launching mass COVID-19 testing in the SARS-CoV-2-positive areas, designating a new high- or medium-risk area, locking down the corresponding community in response to new COVID-19 cases.
Case E in Jilin	Jan. 5 2021	Regular screening for high-risk populations (e.g. people from high- or medium-risk area) → Looking for the case with positive nucleic acid test → aggressive contact tracing → launching COVID-19 testing → Discovering asymptomatic carrier ("patient Zero" of this epidemic)		launching mass COVID-19 testing in the SARS-CoV-2-positive areas, designating a new high- or medium-risk area, locking down the corresponding community in response to new COVID-19 cases.

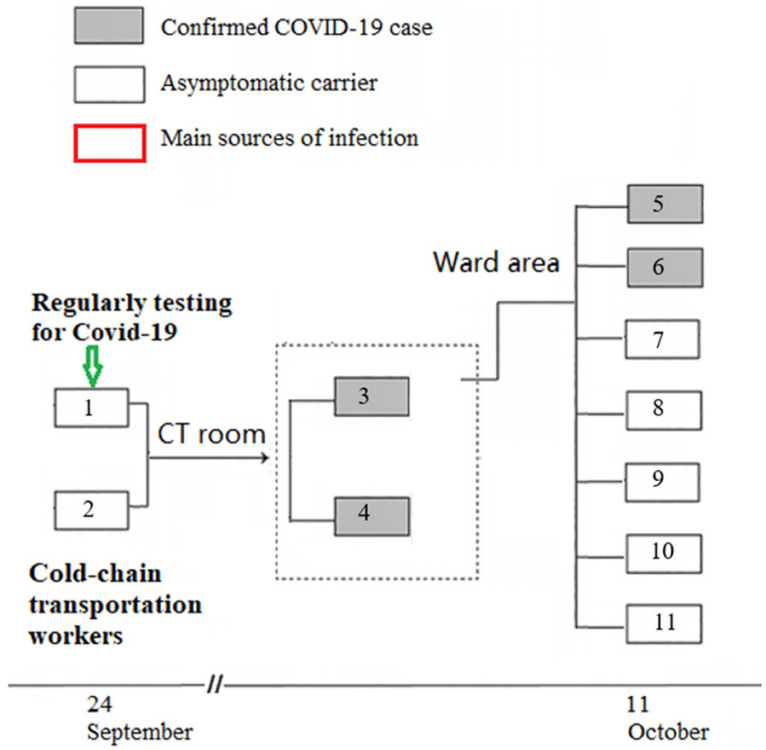

Figure 3. Timeline of exposure and connections between SARS-CoV-2 cases among persons in Qingdao, China. Cases 1 and 2 were quarantined in the hospital when they tested positive for SARS-CoV-2 nucleic acid on September 24, 2020, who were determined to have asymptomatic infection. By October 16, 2020, Qingdao city had reported 13 confirmed cases since the asymptomatic cases were first detected in September 24, 2020.

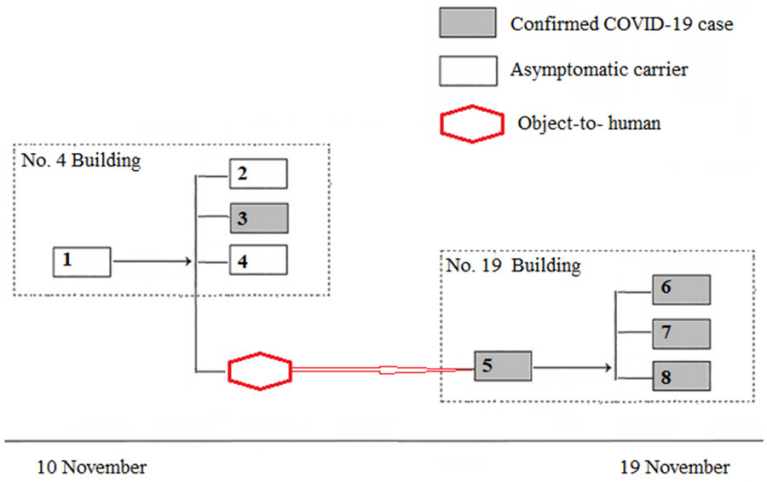

Figure 4. Timeline of exposure and connections between SARS-CoV-2 cases among persons in Tianjin, China. Case 1 in No. 4 Building was first tested positive for SARS-CoV-2 on November 10, 2020, who was an asymptomatic carrier. Cases 5-8 in No. 19 Building were infirmed as COVID-19 case on November 19, 2020. Epidemiological investigation showed that there was an SARS-CoV-2 transmission chain between No. 4 Building and No. 19 Building.

cases were first detected in September 24, 2020.

Transmission chain analysis of Case B (Tianjin)

On November 10, 2020, Case 1 was first tested positive for SARS-CoV-2 in No. 4 Building, who was an asymptomatic carrier (**Figure 4**). Cases 1-3 shared the same room. Case 2 (asymptomatic case) and 3 (infirmed case) were tested positive for SARS-CoV-2 on November 17, 2020. Cases 1-4 lived in No. 4 Building, and Case 4 was tested positive for SARS-CoV-2 (asymptomatic case) on November 18, 2020.

On November 19, 2020, Case 6, his parents (Cases 7 and 8), and Case 5 were infirmed as COVID-19 case. Cases 5-8 lived in No. 19 Building.

The surveillance video from No. 9 Building proved that Case 1 looked for his colleague in No. 9 Building on the evening of November 9, and he coughed and sneezed without wearing a mask in the elevator; On November 10, Case 5 tried to find his colleague of No. 9 Building by the same elevator, and then returned to No. 19 Building. In addition, the samples of the elevator surface in No. 9 Building were tested positive for the SARS-CoV-2 nucleic acid, and they were positive at multiple points, which confirmed that the elevator in No. 9 Building was contaminated. These data suggested that there was an epidemiological link between No. 4 Building and No. 19 Building.

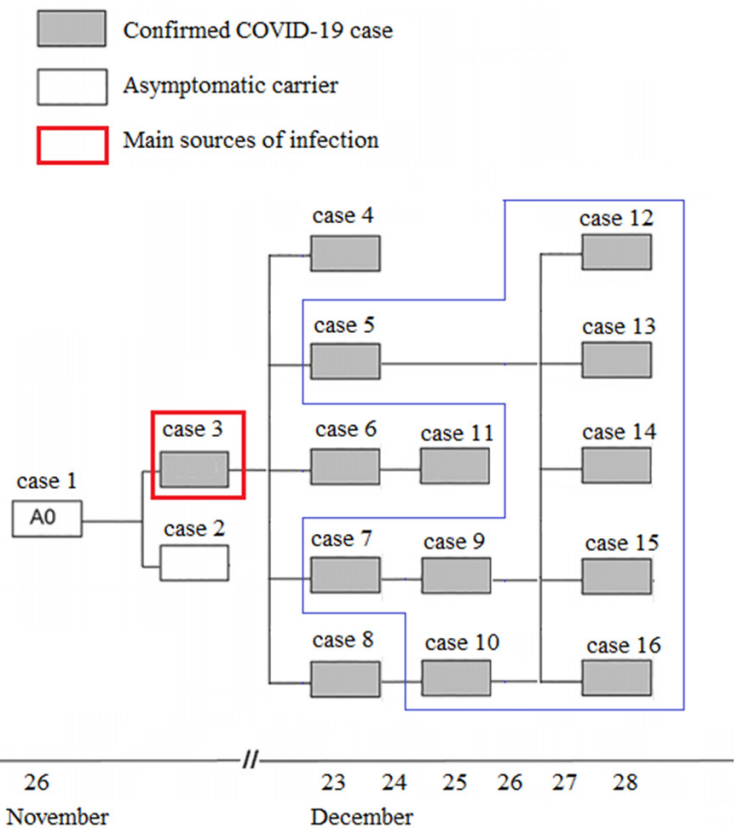

Figure 5. Timeline of exposure and connections between SARS-CoV-2 cases among persons in Beijing, China. On December 10, 2020, A0 (Case 1), Indonesian national, returned to Shunyi District, Beijing after 14 days of isolation in Fujian Province and a negative nucleic acid test. He was diagnosed as asymptomatic infection on December 28. Case 1 was the source of a clustered epidemic and Case 3 is a key case in the transmission chain. Note: The data is based on public reports and might be incomplete.

Disease Control and Prevention of Tianjin Province sequenced the entire genomes of 8 samples from No. 4, No. 9, and No. 19 Buildings. The results showed that these viruses belonged to the European family branch 1 of the L genotype, indicating that SARS-CoV-2 among three buildings came from the same point of origin.

Transmission chain analysis of Case C (Beijing)

On December 10, 2020, A0 (Case 1), an Indonesian national, returned to Shunyi District, Beijing after 14 days of isolation in Fujian Province and a negative nucleic acid test. He was a close contact with a seat on the same flight from Indonesia on November 26, 2020. He had negative SARS-CoV-2 nucleic acid and positive serum IgM antibody on December 26, and the detection of SARS-CoV-2 nucleic acid in the environment of his residence and work place was positive. He had positive SARS-CoV-2 nucleic acid on December 28. These data suggested that he was diagnosed with asymptomatic infection (**Figure 5**).

Case 2 was Case 1' tenant in a shared house, and the virus of Case 1 spread to Case 2. Case 1 also spread to a supermarket employee (Case 3) during shopping.

Case 3 spread to her customer Case 4 (the first reported confirmed case of this epidemic), her husband Case 5, an online ride-hailing driver Case 6, and her friend Cases 7 and 8. Case 6 spread to driver Case 11 through a shared meal. Cases 7 and 8 were transmitted to their husbands (Cases 9 and 10). Cases 5, 7, 9, and 10 worked in the same Industrial District, and their collective activities resulted in Cases 12-16 infection.

Furthermore, Beijing CDC conducted a whole-genome sequencing analysis of Cases 1-16 and related environmental samples of the virus and the results showed that the viruses all came from the European family branch 2.3 of the L genotype, which is the same transmission chain.

Transmission chain analysis of Case D (Dalian city)

On December 15, 2020, Cases 1-4 had positive SARS-CoV-2 nucleic acid tests during regular COVID-19 testing for cold-chain transportation workers (**Figure 6**). Their close contacts, Cases 5 and 6, subsequently tested positive for SARS-CoV-2 on December 16 or 17. In addition, Cases 1-4 and Cases 7-10 gathered in the Restaurant 1 on December 12. Cases 7-10 had positive SARS-CoV-2 nucleic acid tests on December 17. After nucleic acid testing of all employees in Case 7's local community on

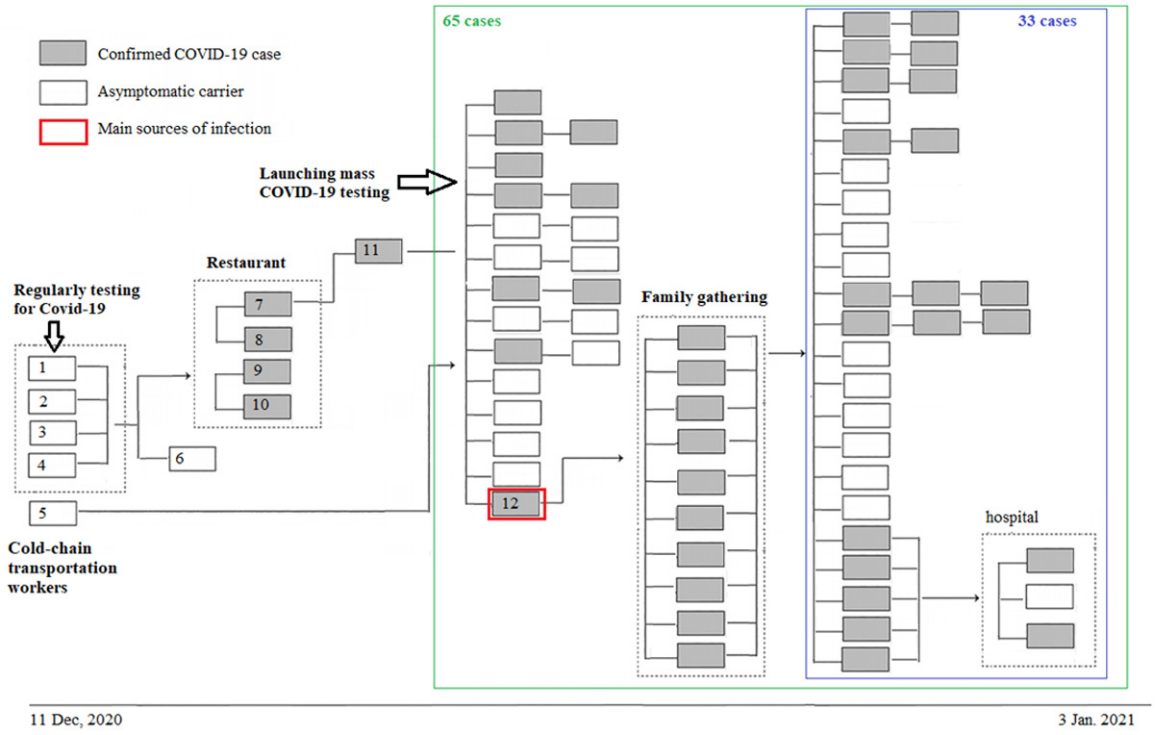

Figure 6. Timeline of exposure and connections between SARS-CoV-2 cases among persons in Dalian, China. During regularly COVID-19 testing for cold-chain transportation workers, Cases 1-4 had positive SARS-CoV-2 nucleic acid tests on December 15, 2020. Their close contacts, Cases 5-10, subsequently tested positive for SARS-CoV-2. Cases 5, 7 and 11 brought the SARS-CoV-2 virus to the Commercial Building 1 and multiple communities, leading to further infections. As of January 3, 2021, Cases 1-5 remained asymptomatic.

December 19, Case 11 had positive SARS-CoV-2 nucleic acid tests on December 20.

Investigators learned that Case 5 had ever been to Commercial Building 1 on December 11 (**Figure 6**). At the beginning of December 20, all staffs of Commercial Building 1 and Case 11's big community were launched mass COVID-19 testing. A cluster of 65 COVID-19 cases (including Case 12) was identified from December 11 to 21, 2020. Epidemiological investigation showed that 65 cases were associated with Commercial Building 1, located in Case 11's big community.

After Case 12 took part in a family gathering, a total of 10 other persons were infected with SARSCoV-2. All persons associated with the 10 cases, including those who lived in the same community and had close contact with SARS-CoV-2-positive cases or visited the hospital during December 1-20, were tested for SARS-CoV-2 nucleic acids. Results showed that 33 cases were infected with SARSCoV-2, including 21 infirmed cases and 12 asymptomatic cases. Among 33 cases, 10 cases were nosocomial infection. By January 3, 2021, Cases 1-5 remained asymptomatic.

Transmission chain analysis of Case E (Jilin)

On January 5, 2021, case-patient A0, an individual marketer, came to Changchun city, Jilin Province from Wangkui County, Heilongjiang Province. He gave speeches in Market-training Hall 1 and 2 of different cities on January 8 and 10, respectively (**Figure 7**).

Patient B1, B2 and A0 were in the same train carriage on January 5, 2021. Both B1 and B2 tested positive for SARS-CoV-2 on January 11, and remained asymptomatic, indicating that B1 and B2 were previously infected with SARS-CoV-2 and were asymptomatic carriers. Based on epidemiological surveillance, A0 had positive SARS-CoV-2 nucleic acid tests on January 12 and noted symptoms of COVID-19 on January 16, suggesting A0 was the first confirmed case in this cluster, raising Jilin's health commission concerns.

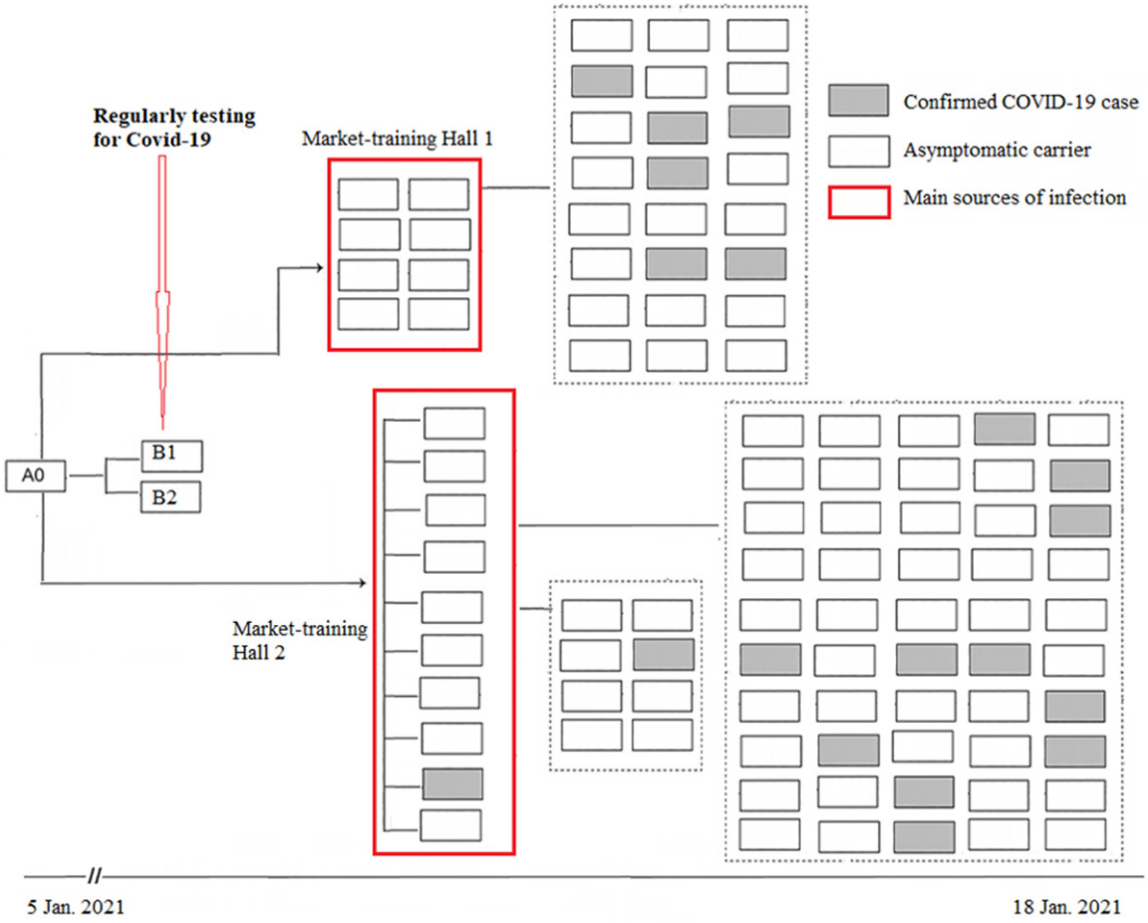

Figure 7. Timeline of exposure and connections between SARS-CoV-2 cases among persons in Jilin Province, China. A0 came to Changchun city from Heilongjiang Province on January 5, and A0, B1 and B2 were in the same train carriage. Both B1 and B2 had positive SARS-CoV-2 nucleic acid tests on January 11 and remained asymptomatic, indicating that B1 and B2 were previously infected with SARS-CoV-2 and likely were asymptomatic carriers. Based on epidemiological surveillance, A0 had positive SARS-CoV-2 nucleic acid tests on January 12 and noted symptoms of COVID-19 on January 16, suggesting A0 was the first confirmed case in this cluster.

Jilin launched mass COVID-19 testing in some areas including Market-training Hall 1 and 2 on January 11. From 11 to 18 January 2021, 34 new COVID-19 cases and 80 asymptomatic carriers had been identified in the Jilin Province. Among these cases, 102 were related to case-patient A0. By February 9, 2021, Jilin Province had reported 3 deaths among 573 confirmed cases since the asymptomatic cases were first detected in the Changchun city in 11 Jan. 2021.

Discussion

Main findings of new sporadic outbreaks with COVID-19 from June 2020 to May 2021 in China were as follows: (1) the importance of regular screening for high-risk groups, which was key part of the COVID-19 surveillance; (2) differential control strategies for different epidemiological characteristics of 5 series cases with COVID-19 outbreaks caused by asymptomatic carriers. Here we offered a narrative research of SARS-CoV-2 transmission chain in 5 series cases with COVID-19 outbreaks. In addition, we also described the occupational distribution of high-risk groups, epidemiological characteristics, and the occupational distribution of asymptomatic carriers in 5 COVID-19 outbreak regions. Chinese management measures including regular screening for high-risk populations, aggressive contact tracing and quarantine of close contacts of people with asymptomatic or confirmed infection, were found to be effective in mounting a rapid

response and minimized the impact of a new outbreak.

Regular screening for high-risk populations provides a standardized model of early identification for the asymptomatic carrier with SARS-CoV-2 [27]. SARS-CoV-2 testing of high-risk groups may identify the asymptomatic carriers and infected people before widespread transmission of the highly contagious COVID-19 occurs. Screening millions of people for SARS-CoV-2 testing in a short period is challenging and requires the understanding of the occupational distribution of high-risk populations. Our results have shown that the occupational distribution of high-risk populations includes cold-chain transportation workers, imported businessmen and an individual marketer. To minimize testing time and conserve health resources, a pooled testing approach has attracted worldwide attention [27, 28].

An asymptomatic carrier with the causative pathogen is well-known to cause rapid spread of SARS-CoV-2 [29-32]. At the early stage of 2020, Chinese physicians have rapidly identified the importance of the asymptomatic carriers in local rapid spread of SARS-CoV-2. Some studies have identified asymptomatic transmission of SARS-CoV-2 as a likely major factor for the superspreader events [26]. Our data have reported the main source phenomenon of COVID-19 infection in 4 cities, suggesting that there are superspreader events in China. Such super spreaders are of particular concern in COVID-19 outbreaks [33, 34]. The superspreading phenomenon is an important outbreak alarm, and this requires careful planning to facilitate coordinated management of COVID-19 outbreaks, including effective coordination and execution in community, along with cooperation of residents.

Though human-to-human is the main transmission route of COVID-19, our data showed environment-to-human transmission in 3 cities. Environment-to-human transmission is defined as the transfer of virus from virus-laden objects to humans upon contact. It is well known that the environment may play an important role in the transmission and spread of the coronavirus [35, 36]. This transmission can only happen under the following three conditions: (1) The object is seriously contaminated by the virus; (2) The object's surface is able to keep the virus alive for a fairly long time; (3) The person coming in contact with virus-laden objects does not take adequate protection measures. There have been multiple reports that most cases of environment-to-human transmission in China are linked with imported products, such as frozen foods [7, 8, 37].

In conclusion, China has ignited tremendous efforts to unravel the epidemiological characteristics of SARS-CoV-2, which constitutes the foundation for international public health development strategies [38, 39]. Our results show the importance of regular screening for high-risk populations and different control strategies for epidemic control, which provide an objective basis for suppressing the spread of the SARS-CoV-2 virus. These important experiences can be used for reference to minimize the subsequent spread of virus mutants in various places.

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Disclosure of conflict of interest

None.

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