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Cluster infections play important roles in the rapid evolution of COVID-19 transmission: a systematic review

Tao Liu¹, Dexin Gong¹, Jianpeng Xiao, Jianxiong Hu, Guanhao He, Zuhua Rong, Wenjun Ma*

Guangdong Provincial Institute of Public Health, Guangdong Provincial Center for Disease Control and Prevention, Guangzhou, China

¹ These authors contributed equally to this work.

*Corresponding author

Correspondence to:

Wenjun Ma, Guangdong Provincial Institute of Public Health, Guangdong Provincial Center for Disease Control and Prevention, Guangzhou 511430, China

mawj@gdiph.org.cn

Telephone: 86-020-31051602

Fax: 86-020-31051652

Highlights

- We summarized the major types of cluster infections of SARS-COV-2 worldwide.
- Sixty-five studies were included involving 108 cluster infections.
- The major types of clusters are family cluster, community transmission, etc.
Abstract

Objectives: To summarize the major types of cluster infections of SARS-CoV-2 all over the world through a comprehensive systematic review.

Methods: We searched all of the studies published between January 1, 2020 and June 15, 2020, on the cluster infections of COVID-19 in the English electronic databases including PubMed, Embase, Web of Knowledge, and Scopus. All included studies were independently screened and evaluated by two authors, and information of each study was extracted using a standard form.

Results: A total of 65 studies were included in this study which involved 108 cluster infections from 13 countries, areas or territories. Out of the cluster infections, 72 (66.7%) were reported in China. The major types of cluster infections include family cluster, community transmission, nosocomial infection, transmission in gathering activities, on transportations, in shopping malls, on conference, among tourists, in religious organizations, among workers, in prisons, office, and in nursing home.

Conclusions: The SARS-CoV-2 can be transmitted in various circumstances, and cluster infection plays important roles in the rapid evolution of COVID-19 transmission. Prevention and control measures such as social distance must be strictly implemented to contain the cluster infections.

Key words: novel coronavirus, COVID-19, SARS-CoV-2, cluster infection, systematic review
Introduction

In December of 2019, an emerging infectious disease named as COVID-19 caused by SARS-CoV-2 virus was first reported in Wuhan, Hubei Province, China (Epidemiology Working Group for NCIP Epidemic Response, 2020). Since then, more and more countries also reported COVID-19 all over the world (Liu et al., 2020a). The World Health Organization (WHO) has declared the COVID-19 a public health emergency of international concern January 30, 2020 (WHO, 2020a), and further declared the COVID-19 a pandemic on March 11, 2020 (WHO, 2020b). As of June 24, 2020, a total of 9,273,773 confirmed cases with 477,807 deaths were in more than 210 countries, areas or territories (Hopkins, 2020).

Although the whole world is endeavoring to contain COVID-19, and several countries have successfully controlled the epidemic, this novel norovirus is still widely spreading in many countries. Since the late of May 2020, daily confirmed cases exceeded 100,000, and had an increase trend worldwide, which indicates that epidemic of COVID-19 is still serious. Additionally, studies have reported characteristics of SARS-CoV-2 different from other coronaviruses (Tan et al., 2005). For example, people could be infected with SARS-CoV-2 by asymptomatic carries and presymptomatic patients (Qian et al., 2020, Zhang et al., 2020a), which could prolong the infectious period. Meteorological factors including temperature and UV radiation may not impact the transmission risk of SARS-CoV-2 (Yao and Pan, 2020). Several super-spreaders of COVID-19 were reported in settings such as religious organizations (Wikipedia, 2020). These characteristics partially contribute the high transmission risk of SARS-CoV-2, and indicate that more research workers are needed to further understand this infectious disease.
Understanding the transmission routes and circumstances of SARS-CoV-2 as a novel coronavirus is critical for preventing and controlling its spreading. In the early stage of epidemic, the transmission routes of SARS-CoV-2 were reported mainly from wild animals to human, and limited transmissibility between humans. However, in the progress of COVID-19 rapidly spreading, more and more transmission routes and circumstances were reported, including family, community, nosocomial infections, etc. However, no study has systematically summarized the types of cluster infections of SARS-CoV-2. In the study, we summarized the major types of cluster infections of SARS-CoV-2, which could provide critically important implications for the prevention and control of COVID-19 worldwide.

Methods

Data Sources and Search Strategy

According to the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) (Moher et al., 2009), the literature search was conducted in English databases including PubMed, Embase, Web of Knowledge, and Scopus. Time was restricted between 1st Jan 2020 and 15th June 2020 and no other limitations were applied.

The search terms were (“novel coronavirus” OR “2019-nCoV” OR “COVID-19” OR “SARS-CoV-2”) AND (“cluster” OR “infection”). We included “2019-nCoV” in the search terms because the novel coronavirus was temporally named as 2019-nCoV in the early stage of the epidemic. All records were retrieved, and duplicates identified by title and author were removed. The remained records were initially screened on title and abstract. Full text will be retrieved for the potential
eligible records and be further assessed. Reference lists of full-text articles were also screened for additional publications. Two authors (T. L and DX. G) searched and screened independently to identify eligible studies. Disagreement between them were reconciled by a third author.

Selection criteria

Studies were included if they reported an aggregation of COVID-19 cases in any settings, such as in household, vehicle, shopping mall, community, etc. The exclusion criteria were editorial, comment, and letter or articles with irrelevant topics. For studies sharing a same case series, the one with the most meaningful information was included.

Data extraction

The following information were independently extracted by two authors: author names, time of publish, study setting, type of cluster infection, and number of infections involved. Differences were addressed by a third author. Authors of studies with unclarified data were contacted to update information.

Results

The search strategy initially identified 981 records and 5 reference was added by referring to reference sections. We excluded 500 duplicated articles through screening their titles and abstracts. In the left 486 articles, 417 articles were excluded because these articles are related to epidemiological characteristics of COVID-19 cases (n=90), clinical characteristics or therapy (n=115), spatial analysis (n=10), policies or recommendations (n=54), genome and phylogeny
(n=25), testing/screening/immunity (n=14), or others such as review, comment (n=109). In the 69 potentially eligible studies, we further excluded four repeated studies, and 65 studies were finally included in this study (Figure 1). The included 65 studies involved 108 cluster infections in 13 regions. Out of the cluster infections, 72(66.7%) were reported in China, and 58(53.7%) were family clusters (Table 1). The major types of clusters are family cluster (62), in community (4), nosocomial infection (3), transmission in gathering activities (15), on transportations (6), in shopping malls (3), on conference (4), during tourists (6), and in religious organizations (5).

**Family cluster**

Family is the dominated circumstance where the cluster of SARS-CoV-2 infection occurs. World Health Organization reported that 78-85% of infection clusters occurred in families in the early stage of COVID-19 epidemic in China (Mission, 2020). The first family cluster was reported as early as on January 24, 2020 in Shenzhen, China, in which a household member who had no travel history to Wuhan or exposure to wild animals were infected by a COVID-19 case who traveled from Wuhan (Chan et al., 2020). This is the first study that confirmed the transmission of SARS-CoV-2 from human to human. Since then, many family clusters of COVID-19 were reported across the world (Qian et al., 2020, Zhang et al., 2020a, Chan et al., 2020, Xu et al., 2020, Wolf et al., 2020, Chiu et al., 2020, To et al., 2020, Qiu et al., 2020a, Liu et al., 2020b, Wei et al., 2020a, Zhang et al., 2020b, Ye et al., 2020, Tang et al., 2020, Ji et al., 2020, Phan et al., 2020, Deng et al., 2020, Du et al., 2020, Huang et al., 2020a, Jiang et al., 2020a, Liu et al., 2020c, Xiong et al., 2020, Gao et al., 2020a, Chen et al., 2020a, Yu et al., 2020, Yang et al., 2020, Tong et al., 2020, Qiu et al., 2020b, Pan et al., 2020, Luo et al., 2020, Lu et al., 2020a, Li et al., 2020a, Li et al., 2020b, Huang et al.,
Family cluster usually has higher risk of infection in household members due to their close and frequent contacts (Bi et al., 2020). Hence, prevention of infection among household members is an important strategy to contain the transmission of COVID-19 worldwide. For example, it is crucial to quarantine their close contacts in families of confirmed COVID-19 cases and detect SARS-CoV-2 as early as possible.

Community transmission

Community transmission is one of the most important modes facilitating the widespread of COVID-19. Several studies have reported community transmission cases (Ghinai et al., 2020, Lu et al., 2020b, Liu et al., 2020e, Kim et al., 2020, The Centre for Health Protection, 2020). For example, the Centers for Disease Control and Prevention (CDC) reported community transmissions occurred in Chicago in April, in which 16 COVID-19 cases were infected in nonhousehold gatherings (a birthday party, funeral and church attendance) (Ghinai et al., 2020). These cases indicate the importance of social distancing for prevention of COVID-19 transmission. Additionally, studies showed extensive environmental contamination of SARS-CoV-2 (Jiang et al., 2020a, Ong et al., 2020), suggesting the contaminated environments as a potential medium of virus transmission among families in the communities. Environmental management and disinfection are also important for preventing the community transmission of COVID-19.

Nosocomial infection
Nosocomial infection is also an important mode of COVID-19 transmission, which is similar to Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS) (Tsang et al., 2003, Assiri et al., 2013, Sina News, 2020). It was reported that as of February 11, 2020, a total of 3,019 healthcare workers have been infected by SARS-CoV-2 in China, with 1,716 confirmed cases and 5 have died (0.3%) (The Novel Coronavirus Pneumonia Emergency Response Epidemiology, 2020). Another report on 138 COVID-19 cases in Zhongnan Hospital of Wuhan University in Wuhan during the early period of COVID-19 outbreak presumed that nosocomial transmission of 2019-nCoV was suspected in 41% (57/138) of patients, including 40 healthcare workers and 17 patients who were already hospitalized for other reasons (Wang et al., 2020).

These nosocomial infections were mainly due to the lack of understanding on the novel coronavirus, and insufficient personal protection equipment (PPE) in the early stage of epidemic. As knowledge of COVID-19 increases, nosocomial infections dramatically decreased in China. For example, more than 42,000 healthcare workers were sent to assist Wuhan from other provinces in China, but none of them was infected (Liu et al., 2020f). Nosocomial infections were also reported in many other studies (Cao et al., 2020, von Freyburg et al., 2020, Wei et al., 2020b, Hara et al., 2020, WHO, 2020c). It was reported that over 90,000 health workers were infected with COVID-19 worldwide (Mantovani, 2020). Healthcare workers play an essential role in containing the COVID-19 outbreak. They provide care for patients during routine health service, offer critical care to severe patients, and ensure that the infection prevention and control measures are implemented and adhered to in healthcare facilities in order to limit nosocomial infections. Before a vaccine of SARS-CoV-2 available, healthcare workers remain susceptible to COVID-19. However, evidence from Wuhan,
China illustrated that appropriate personal protective equipment in addition to adhering to standard recommendations could effectively protect them from SARS-CoV-2 infection even in the clinical settings with higher risk of exposure (Liu et al., 2020f). Hence, healthcare workers must be given priority to procurement and distribution of PPEs, and provided adequate training of protecting themselves from infection.

Transmission in gathering activities

Indoor gathering activities could also lead to cluster infections of COVID-19. Transmission in gathering activities were reported in several studies (Jiang et al., 2020b, Emma, 2020, Danis et al., 2020, Jang et al., 2020). For example, Danis et al. reported a confirmed case infected in a chalet in France (Danis et al., 2020). The index case had attended an international conference in Singapore linked to COVID-19 confirmed cases. He flighted to France and had a gathering activity with several English tourists and French residents, which led to 11 people infected. Such transmissions also occurred in other countries (Jang et al., 2020, Takeuchi, 2020). People in gathering activities rarely wear PPEs such as face masks, which make them in higher risk of infection. These transmissions further support the WHO recommendations to stay at home during the epidemic, and avoid any gatherings with persons from multiple households.

Transmission on transportations

Transportation is another circumstance occurring the transmission of COVID-19, including flight, train, taxi, bus, cruise, etc. (Qiu et al., 2020a, Pongpirul et al., 2020, Shen et al., 2020, Eldin et al., 2020, Kakimoto et al., 2020) For example, Yang et al. reported that ten out of 325 passengers and
crew members were infected in a flight from Singapore to Hangzhou, China (Shen et al., 2020). Pongpirul et al. reported a confirmed case infected in a taxi in Thailand. The transportations usually have an enclosed space. Passengers usually have close contacts, and droplets can be easily generated in the enclosed space, which may transmit the SARS-CoV-2 from those carriers. Previous studies have demonstrated that SARS-CoV transmission in transportations was more likely through airborne (Chan et al., 2020), small-particle (Setti et al., 2020), and close contacts (Olsen et al., 2003). Therefore, travelers should avoid all nonessential travels during the epidemic, and must implement strict measures to protect themselves on the transportations once they have to travel, such as wearing face masks, sanitation and disinfection.

**Transmission in shopping malls**

A shopping mall is a place with high density of people, which can increase the transmission risk of SARS-CoV-2. Cai et al. reported a cluster of 35 confirmed cases associated with a shopping mall in Wenzhou, China (Cai et al., 2020). A similar cluster of COVID-19 was reported in a shopping mall in Tianjin, China, which has caused 42 confirmed cases by February 22 (Tianjin Health Commission, 2020). It was proposed that SARS-CoV-2 in shopping mall may spread via fomites (e.g., elevator buttons or restroom taps) or virus aerosolization in confined public places (e.g., restrooms or elevators) (Cai et al., 2020). A report from Guangzhou, China also detected the nucleic acid of SARS-CoV-2 on a doorknob at a patient’s house (Guo, 2020), which further clarified the transmission of SARS-CoV-2 in the shopping mall. In addition, close contacts among people in the shopping mall may also lead to low intensity transmission. In order to prevent the spread of COVID-19 in shopping places, many commercial activities were prohibited during the epidemic worldwide.
In addition, customers are suggested to wear face mask, practice social distancing while shopping, and wash hands.

**Transmission on conference**

Conference is also a circumstance favoring the transmission of SARS-CoV-2. A typical case was reported in Singapore where 109 persons from several countries attended an international conference, which led to at least seven confirmed cases (WHO, 2020d). More importantly, these infected cases spread the SARS-CoV-2 to many other countries including Malaysia, UK, France, and Spain through international flight. Therefore, many countries firstly stopped the international flights to and from those epidemic regions.

**Transmission among tourists**

Tourists usually have close contacts, such as taking the same transportation, having meals together, staying in the same hotel. Hence, the infection risk is high once anyone of them was a virus carrier. A such cluster of cases was reported in India. A group of 23 Italian tourists along with three Indians visited several tourist places, and the index case infected 16 tourists with an attack rate of 65.4% (Vivian et al., 2020), which was higher than existing literature such as 5.7% in Shenzhen, China (Bi et al., 2020). Another study also reported a cluster of eight cases infected in a hotel in Spain (Hoefer et al., 2020). These studies illustrated the high risk of infections among tourists, and protection measures must be strictly implemented among those tourists.

**Transmission in religious organizations**

Outbreak of COVID-19 was also reported in religious organizations (Qian et al., 2020, Wei et al.,
2020a, Zhang et al., 2020b, Pung et al., 2020, Kupferschmidt, 2020, The Ministry of Health and Welfare, 2020). One outbreak event occurred in South Korea, where the index case, a devout follower of the Shincheonji Church of Jesus, infected at least 456 confirmed cases in a series of church activities (The Ministry of Health and Welfare, 2020). Another example was reported in Malaysia. A religious gathering activity was held in Sri Petaling Mosque located in Kuala Lumpur, and 16,000 people attended the activity, which led to at least 3,375 confirmed cases linked to the activity (Wikipedia, 2020). Super-spreading event occurred in both examples. Therefore, the risk of SARS-CoV-2 transmission is very high in such large gathering activities which must be prohibited during the epidemic.

**Transmission in workers**

Workers such as miners, and migrant workers usually constitute an underserved, isolated, medically vulnerable and often underinsured population. In addition, these workers usually do a job in an enclosed space, and had close contacts with each other. Hence, they are susceptible to the COVID-19 which easily outbreak once the virus appears among the population (Sood et al., 2020). For example, COVID-19 hit the first Quantum’s Cobre Panamá mine, and killed workers (Latin America Copper, 2020). It was reported that miners account for almost 20% of COVID-19 cases in Poland who had closed more than 10 coal mines to contain the epidemic of COVID (Barteczko, 2020). Sood et al. call for intensifying the implementation of prevention and control measures among those workers (Sood et al., 2020), such as providing primary care, health education, providing separate or isolated living space, disinfecting high-touch common areas, providing hand-washing stations and hand sanitizer, and providing adequate PPEs.
Others

Cluster infections of SARS-CoV-2 were also reported in other circumstances, including prisons (Xinhuanet, 2020), office (Zhang et al., 2020b), nursing home (The Beijing News, 2020). For example, five prison epidemics of COVID-19 including 511 confirmed cases were reported in China at the end of February 2020. (Xinhuanet, 2020) A cluster of cases infected in an office were reported in a German company (Rothe et al., 2020, Böhmer et al., 2020). Nursing home is another important setting with high risk of SARS-CoV-2. It has been demonstrated that older people are more susceptible to SARS-CoV-2, and older COVID-19 patients had poorer prognosis (Guan et al., 2020). Statistics from the Swedish Board of Health and Welfare showed that 90% of COVID-19 patients who had died as of April 28 were over the age of 70, and half were nursing home residents (Bangkok Post, 2020). These results suggest that transmission of SARS-CoV-2 could occur in various circumstances, which increases in the difficulties of control and prevention on the spread of COVID-19. These characteristics of COVID-19 also differ from SARS and MERS (Kwok et al., 2019). The majority of SARS and MERS cases occurred in healthcare setting. While most SARS cases were among health care workers, substantial number of MERS cases were patients.

Conclusions

Studies have demonstrated that SARS-CoV-2 had a stronger transmissibility than other coronaviruses including SARS-CoV and MERS-CoV (Petrosillo et al., 2020). Out of the many driving factors of the strong transmissibility, cluster infections play critical roles in the rapid evolution of COVID-19 transmission, which exponentially increases the number of cases and drive the new emerging disease to spread worldwide through modern transportation.
COVID-19 is still spreading over the world, countries that are in pandemic should be particularly cautious about cluster infectious in various settings. Governments are advised to track COVID-19 cases and conduct extensive epidemiological investigation as early as possible. Additionally, proper and effective risk communication are essential when taking social restrictions to minimize people’s gatherings (meals, religions, etc.) and journeys outside home. Preventing and controlling the cluster infections of SARS-CoV-2 is an important strategy to contain the spread and to flatten the curve of COVID-19. As we continue to face many challenges on containing this infectious disease, collaboratively work and efforts from global community to reduce cluster infections are particularly important to suppress its spreading.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical approval: Not required.

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Author contributions

TL and DG performed the database research, done the statistical analysis, and wrote the first draft of the manuscript; JX, JH, GH and ZR reviewed the manuscript critically for contents; WM concepted and guaranteed this study. All authors are in agreement with the content of the manuscript and approved the final manuscript.

Competing interests: None declared.
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Kupferschmidt K. COVID-19 Case clustering emerges as key pandemic puzzle. Science


The Novel Coronavirus Pneumonia Emergency Response Epidemiology T. Vital Surveillances: The


To KLA, Fok YYY. Homeopathic Clinical Features of 18 Patients in COVID-19 Outbreaks in Hong Kong. Homeopathy 2020.


Wikipedia. COVID-19 pandemic in Malaysia; 2020. Available from:


Records identified through database search (n = 981)
PubMed: 441
Embase: 224

Additional records identified through other sources

Records screening title and abstract

Records excluded (n = 917):
- Duplicates identified: 500
- Epidemiological characteristics: 90
- Clinical characteristics /therapy: 115
- Spatial analysis: 10
- Policies/recommendations: 54
- Genome and phylogeny: 25

Full-text articles assessed for eligibility

Four articles were excluded because of sharing the

Studies included in this study (n = 65)
Figure 1 Flowchart for literature search and selection in systematic review.
Table 1 Detailed characteristics of studies included in the systematic review

<table>
<thead>
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<th>Study name</th>
<th>Region</th>
<th>Type of cluster</th>
<th>Number of infections involved</th>
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