

A New Features of SARS-CoV-2 Infection in a City of China

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Research article

Keywords: Severe acute respiratory syndrome coronavirus 2(SARS-CoV-2), Coronavirus Disease 2019 (COVID-19), Asymptomatic patient

Posted Date: April 14th, 2020

DOI: <https://doi.org/10.21203/rs.2.23945/v2>

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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, a cross-sectional study was executed with 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.

CONCLUSIONS: 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 6th, 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

The case with SARS-CoV-2 was confirmed by high-throughput sequencing or real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay performed by the local Center for Disease Control and Prevention or designated hospital of COVID-19 according to the official guidelines[13]. 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>). The patients were divided into severe and non-severe groups according to the American Thoracic Society guideline on admission[14].

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)"[15]. 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 link to Wuhan city nor a history of intimate contact with patients or individuals from Wuhan without any 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. The RT-PCR assay was performed in accordance with the protocol established by the World Health Organization[16]. 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 (SPSS Inc).

Results

Characteristics of the studied patients

As shown in **Figure 1**, of all 490 patients reported as of January 12th 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 and were described in **Table 1**. 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.

New features of SARS-CoV-2 in WZ differing from Wuhan

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** and **Figure 2**, 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 link to Wuhan city nor a history of intimate contact with patients or individuals from Wuhan without any symptoms, 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 one without, and then made a time distribution chart based on the time of onset of diseases. As indicated in **Figure 3**, 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%. It was five days that between the peak of daily number of new cases who have no link to initial epidemic area and who have link to initial epidemic area. On January 23, initial epidemic city was on lockdown by government of China so that the daily number of new cases who had link to initial epidemic area decreased gradually. And on the same day, Zhejiang Province activated first-level public health emergency response so that the daily number of new cases who had no link to initial epidemic area begun to decreased gradually after three days. 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. (**Figure 1**).

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 (**Figure 4**). 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.

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 link to Wuhan nor a history of intimate contact with patients or individuals from Wuhan without any symptoms, indicated that the COVID-19 presence and prevalence may be underestimated at present.

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[17]. 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, 18]. 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[19]. 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[20]. 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. 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, 21]. 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 [13] 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.

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. 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.

Funding

This study was supported by the National Natural Science Foundation of China 81872694, 81673267 and 81473040 (J. Lu); 81602289 and 81872127 (F. Qiu).

Local Innovative and Research Teams Project of Guangdong Pearl River Talents Program 2017BT01S155(J Lu); Health Industry Scientific Research Project of Gansu Province GSWSKY2018-18(H Zhao). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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.

Acknowledgements

Not applicable.

References

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, Wang B, Xiang H, Cheng Z, Xiong Y et al: Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA 2020.

2. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X et al: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020.
3. Rodriguez-Morales AJ, MacGregor K, Kanagarajah S, Patel D, Schlagenhauf P: Going global - Travel and the 2019 novel coronavirus. *Travel Med Infect Dis* 2020:101578.
4. Ki M, nCo VT: Epidemiologic characteristics of early cases with 2019 novel coronavirus (2019-nCoV) disease in Republic of Korea. *Epidemiol Health* 2020:e2020007.
5. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, Hu Y, Tao ZW, Tian JH, Pei YY et al: A new coronavirus associated with human respiratory disease in China. *Nature* 2020.
6. Chan JF, Yuan S, Kok KH, To KK, Chu H, Yang J, Xing F, Liu J, Yip CC, Poon RW et al: A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020.
7. Phan LT, Nguyen TV, Luong QC, Nguyen TV, Nguyen HT, Le HQ, Nguyen TT, Cao TM, Pham QD: Importation and Human-to-Human Transmission of a Novel Coronavirus in Vietnam. *N Engl J Med* 2020.
8. Rothe C, Schunk M, Sothmann P, Bretzel G, Froeschl G, Wallrauch C, Zimmer T, Thiel V, Janke C, Guggemos W et al: Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. *N Engl J Med* 2020.
9. National Health Commission of the People's Republic of China: <http://www.nhc.gov.cn>. Assessed 7th February, 2020.
10. Kui L, Fang YY, Deng Y, Liu W, Wang MF, Ma JP, Xiao W, Wang YN, Zhong MH, Li CH et al: Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province. *Chin Med J (Engl)* 2020.
11. Battegay M, Kuehl R, Tschudin-Sutter S, Hirsch HH, Widmer AF, Neher RA: 2019-novel Coronavirus (2019-nCoV): estimating the case fatality rate - a word of caution. *Swiss Med Wkly* 2020, 150:w20203.
12. National Health Commission of the People's Republic of China: <http://www.nhc.gov.cn>. Assessed 8th February, 2020.
13. Lin L, Li TS: [Interpretation of "Guidelines for the Diagnosis and Treatment of Novel Coronavirus (2019-nCoV) Infection by the National Health Commission (Trial Version 5)"]. *Zhonghua Yi Xue Za Zhi* 2020, 100(0):E001.
14. Metlay JP, Waterer GW, Long AC, Anzueto A, Brozek J, Crothers K, Cooley LA, Dean NC, Fine MJ, Flanders SA et al: Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med* 2019, 200(7):e45-e67.
15. National Health Commission of the People's Republic of China. New coronavirus pneumonia case surveillance program. <http://www.nhc.gov.cn>.
16. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance.

(<https://www.who.int/docs/default-source/coronaviruse/clinical-management-of-novel-cov.pdf>. opens in new tab). January 28, 2020.

17. Novel coronavirus (2019-nCoV): **Situation Report-23**. 12 February 2020. Geneva: World Health Organization.
18. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, Ren R, Leung KSM, Lau EHY, Wong JY et al: Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. *N Engl J Med* 2020.
19. Li C, Ji F, Wang L, Wang L, Hao J, Dai M, Liu Y, Pan X, Fu J, Li L et al: Asymptomatic and Human-to-Human Transmission of SARS-CoV-2 in a 2-Family Cluster, Xuzhou, China. *Emerg Infect Dis* 2020, 26(7).
20. Mao ZQ, Wan R, He LY, Hu YC, Chen W: The enlightenment from two cases of asymptomatic infection with SARS-CoV-2: is it safe after 14 days of isolation? *Int J Infect Dis* 2020.
21. Nishiura H, Kobayashi T, Yang Y, Hayashi K, Miyama T, Kinoshita R, Linton NM, Jung SM, Yuan B, Suzuki A et al: The Rate of Underascertainment of Novel Coronavirus (2019-nCoV) Infection: Estimation Using Japanese Passengers Data on Evacuation Flights. *J Clin Med* 2020, 9(2).

Table

Table 1. The clinical characteristics of patients with SARS-CoV-2 infection.

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%)
Uncontacted	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)

Figures

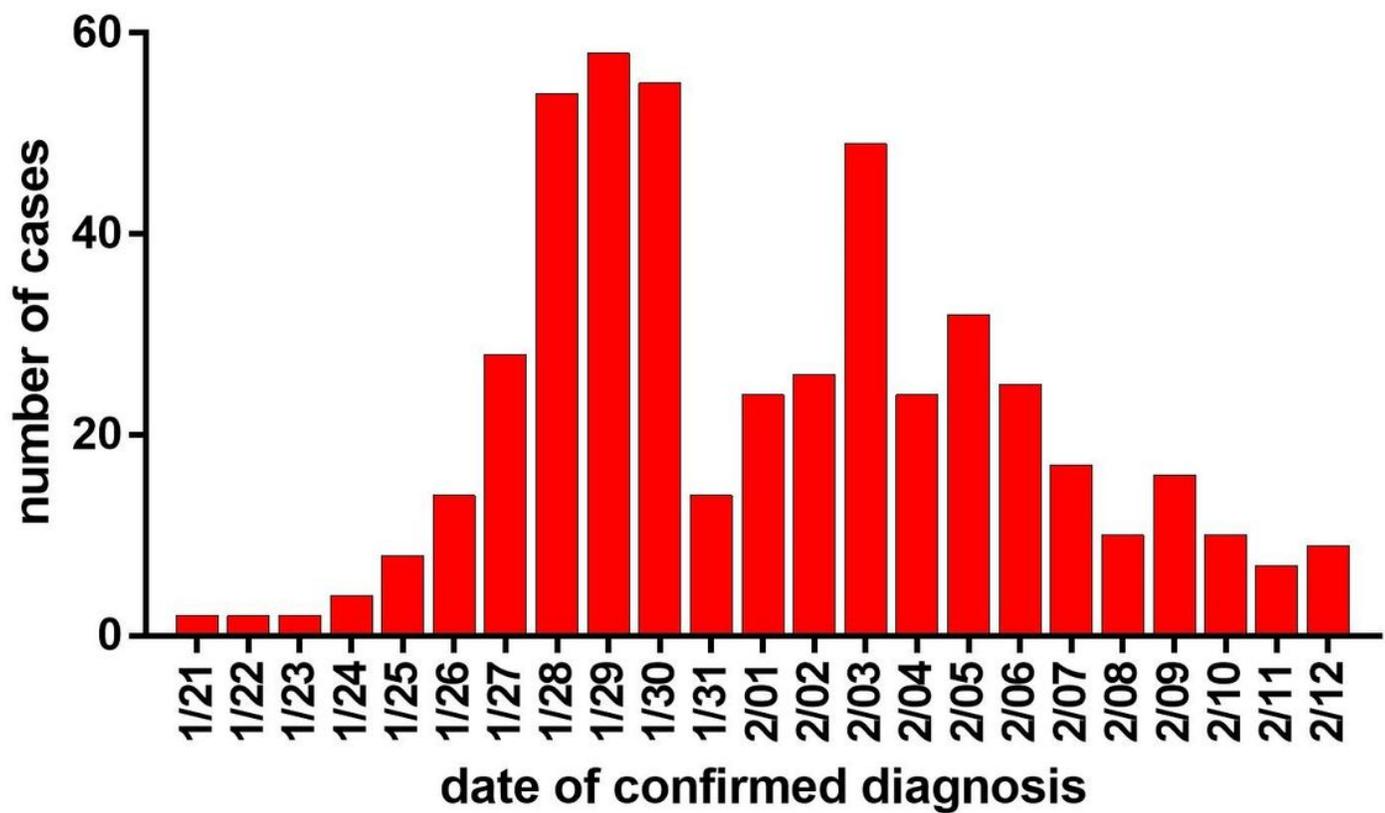


Figure 1

According to the date of confirmed diagnosis, the temporal distribution of confirmed cases by the nucleic acid detection by RT-qPCR.

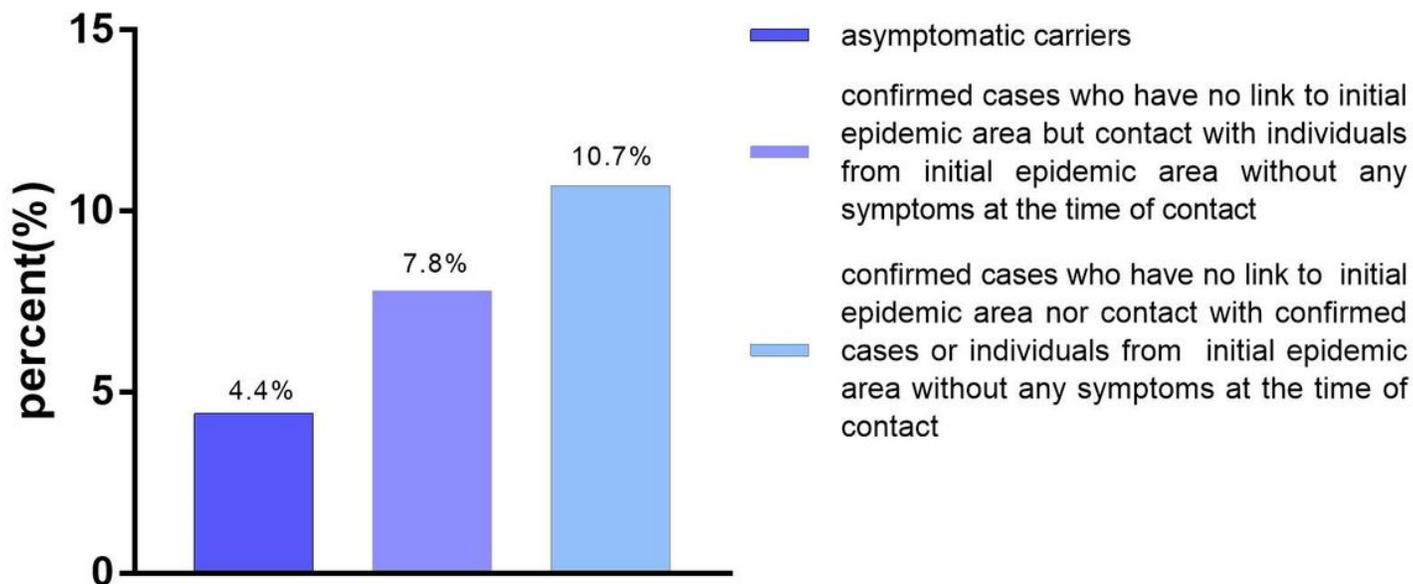


Figure 2

The emergence of three kinds of un conventionally confirmed cases with COVID-19.

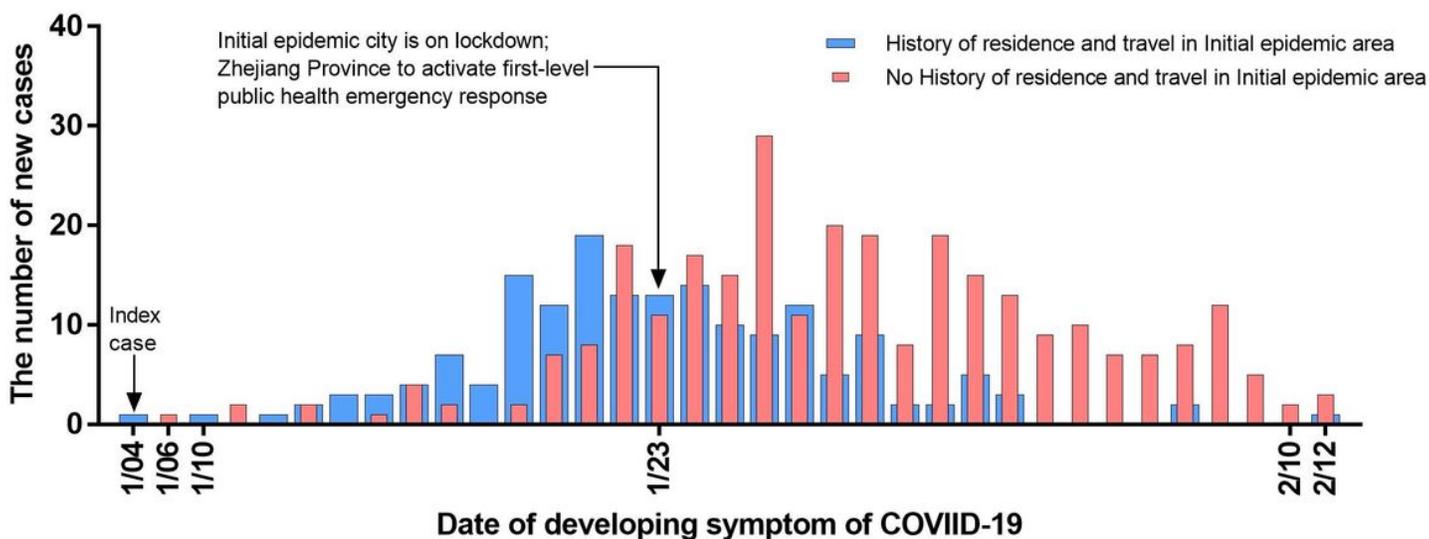


Figure 3

According to the date of onset of symptoms, the temporal distribution of cases with and without a history of residence and travel in Wuhan.



Figure 4

An outbreak of infection in a public place at the Yintai world trade center in WZ city.