

Transmission Dynamics of SARS-CoV-2 in a Mid-size City of China

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Research article

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Abstract

Background: An outbreak of pneumonia associated with the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan city and then to other city. It is very urgent to delineate the epidemiological and clinical characteristics of these affected patients.

Methods: To investigate the epidemiological characteristics of the COVID-19, we describe a case series of 459 patients with confirmed COVID-19 in WZ of China from January 27 to February 12, 2020.

Results: The median age of all patients was 48.0 years, and 46.8% were females. 37.5% of patients had a history of residence in Wuhan. Fever (72.1%) and cough (43.6%) were the most frequent symptoms. In addition, three kinds of unconventional cases were observed, in which included 4.4% confirmed virus carrier who were asymptomatic, 7.8% confirmed patients who had no link to Wuhan city but contact with individuals from Wuhan without any symptoms at the time of contact, and 10.7% confirmed patients who had no link to Wuhan city nor a history of intimate contact with patients or individuals from Wuhan without any symptoms, respectively.

Conclusion: Our findings presented the possibility of asymptomatic carriers affected with SARS-CoV-2, and this phenomenon suggested that chances of uncontrollable transmission in the larger population might be higher than formerly estimated, and transmission by these three kinds of unconventional patients in WZ may be one of the characteristics of infection in other Chinese cities outside the Wuhan epidemic area.

Background

It has been a month since a number of life-threatening pneumonia associated with the severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) were reported in Wuhan, China on December 31, 2019[1, 2]. In the past few days, the epidemic was rapidly spread other Chinese cities and circulating in a few other countries in the world [3-5]. An increasing number of epidemiological evidence indicated that person-to-person transmission in hospital and family settings were observed [6-8], suggesting a formidable challenge of prevention and control for this novel coronavirus pneumonia (NCP).

Recently, the World Health Organization had declared the Corona Virus Disease 2019(COVID-19) as a "Public Health Emergency of International Concern" and officially termed this NCP as Corona Virus Disease 2019 (COVID-19). As of February 6, 2020, the Chinese government reported 27,460 confirmed cases in mainland China[9]. Apart from Wuhan city, which including initial epidemic city and its surrounding cities, other major cities in China has been likely to be experience localized outbreaks and other countries[10, 11]. Despite the outbreak propagates worldwide, the clinical characteristics of SARS-CoV-2 have not been fully clarified. Huang *et al* first reported the cases of COVID-19 in which most patients had a history of exposure to a Seafood Wholesale Market [2]. And Wang *et al* identified patients with COVID-19 had common symptoms included fever, fatigue and dry cough[1]. Furthermore, several case reports confirmed the human-to-human transmission [6, 7].

To better understand and control the COVID-19 outbreak, an updated analysis of this epidemic in other China areas is urgently warranted. As of February 8th, except for Hubei Province, the slowdown of the increase rate of confirmed patients and suspected patients, also indicated that the measures and strategies of prevention and control had proven effective [12]. A city (named WZ) of China is a prefecture-level city of Zhejiang province and has been designated as an epidemic area because of the city with the largest number of confirmed cases outside initial epidemic area. There are many people of this city engaged in business so that businessmen of this city are famous and distributed throughout China even the world. The important thing is that many people returned to this city from initial epidemic area before lockdown because of Spring Festival. And there also was evidence that indicated the epidemic situation in some city might potentially shift from the import stage to the community spread stage in the coming time period. And the emergence of unconventional cases also suggested that we need to be alert to the trend of the epidemic shifting from the import stage to the community spread stage, while continuing or implement the measures and strategies of prevention and control to stop the spread of SARS-CoV-2.

Materials And Methods

Data collection

Epidemiological investigators conducted epidemiological survey on confirmed cases for collecting and organizing information and finding close contacts. Then all epidemiological, clinical and laboratory characteristics and outcomes information were published by Municipal Health Commission (**Website:** <http://wjw.wenzhou.gov.cn/col/col1209919/index.html>).

Study definitions

The COVID-19 patient of was determined by a positive result by real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) assay of the SARS-CoV-2 virus in patient's pharyngeal and anal swab specimens. Only the laboratory-confirmed patients were included in the final analysis.

Asymptomatic patient was defined as someone who was patients with no clinical symptoms and a positive result of SARS-CoV-2 on RT-PCR, who were mainly found through close contact screening, cluster epidemic investigation and source trace investigation based on the official document "New coronavirus pneumonia case surveillance program (from Second to Sixth Edition)"[13].

The exposure is defined as the following situations within 14 days before the onset of illness applicable to individuals: 1) traveling to or living in Wuhan or other regions with severe epidemics abroad ; 2) having contact with SARS-CoV-2 infected individuals whose nucleic acid test was positive or with patients who had fever or respiratory symptoms coming from Wuhan or other regions abroad that have been severely affected by the epidemic; 3) having been to 2 or more cases occurred fever or respiratory symptoms in a small area (such as home, office, school class, etc.).

Cluster outbreak was defined that 2 or more cases occurred fever or respiratory symptoms in a small area (such as home, office, school class, workshop, construction site, etc.) within 14 days, which was the possibility of interpersonal transmission and being infectious due to co-exposure.

Close contacts referred to people who had not taken effective protection from close contact with suspected or confirmed case since 2 days before the onset of symptoms or 2 days before the collection of asymptomatic specimens.

Suspected case was defined included epidemiological history and clinical characteristics. For epidemiological history: (1) Having a history of travelling or living Wuhan and surrounding areas, or other communities in China with case reports, or countries or regions with severe epidemics abroad within 14 days before the onset of illness; (2) History of contact with SARS-CoV-2 infected persons (person who nucleic acid test was positive) within 14 days before the onset of illness; (3) History of contact with patients who had fever or respiratory symptoms from Wuhan and surrounding areas, other communities with case reports in China, or countries or regions with severe epidemics abroad within 14 days before the onset of illness; (4) Cluster onset: 2 or more cases occurred fever or respiratory symptoms in a small area (such as home, office, school class, workshop, construction site, etc.) within 14 days. For clinical characteristics: (1) Occurred fever and / or respiratory symptoms; (2) With radiologic imaging features of SARS-CoV-2 pneumonia; (3) The total count of white cells was normal or decreased, or the lymphocyte count was normal or decreased in the early stage of onset; Any one of epidemiological history meets any two of the clinical characteristics; those without a clear epidemiological history meet three of the clinical characteristics. Co-exposed persons are defined as people who shared the same risks of exposure as a suspected or confirmed case of COVID-19.

The unconventional patients included asymptomatic patients, and patients who had no link to Wuhan city but contacted with individuals from Wuhan without any symptoms at the time of contact, and patients who had no known direct source of transmission. **The conventional patients** who had known direct source of transmission and symptoms.

Laboratory confirmation

Laboratory confirmation of the SARS-CoV-2 by RT-PCR assay was conducted in WZ Center for Disease Prevention and Control and the ZJ Provincial Center for Disease Prevention and Control[14]. The RT-PCR assay was performed in accordance with the protocol established by the World Health Organization[15]. SARS-CoV-2 nucleic acid testing was performed using RT-PCR assay according to the National Health Commission guidelines for laboratory testing of pneumonia with novel coronavirus infection(Second Edition, Third Edition) [2].

Statistical analysis

Continuous variables were presented using mean and standard deviation or median and interquartile range (IQR) as appropriate, and categorical variables were described as frequency rates and percentages.

All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 16.0 software (SPS)

Results

Characteristics of time distribution

The first patient (index patient) with COVID-19 was diagnosed on January 21, 2020 in WZ. He, the earliest date of onset patient, recalled his onset date with symptoms to be on January 4, 2020, when he was interviewed by field epidemiologist of WZ Centre for Disease Control and Prevention (WZCDC). The time distribution of all COVID-19 patients was shown by dates of diagnosis in **Figure 1**, The majority of the 490 cases (406 cases, 82.9%) occurred during January 27 and February 7, as shown in the diagnosis dates curve. There were four relatively high peaks on January 28, 29, 30 and February 3, respectively. The number of cases decreased significantly after that.

As of February 12, 2020, 42 out of all 490 confirmed cases were severe, and 398 were mild. There were 89 cases discharged in total, 370 cases staying, and no death occurred in WZ.

Characteristics of the studied patients

As shown in **Table 1** and **Figure 2**, of all 490 patients reported as of January 12 in a city of China, 31(6.3%) patients were excluded due to the complete information (including clinical outcomes and symptoms) of them were not published in time for the day, because the complete information collection and organization needs a certain amount of time, and 459(93.7%) patients had completed characteristics. The median age was 48 years (IQR, 37-56; range, 2-93 years), and 215 (46.8%) were females. The median time from onset to diagnosis was 6.0 days (range: 0-23 days). Of these patients, 42(9.2%) were severe patients and 417(90.8%) were non-severe patients. Fever (72.1%) and cough (43.6%) were the most common symptoms, whereas diarrhea or castalgia (3.3%) were rare. 172 (37.5%) patients had a history of travel or residence to Wuhan. No deaths occurred in the total patients.

Features of Asymptomatic Transmission of SARS-CoV-2 in WZ

The point worth noting about this novel coronavirus pneumonia in WZ city, was that the emergence of three kinds of unconventional cases. As shown in **Table 1**, there were 20 asymptomatic carriers accounted for 4.4% of the total patients, 36 (7.8%) patients who had no link to Wuhan city but contact with individuals from Wuhan without any symptoms at the time of contact and 49 (10.7%) patients who had no known direct source of transmission, which suggests that asymptomatic carriers were also likely to transmit the virus. We divided all patients into two groups, one with a history of residence and travel in Wuhan and other without, and then made a time distribution chart based on the time of onset of diseases. As indicated in **Figure 2**, in addition to the change in daily number of new cases with a history of residence and travel in Wuhan, we can see the change of daily number of new cases with no link to Wuhan. There were 287 cases who had no link to initial epidemic area accounted for 62.5% of 459 cases

and 172 cases had links to initial epidemic area accounted for 37.5%. We described the curve of onset dates for both imported and local cases in **Figure 2**. The earliest onset time of the imported cases was January 4th, with the peak on the January 21. The number of new cases gradually reduced after January 27. The local cases started to onset on January 6, and the peaks on January 26. The number of cases decreased significantly after that. All these evidences indicated that the epidemic situation in this city of China might potentially shift from the import stage to the community spread stage in the coming time period. However, the slowdown of the increase rate of new patients, also indicated that the measures and strategies of prevention and control in this city have proven effective.

An outbreak of infection in a public place

Moreover, there was an outbreak of infection in a public place at the Yintai world trade center. On January 20, a 39-year-old saleswoman went to local hospital for treatment by herself after breaking out with a fever at 38.5° C, accompanied with chills, dizziness and headache, and symptoms of soreness and fatigue. She was subsequently diagnosed COVID-19 on January 28, but the source of which is unknown. As of the date of publication, a total of 16 additional patients resulting from this mall have been confirmed, namely two staff members, two sales persons, one janitor, nine customers, and two individuals outside the mall but close contact with one of the above.

Table 1. Clinical and epidemiological characteristics of the studied patients

Early clinical symptoms	WZ
	n/459(%)
Female sex-No.,%	215/459(46.8%)
Age, Median (range) – years	48.0(2-93)
Travel or residence history within 14 days-No.,%	
Recently been to Wuhan	172/459(37.5%)
Outside Wuhan or WZ city	10/459(2.2%)
No	277/459(60.3%)
Contact with source of transmission within 14 days-No.,%	
Contacted with people from Wuhan	36/459(7.8%)
Contacted with patient	187/459(40.8%)
Related the Yintai world trade center	17/459(3.7%)
Unknow	219/459(47.7%)
Discovered source of transmission	
Undiscovered source of transmission	49/459(10.7%)
Symptoms	
Asymptom-No.,%	20/459(4.4%)
Symptoms	
Fever	331/459(72.1%)
Headache	31/459(6.8%)
Cough	200/459(43.6%)
Sore throat	39/459(8.5%)
Sputum production	49/459(10.7%)
Fatigue	57/459(12.4%)
Diarrhea or castalgia	15/459(3.3%)
Muscle soreness	29/459(6.3%)
Disease severity	
Severe-No.,%	42/459(9.2%)

Clinical outcomes

Discharge from hospital	89/459(19.4%)
Staying in hospital	370/459(80.6%)
Death	0/459(0%)
Time from onset to diagnosis (days)	
Median(range)	6.0(0-23)

Discussion

In the current study with a total of 459 patients with COVID-19 in a city of China, we found that there were the emergence of three kinds of unconventional patients including 4.4% cases with asymptomatic, 7.8% patients who had no link to Wuhan but contact with individuals from Wuhan without any symptoms at the time of contact, and 10.7% cases who had no known direct source of transmission, indicated that the COVID-19 presence and prevalence may be underestimated at present increasing the difficulty of prevention and control.

Along with the epidemic of SARS-CoV-2 spreads rapidly throughout China and worldwide, more concerns and new strategies should be undertaken in the next a few days[16]. It is untoward to differentiate and screen patients with atypical symptoms, and the rapid human-to-human transmission among close contacts is a crucial peculiarity for SARS-CoV-2[7, 17]. A recent study indicated that WZ had become the city with the most patients of SARS-CoV-2 outside of Wuhan in China[12]. In addition, previous studies had reported that asymptomatic transmission of SARS-CoV-2 infection through close contacts in both familial and hospital settings had been observed[18]. Also, clustered outbreaks caused by asymptomatic individuals were reported. Based the fact that the SARS-CoV-2 virus can be positively detected in asymptomatic patients, we could reasonably speculate that these asymptomatic patients may carry a certain amount of active virus in the body and might pollute the surrounding environment, and thus became a potentially threatening source of SARS-CoV-2 infection[19]. In this study, we found a emergence of unconventional patients with COVID-19, and this phenomenon suggested that chances of uncontrollable transmission in the larger population might be higher than formerly estimated, and asymptomatic transmission may be one of the characteristics of infection in other area. There were likely to three aspects of source infection, indirect transmission, aerosol transmission and fecal-oral transmission.

The indirect transmission of the causative virus occurred, maybe resulting from virus contamination of surfaces of objects. The Guangzhou Center for Disease Control and Prevention detected the nucleic acid of SARS-CoV-2 on a doorknob at a patient's house [20]. Researchers have detected SARS-CoV-2 on surfaces of objects in a symptomatic patient's room and toilet area[21]. Guo, et.al tested surface and air samples from an intensive care unit (ICU) and a general COVID-19 ward (GW) at Huoshenshan Hospital in Wuhan, China.[22] The surface of objects positive results were concentrated in the contaminated areas

ICU or GW for floor swab samples, the floor of the pharmacy, the floor of medical staff dressing room, half of the samples from the soles of the ICU medical staff shoes; there were positive results that were frequently touched by medical staff or patients for computer mice, sickbed handrails, doorknobs, patient masks, sleeve cuffs and gloves of medical staff. Hence, SARS-CoV-2 was widely distributed on object surfaces, implying a potentially high infection risk spread via fomites.

The aerosol to mean the small respirable particles <5-10 μ m that can remain airborne and are capable of short and long-range transport. [23-25] Morawska, et.al studies that normal breathing and talking result in size distributions of droplets with the majority, 80-90%, in the <1 μ m range.[26] In the United States, the likelihood of an airborne aerosol form of active SARS-CoV-2 was the Skagit Valley Chorale rehearsal in Mount Vernon, Washington, that took place on March 10, implying the forceful breathing action of singing may have increased dispersion of the virus at the church.[27] Tang et al found for SARS-CoV-1 that “particles of diameters 1-3 μ m remained suspended almost indefinitely, 10 μ m took 17 min, 20 μ m took 4 min, and 100 μ m took 10 seconds to fall to the floor”. [28] Pathogen-bearing droplets are reported to travel up to 23-27 feet, with droplet size, turbulence, speed of the gas cloud, humidity, and temperature being important factors for the distance travelled.[29] long-range aerosol transport was implicated as the cause of the spread of the disease in several studies. For the aerosol and surface stability of virus, SARS-CoV-2 can remain viable and infectious in aerosols for hours and on surfaces up to days, so aerosol and contact transmission of the virus is reasonable. [30]

SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV), are known to cause respiratory and enteric symptoms. In the SARS outbreak of 2002-03, 16%-73% of patients with SARS had diarrhea during the course of the disease. [31] 138 consecutive hospitalized patients with COVID-19, investigators reported that approximately 10% of patients initially presented with gastrointestinal symptoms, prior to the subsequent development of respiratory symptoms. [32] Studies have identified the SARS-CoV-2 in anal/rectal swabs and stool specimens of COVID-19 patients, even after the clearance of the virus in the upper respiratory tract.[33-37] The viral receptor angiotensin converting enzyme 2 (ACE2) was found to be expressed in gastrointestinal epithelial cells. [38, 39] So that SARS-CoV-2 can actively infect and replicate in the gastrointestinal tract. Although there been no solid evidence to confirm that SARS-CoV-2 can be transmitted through the fecal-oral route, this possibility exists as the virus has been successfully isolated in a stool or anal swab of patients with COVID-19, which is almost as accurate as a pharyngeal swab.

The epidemic characteristics of SARS-CoV-2 in WZ may be typical of the outbreaks in other Chinese cities outside of Wuhan. Besides, since the outbreak of SARS-CoV-2 in a public place in WZ city occurred, this is a typical incidence of outbreak that should be of great concern.

The epidemic situation might potentially shift from the import stage to the community spread stage in the coming time period. Although the slowdown trends of the increase number of new patients in recent days, we need to find and control the infection source of patients affected with SARS-CoV-2[8, 40]. In light of the emergence of unconventional patients, and Diagnosis and Treatment of Pneumonitis Caused by

New Coronavirus (trial version 5) published by China National Health Commission [14] indicated that asymptomatic infected individuals may also be the source of infection, and there were evidences that asymptomatic infections has a certain infectivity[8]. Based on the above, it suggested that suspected patients should include patients with clinical symptoms and who, in the history of epidemiology, intimate contact with individuals from Wuhan, although these individuals from Wuhan are not confirmed cases and without any symptoms at the time of contact. So far, our understanding of the epidemic characteristics of SARS-CoV-2 is still insufficient, and we still need to track the development closely, further collect and analyze information through epidemiological investigations.

Our study had some obvious limitations. Firstly, the case information of WZ was extracted from the website of Wenzhou Health Commission, which were incomplete (38 cases) in the early stage of the epidemic. Secondly, it is necessary to dynamically observe for a period of time to determine whether without symptomatic patients is asymptomatic and pro-symptomatic. We did not have dynamic observation therefore we could not distinguish the asymptomatic and pro-symptomatic patients. Lastly, our study was based on case report data, which were more likely to report patients with severe or obvious symptoms resulted in the proportion of asymptomatic infections was underestimated.

Conclusions

In summary, the epidemic characteristics of SARS-CoV-2 in WZ may be typical of the outbreaks in other Chinese cities outside of Wuhan. The asymptomatic infected individuals have a certain infectivity and may be the source of infection. There were likely to indirect transmission, aerosol transmission and fecal-oral transmission.

Therefore, we need to be alert to the trend of the epidemic shifting from the import stage to the community spread stage, while continuing or implement the measures and strategies of prevention and control to stop the spread of SARS-CoV-2.

Abbreviations

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2

NCP: Novel coronavirus pneumonia

COVID-19: Corona virus disease 2019

IQR: Interquartile range

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Guangzhou Medical University. We collected data from the official website of Municipal Health Commission (**Website**: <http://wjw.wenzhou.gov.cn/col/col1209919/index.html>), which was considered exempt from approval.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare no competing interests.

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Authors' contributions

HJZ and JCL designed the study. BQR collated the data, and TGL analyzed epidemiologic data. DDW and DW contributed to interpreting the results.

HJZ wrote the manuscript and analyzed the results. XXL, FMQ and ZCY revised the manuscript. All authors read and approved the final manuscript.

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Figures

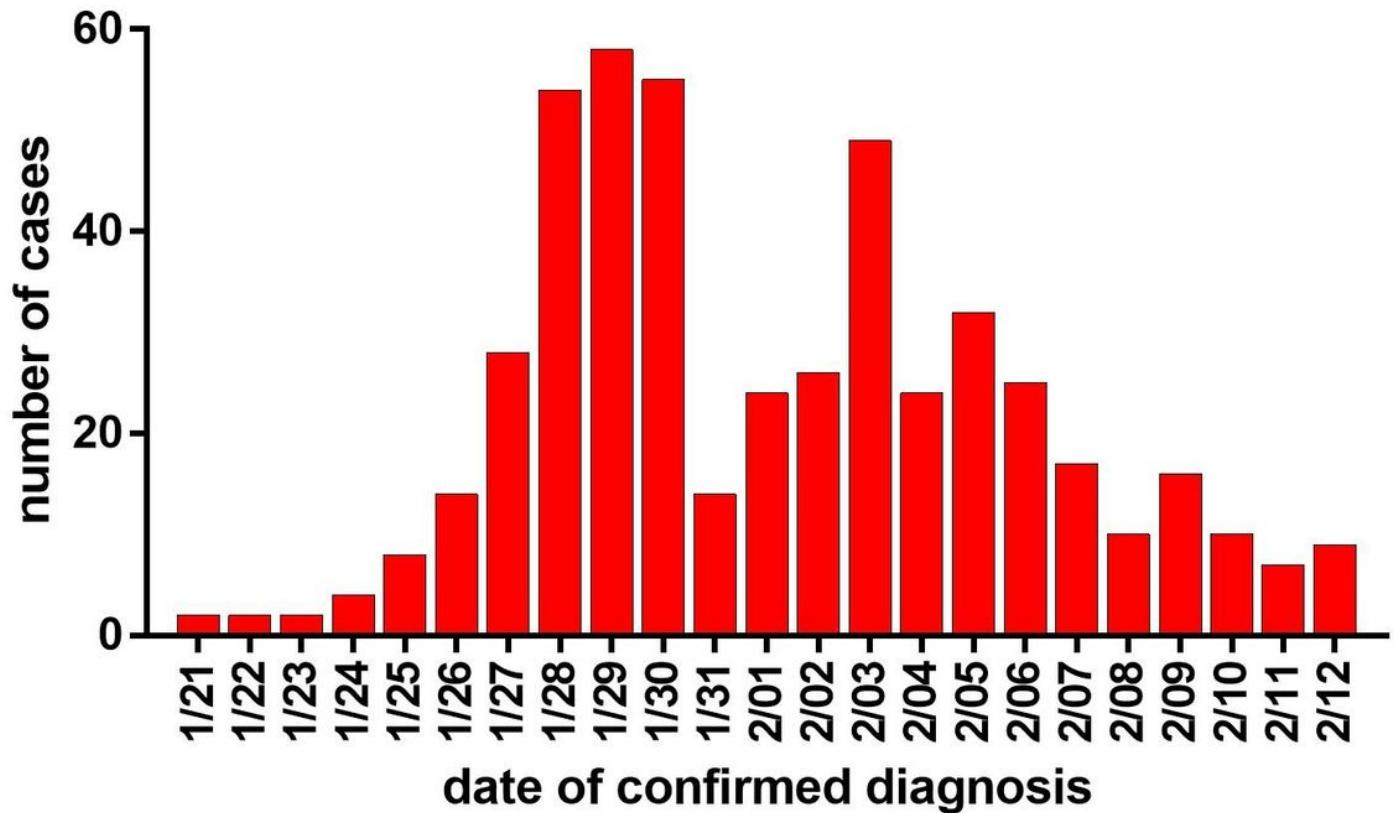


Figure 1

The dates of diagnosis distribution of cases

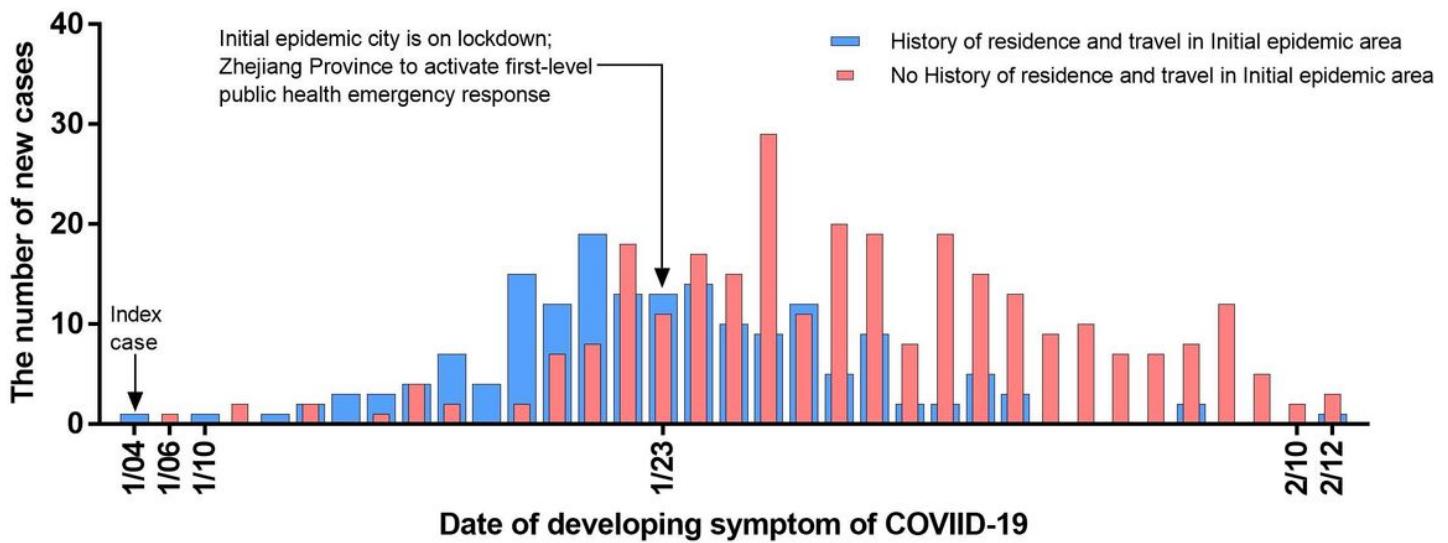


Figure 2

The time distribution of imported and local cases