

Descriptive study of the first 63 cases of the ongoing SARS-CoV-2 outbreak at the transportation hub city Xuzhou in China

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Abstract

A novel coronavirus (SARS-CoV-2) outbreak from Wuhan, China has, as of February 13, 2020, infected nearly 60,000 people in China with the death toll passing 1300. The virus is also spreading worldwide rapidly, with 490 confirmed cases in 24 countries and 1 death at current stage. Numerous studies have recently been published in terms of genome structure, transmission, infection mechanism, and drug development of the SARS-CoV-2 virus. In this study, we performed a descriptive study by focusing on the first 63 confirmed COVID-19 cases in Xuzhou, a major city and a transportation hub with 10.44 million population (National Bureau of Statistics of China, 2019) on the east coast of China. Among the 63 patients with confirmed COVID-19, the median age is 45-year-old and 49.21% are male. 23 cases (36.51%) are imported. 23 cases (36.51%) were confirmed between from January 26 to 31 while 40 cases (63.49%) from February 1 to 10. The mean period from isolation to confirmation is 4.95 days. Among the ten administrative divisions of Xuzhou city, Suining county (n=17) and Pizhou City (n=15) have the most cases while Tongshan district has none. A representative familial cluster was analysed in detail in order to get a better understanding of the transmission routes of the virus. Clinical symptoms associated with COVID-19 in 41 confirmed cases were analysed, which could provide a meaningful understanding during the initial screening of the disease. In sum, this study provides an epidemiological overview of the SARS-CoV-2 outbreak in Xuzhou, the economic hub of Huaihai Economic Zone (HEZ) and an important transportation center in China. Considering the ongoing situation of this newly emerged infection both domestically and internationally, more efforts should be required to reduce the transmission of the virus so as to avoid further casualties, economic losses, and global pandemic.

Authors Liang Wang, Jiawei Yan, and Zhanzhong Liu contributed equally to this study.

Introduction

A novel coronavirus pneumoniae outbreak, previously abbreviated as novel coronavirus pneumoniae (NCP) by China National Health Commission (CNHC) and now officially named by WHO as COVID-19¹, has been traced back to Huanan (Southern China) seafood wholesale market in Wuhan, China². This coronavirus, temporarily known as 2019-nCoV, has now been entitled by WHO as severe acute respiratory syndrome-related coronavirus 2, or SARS-CoV-2 because it is confirmed as a variant of the SARS-CoV³. According to the real-time data released by CNHC, the virus has causes nearly 60,000 infections with death toll passing 1300 as of February 13, 2020. The outbreak has led to the spread of SARS-CoV-2 into all 34 provincial administrative divisions (23 provinces, 4 autonomous regions, 5 municipalities, 2 special administrative regions) in China. In addition, 490 more cases have also been identified in 24 countries with 1 death in Philippines. The rapid spread of the virus is partially due to the role of Wuhan, capital city of Hubei province, as a major hub of road, rail and flight and also due to the annual Spring Festival travel rush starting from Jan 10, 2020 at the time of the outbreak. Basic reproduction number R_0 , a parameter for describing the contagiousness or transmissibility of an infectious agent⁴, was estimated by using exponential growth model method⁵. Current estimation of R_0 for SARS-CoV-2 ranges from 2.24 to 3.58

⁵, which is generally similar with SARS-CoV ⁶. However, based on epidemiological analysis, the fatality rate of SARS-CoV-2 (2%) is much lower than SARS-CoV (9.6%) ⁶. Thus, as far as we know, the novel SARS-CoV-2 outbreak is highly contagious and less fatal.

Unbiased whole genome sequencing of samples from patients with pneumonia, via a combination of Illumina and Nanopore platforms, revealed that SARS-CoV-2 is similar with some betacoronavirus detected in bats and forms a clade within the subgenus sarbecovirus, Orthocoronavirinae subfamily ⁷. Further sequencing analysis decoded another ten complete SARS-CoV-2 genome, revealing that the virus is about 88% similar to bat-SL-CoVZC45 and bat-SL-CoVZXC21, two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses while more distantly related with SARS-CoV and MERS-CoV ⁸. Thus, it was indicated that the original host of SARS-CoV-2 could be bats. Normally, intermediate host is likely to be involved in the cross-species transmission of novel human viruses, which is the case for 2003 SARS-CoV outbreak ⁹. A new study focusing on the recombination of spike glycoprotein in SARS-CoV-2 indicated that intermediate host for SARS-CoV-2 could be snake ¹⁰ while another yet to be published metagenomics study suggested that pangolin facilitates the cross-species transmission, both of which, however, caused concerns and criticism due to lack of solid scientific evidence ¹¹. Except for the origin, transmission, and evolution of the novel coronavirus, some studies also pay close attention to the infection mechanisms of the virus and it is currently proposed that binding of the virus to the angiotensin-converting enzyme 2 (ACE2) receptor in humans leads to infection ⁸.

Since the virus continues expanding and the outbreak is still ongoing, epidemiological analysis of the infected population is essential to understand the outbreak, which will also facilitate the virus control management. So far, most of the studies focus on cases in the cities of Hubei province like Wuhan, the center of the outbreak ^{2,6,7,12} while less studies are about other areas, such as prefecture-level cities in China. Xuzhou is a major city with around 10.44 million registered population and 8.8 million resident population; its GDP in 2018 reaches 680 billion RMB and ranks 33 out of 100 major cities in China, according to the newest 2019 Xuzhou Statistical Yearbook. Xuzhou is the center of the Huaihai Economic Zone that includes 18 prefecture-level cities and is an important transportation hub. According to Chinese government report, total railway mileage in Xuzhou is 546.56 kilometers, of which 396.26 kilometers are ordinary railways and 150.3 kilometers are high-speed railways. As a high-speed railway hub, Xuzhou has constructed a strategic radiation layout via 4 high-speed rails, forming a one-hour living circle with 4 provincial capital cities such as Nanjing (Jiangsu Province), Zhengzhou (Henan Province), Jinan (Shandong Province), and Hefei (Anhui Province). In addition, it takes passengers within three hours from Xuzhou to the five major cities in China, that is, Beijing, Xi'an, Wuhan, Shanghai, and Hangzhou via high-speed network, which provides strong support for the central role of Xuzhou in Huaihai Economic Zone. It is also noteworthy that there are multiple trains between Xuzhou and Wuhan each day, which shows the tight linkages between the two industrial cities in terms of population, culture, and economy. Thus, it would be interesting to explore the outbreak of COVID-19 in Xuzhou.

A total of 63 confirmed cases have been reported in Xuzhou, among which, there were 61 mild cases, 1 severe case, and 1 critically severe case, as of Feb 10, 2020. Currently, 1920 close contacts of the 63 confirmed cases have been traced, among which, 1263 medical observations have been made while 657 are still having medical observations. Although global real-time data for the outbreak is publicly available, there is no detailed analysis of infected COVID–19 cases in Xuzhou. In this project, we performed a descriptive study of all confirmed cases as of Feb 10, 2020 in Xuzhou and provided an epidemiological overview of the disease in the prefecture-level city. In addition, we focused on one representative familial cluster in order to better understand how the virus is transmitted. Associated symptoms of 41 confirmed COVID–19 cases via corresponding medical records were also summarized. Through this study, a better understanding of the COVID–19 disease in Xuzhou will be achieved, which might also facilitate epidemic prevention of SARS-CoV–2 in local areas.

Methods

For the descriptive study, all cases diagnosed and confirmed from Jan 26 to Feb 10, 2020 at Xuzhou were included. All patients were confirmed as SARV-CoV–2 positive according to the Xuzhou Center for Disease Control and Prevention (Xuzhou CDC). Epidemiological data used in this study were sourced from Xuzhou Statistical Bureau and Xuzhou CDC. Clinical, laboratory, management, and outcome data were collected from anonymous electronic medical records with the removal of patients' private information (name, age, gender and address, *etc.*) at Xuzhou Infectious Diseases Hospital. This study was approved by the Ethics Committee of Xuzhou Medical University.

Procedures

All epidemiological data were followed up to Feb 10, 2020. Laboratory confirmation of SARS-CoV–2 was stipulated via nucleic acid test (real-time fluorescent RT-PCR) as stated by Xuzhou CDC.

Statistical analysis

All statistical analyses such as cumulative growth curve, average, mean, and histogram were performed in R package and Excel. R, Excel, and PowerPoint were used for all data visualization and transmission route illustration.

Results

Geographic analysis of the 63 confirmed COVID–19 patients reveals that these cases are not evenly distributed among the 10 administrative divisions in Xuzhou. Suining County has the highest confirmed cases of 17. Among these cases, only one case is confirmed as imported (case #P23). Pizhou City has 15 confirmed COVID–19 patients, the second highest among all divisions, among which 9 cases were imported. Both Pei County and Jiawang District has 7 cases, with 4 and 2 imported cases for each of

them, respectively. They are then followed by Yunlong District and Quanshan District with 5 cases each. Both of them have 2 imported cases. In addition, Gulou District has 3 cases with 1 imported case. As for Xinyi City and Feng County, each has only 2 confirmed cases while Tongshan District has no confirmed case. Cases in Xinyi City were both imported while Feng County has no imported cases. For details, please refer to *Figure 1a*. In addition, we compared the resident population for each administrative division in terms of the number of all confirmed cases and the number of imported cases (*Figure 1b*). Known clustered cases are also present in *Figure 1c*.

In order to understand the relationship between resident population and the number of confirmed cases, we compared the imported and local cases in terms of resident population for each administrative division. Pizhou City and Suining County ranks first and fourth in terms of their population and they have the most infected cases. Pizhou City has both high imported cases and locally transmitted cases caused by a familial cluster (green dots in *Figure 1c*). As for Suining County, it has highest number of infections with only one imported case, which indicated high rate of local transmission. However, the imported case has only infected one individual via close contact while no clear transmission routes available for other infected cases. The possible reason is that Suining County is bordered with Gengche Town, Sucheng District, and Suqian City. People move very frequently in this area and the risk of infection greatly increases. In contrast, population in Tongshan District ranks the third of the 10 administrative divisions. However, no confirmed case was reported. One possible reason is that both annual GPD (10,906 million yuan in 2018) and electricity usage (72.785 million kWh in 2018) in Tongshan district are the highest than other administrative divisions, which indicates strong economy in this area. Thus, there might be less population movement. Hence less infected cases. Resident population alone is not sufficient to explain the number of infected cases and other factors should be included for consideration such as transportation, population movement, and family gathering, *etc*.

In order to get a better understanding of the overall trends and dynamic changes of all the confirmed cases as of Feb 10, 2020 in Xuzhou, we analyzed daily new cases and visualized it in the form of a cumulative growth curve. The general trend of all the cases in *Figure 2* shows an approximately linear relationship with time (No. of Cases = $4.07 \times \text{Time}$) and the R-squared value (R^2) is equal to 0.9883. The equation indicates that 4.07 new cases emerge every day in theory. R^2 is a statistical measure that represents the proportion of the variance for a dependent variable that is explained by an independent variable in this linear regression model. Here it means that Time and No. of Cases are highly correlated in a linear mode. On the other hand, linear, polynomial, and logarithmic regressions show no specific patterns for the changing dynamics among daily new cases due to very small R^2 values.

At Feb 5, Feb 9, and Feb 10, 3 patients, 5 patients, and 2 patients were fully recovered and discharged from hospitals (*Figure 2*). For details of the 10 discharged cases, please refer to *Supplementary Table 1*. In particular, Case #P1 was confirmed on Jan 26 via the nuclei acid test of real-time fluorescent RT-PCR and chest CT showing thickening of the lungs and patchy shadows. After 15 days on Feb 9, #P1 was fully recovered and discharged from the hospital. Cases #P4, #P6, #P7, #P8 were all confirmed positive on Jan 27 and later discharged on Feb 9. Their duration of recovery was 14 days. As for cases #P10 and

#P15, it took 8 days for them to recover from the infection while cases #P18 and #P20 were fully recovered in 12 days. Case #P31 was discharged from hospital in 4 days after confirmed infection. In sum, recover time is variable and the averaged recover period is 11.5 days, based on the limited number of discharged cases in this study (*Figure 3*). However, the heterogeneity of the recovery time in population is rather complex and needs further exploration in future studies.

We also performed demographic analysis in terms of age and gender of all the patients so as to understand the features of the infected and susceptible people in the population. In addition, whether the cases were imported or infected locally due to close contact with confirmed case(s) were also analyzed, which could provide a guidance for effective management of the outbreak locally. For details, please refer to *Supplementary Table 2*. According to the result (*Figure 4*), the ages of the infected people range from 13-year-old to 80-year-old with most cases (n = 21) in 40–50 years old. The median age of the infected people is 45-year-old. As for the gender, there are 31 male cases (49.21%) and 32 female cases (50.79%). Thus, there is no gender bias in the confirmed cases. In terms of the infection types, 23 cases (36.51%) were imported while 40 cases (63.49%) were locally infected. Thus, local transmission could be the main reason for the continuously increasing number of infected patients. Thus, the city lockdown policy and the closed-off management of communities currently carried out in many areas in China is important to avoid further spread of the virus.

In order to understand what the COVID–19 associated symptoms are after SARS-CoV–2 infection for Xuzhou cases, we collected 41 anonymized medical records from Xuzhou Infectious Diseases Hospital associated with the cases and extracted 12 indicators for assessment (*Supplementary Table 3*). According to the result, the main symptom is cough (24 [58.54%] of 41), which is followed by other symptom such as rough breath (14 [34.15%]), short breath (13 [31.71%]), fever (13 [31.71%]), chest tightness (11 [26.83%]), sputum (10 [24.39%]) and fatigue (10 [24.39%]). 7 [17.07%] cases have watery stool and 4 [9.76%] cases have headache. COVID–19 does not influence appetite much (3 [7.32%]) and infrequently leads to rales (3 [7.32%]). All urine samples (n = 41) from confirmed cases tested normal.

Among the 63 confirmed cases, we identified 11 clusters with clear case contact history (*Figure 1c*). In order to get a better look of how virus transmits among cases, we studied in details of a representative familial cluster in Pizhou City, Xuzhou (*Figure 5*). A family of three (#P8: father, #P45: mother, #P13: child) drove from Wuhan back to Pizhou on Jan 20, 2020. They had a family gathering with #P11 (mother of #P8), #P12 (father of #P8), and #P14 (sister of #P8) on Jan 21. #P8 felt uncomfortable on Jan 22, took infusion treatment at local clinics on Jan 23, and was isolated on Jan 24 due to lung infection. #P8 was finally confirmed positive through nucleic acid test on Jan 27. As a close contact of #P8, #P45 was isolated on Jan 26 and tested positive on Feb 04. As for #P11, #P12, #P13, and #P14, they were all tested positive on Jan 29.

Discussions

SARS-CoV-2 is a single-strand and positive-sense RNA betacoronavirus, which is previously unknown and has recently been identified as the causing agent of COVID-19⁸. The first genomes of SARS-CoV-2 have been successfully decoded⁷. Another study analyzed 10 SARS-CoV-2 genomes that share 99.98% similarity⁸ and concluded that SARS-CoV-2 should be originated from one source within a very short period when considering the fast mutation rate of the virus (10^{-4} nucleotide substitutions/site/year)⁸. Initially, due to the limited number of infected cases ($n = 41$), it was only postulated that SARS-CoV-2 could be transmissible from human to human². Later, it was confirmed that human-to-human transmission of the virus occurred since the middle of December 2019 through a study of 425 cases¹³. Compared with 8098 cases and 9.6% mortality of the SARS-CoV outbreak in 2003, it has been known now that SARS-CoV-2 appears clinically milder and is highly contagious via human-to-human transmission¹⁴. It was also suggested that human coronavirus could be spread via droplets, contaminated hands or surfaces and its environmental survival on inanimate surfaces could be up to 9 days¹⁵. Thus, it would be important to clean environmental surfaces with water, detergent, and hospital-level disinfectant¹⁵. However, the data should be interpreted carefully because there is currently no available data as such for SARS-CoV-2, though such information is urgently needed for guiding the public health policy and virus control management.

A recent epidemiological analysis of 1099 cases from 552 hospitals in 31 provinces/provincial municipalities until January 29th, 2020 showed an overview of the infected population as median age 47 years, ratio of male and female cases 1.39, and mortality 1.36%¹⁶. In addition, the median incubation period ranges from 0 to 24 days with a median of 3 days¹⁶. So far, most of the confirmed cases are in Wuhan, Hubei province, the center of the outbreak. Our study based on 63 random cases in Xuzhou showed similar findings with some variations, such as median age of infected population at 45 years old and the ration of male and female case at 0.97. In addition, mean time from isolation to confirmation was 4.95 days and there is no mortality for all the infected cases in Xuzhou. Variations between the two studies could be attributed to the different sample sizes. In addition, public health policy and management of local government, together with cultural characteristics could also lead to differential features of the infected cases.

Clustered cases have also been reported in China and overseas^{12,17}. In this study, we identified 11 clustered cases and reported one representative familial cluster in detail. The familial cluster was caused by close contacts with imported cases, which indicates the importance and necessity of the isolation/quarantine policy at current stage to avoid more infected cases. Due to the limitation of available medical records and clinical samples, we cannot track the virus at molecular level via genomic and phylogenomic analysis. Meanwhile, rapid detection and confirmation of suspected cases are also important to control the spread of the virus.

Previous study confirmed that common symptoms at onset of illness due to SARS-CoV-2 infection include fever (40 [98%] of 41 patients), cough (31 [76%]), and fatigue (18 [44%]) while sputum (11 [28%] of 39), headache (3 [8%] of 38), haemoptysis (2 [5%] of 39), and diarrhoea (1 [3%] of 38) are less common

². In our study, we noticed that fever is only present in 31.71% cases while cough is the most obvious symptom. A reason for the symptom difference might be due to the different clinical conditions of the two studied groups. The 41 cases in previous study were the first infected patients and had serious, sometimes fatal, pneumonia, among which 27 were exposed to Huanan seafood market ². However, all patients studied in Xuzhou were mild cases with stable life conditions. It is noteworthy that asymptomatic cases or cases with mild symptoms could pose a high risk since some of them cannot be detected by handheld thermometers or infrared body temperature scanners. Thus, it is urgent to develop novel detection methods to avoid further spread of the virus. T also justifies the lockdown policy of the Chinese government so as to avoid further endemic of SARS-CoV-2 both domestically and internationally.

Conclusion

SARS-CoV-2 is a novel coronavirus that is possible to cause severe respiratory illness similar to SARS-CoV. Since its outbreak in late December 2019, it has caused endemic in 34 provincial divisions in China and spread rapidly to 24 foreign countries. Although many researchers are currently working on SARS-CoV-2 intensively, there are still many gaps in our knowledge in terms of origin, evolution, transmission, molecular mechanism, and clinical outcome of the virus. In this study, we performed a descriptive study of the first 63 cases confirmed in Xuzhou, an important transportation hub city in China. Through dissection of case distribution patterns, features of infected individuals, clustered cases, and clinical symptoms, we have an overview of how SARS-CoV-2 starts and spreads in a prefecture-level city, which is helpful for us to gain a better understanding of the outbreak. It is also noteworthy that the low rate of fever in confirmed cases should draw more attention for public health policy maker because high body temperature is currently used as a screening method in public places for suspected cases. In addition, rapid virus detection kit should be developed to facilitate the screening and confirmation of suspected/asymptomatic cases. Further study should also focus on the virus genomes of confirmed cases in Xuzhou in order to understand how the virus is transmitted locally and evolves at molecular level during transmission and intracellular replication.

Declarations

Conflict of Interest

The authors declare that there is no conflict of interest in the study.

Ethical Statement

All procedures were performed in accordance with the ethical standards of Ethics Committee at Xuzhou Medical University. Informed consent was obtained from all patients or if subjects are under 18, from a parent and/or legal guardian.

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Figures

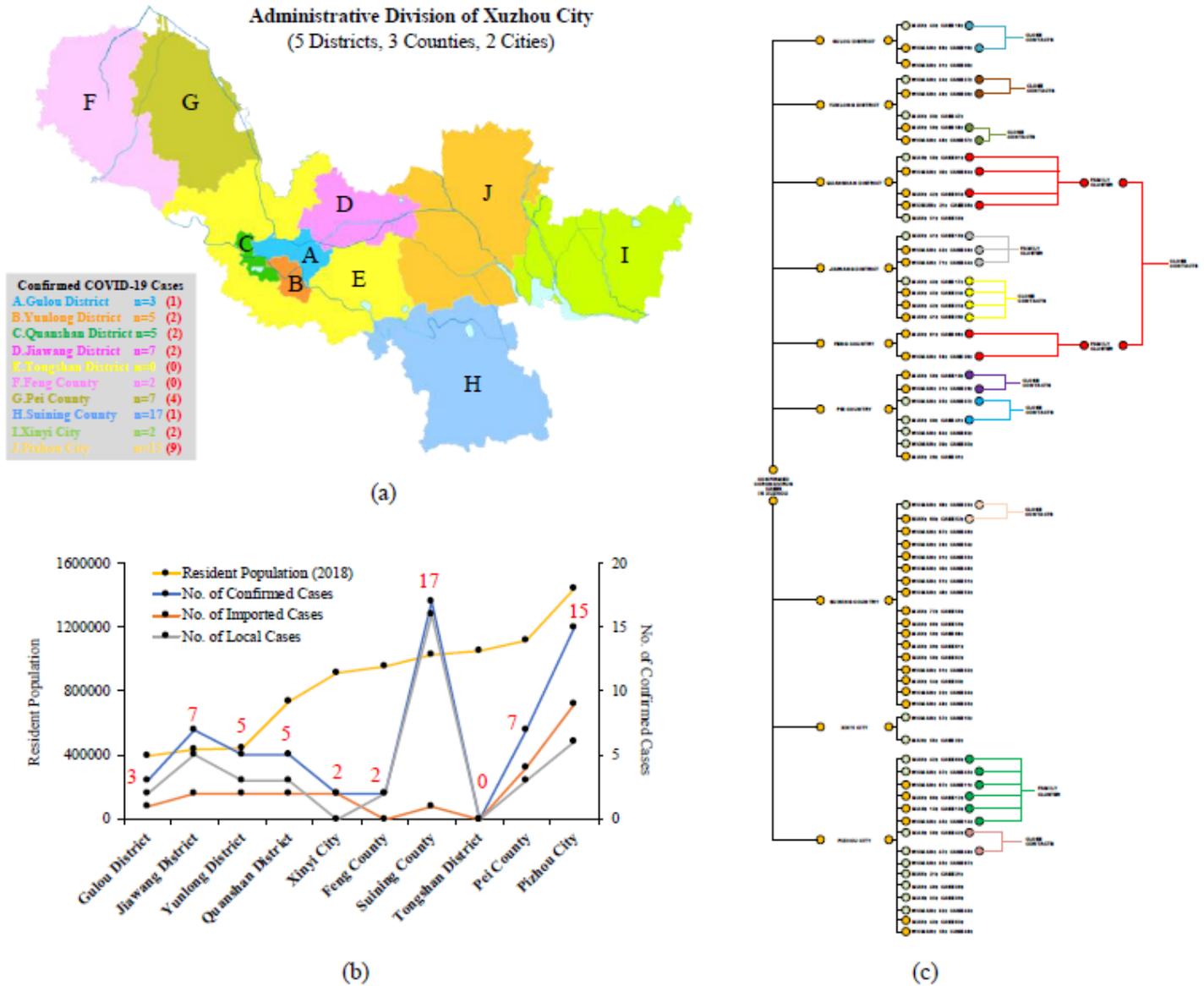


Figure 1

Schematic illustration of geographic distribution, case composition, and clusters of the 63 COVID-19 cases as of February 10, 2020 in Xuzhou, China. (a) A total of 63 cases were confirmed and unevenly distributed in 10 administrative divisions. The top three divisions are Suining County (n=17), Pizhou City (n=15), and Jiawang District (n=7) while the bottom three divisions are Tongshan District (n=0), Xinyi City (n=2), and Feng County (n=2). Red numbers in parenthesis indicate the number of imported cases. (b) Composition of imported and local cases in terms of resident population in each administrative division. (c) 11 known clusters and the corresponding connections among 63 COVID-19 cases in Xuzhou. All imported cases are in light green dots with letter I.

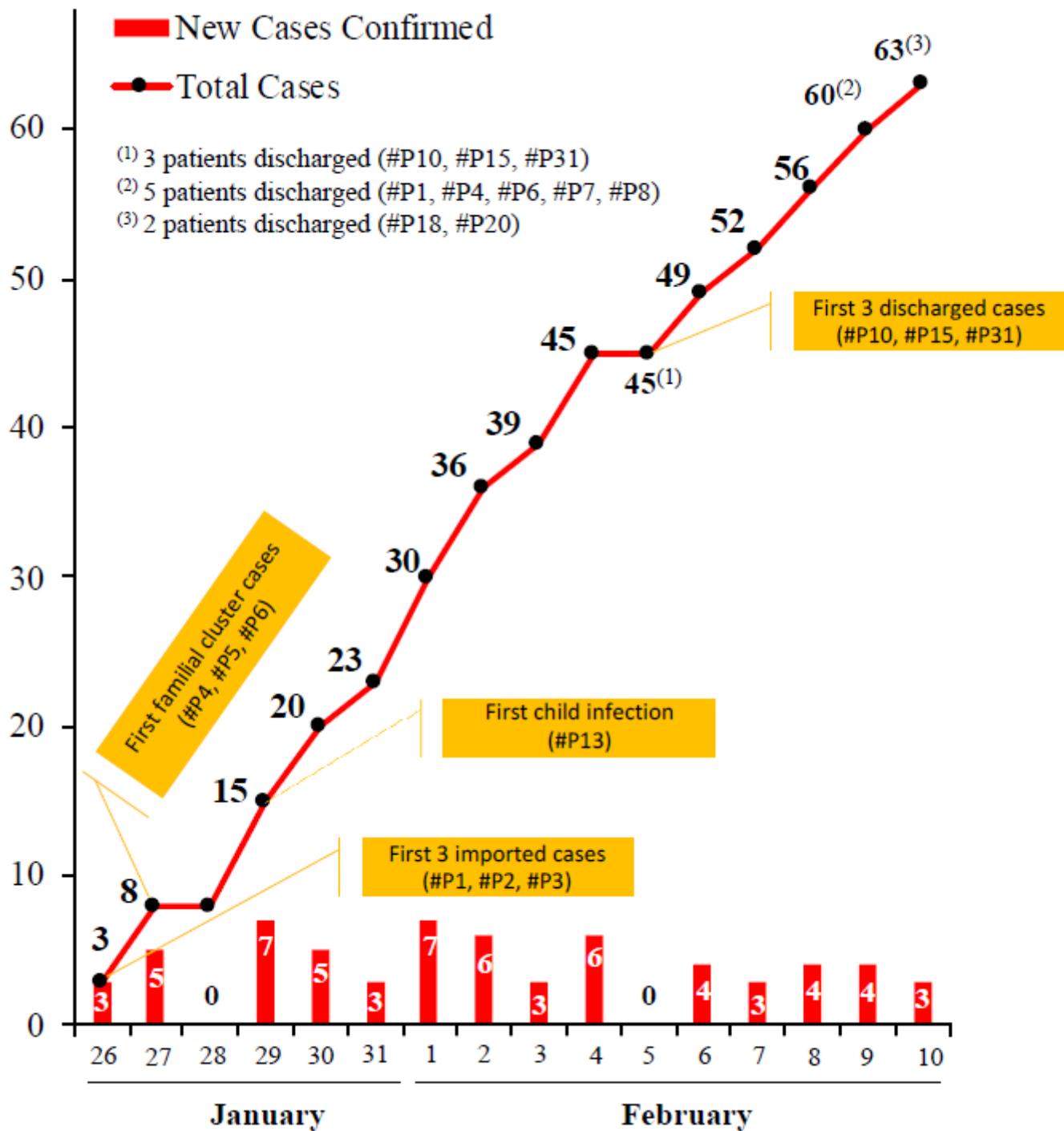


Figure 2

Daily new cases and cumulative sum curve of the confirmed COVID-19 patients in Xuzhou, China. Continuously increasing trend of confirmed cases could be observed. The first 3 cases (#P1, #P2, #P3) reported on Jan 26 were all imported and had Wuhan travel history. On Feb 5, first 3 recovered patients (#P10, #P15, #P31) were discharged from hospital.

COVID-19 Cases in Xuzhou: Patients Discharged

■ Date Confirmed ■ Date Discharged

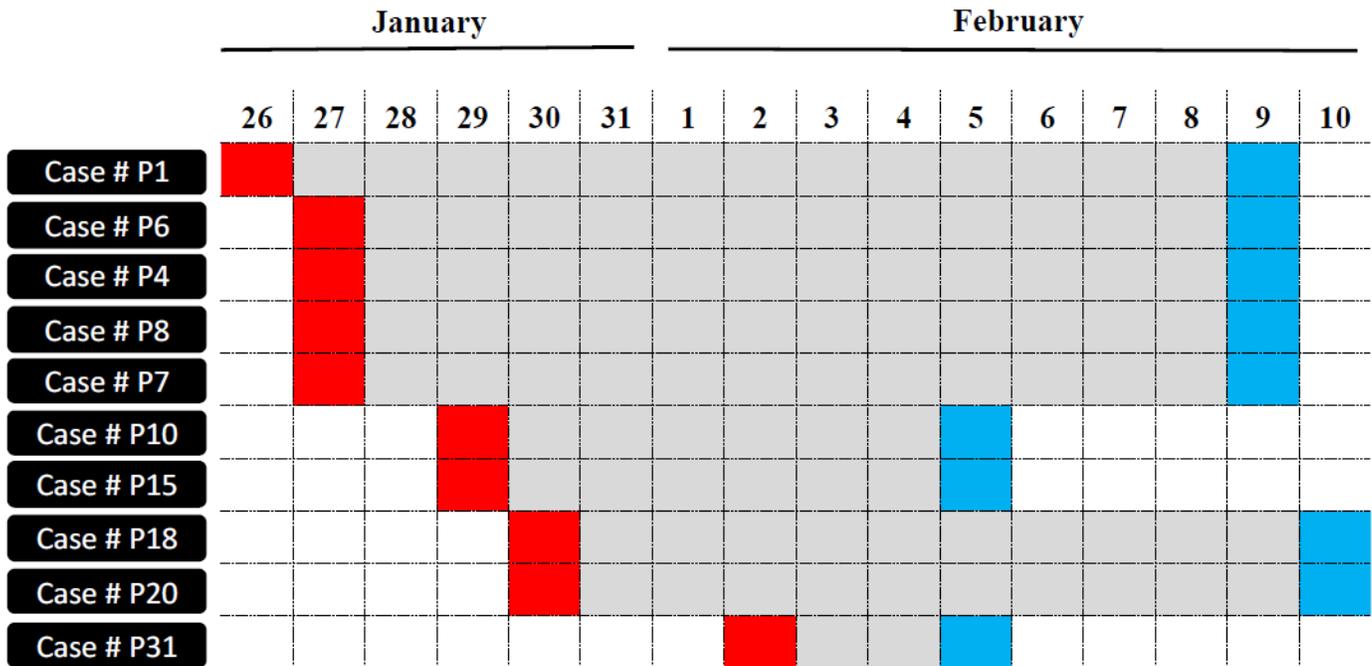


Figure 3

Illustration of hospitalized duration of the 10 discharged patients as of Feb 10, 2020. Red and blue cubes represent confirmed date and discharged date, respectively.

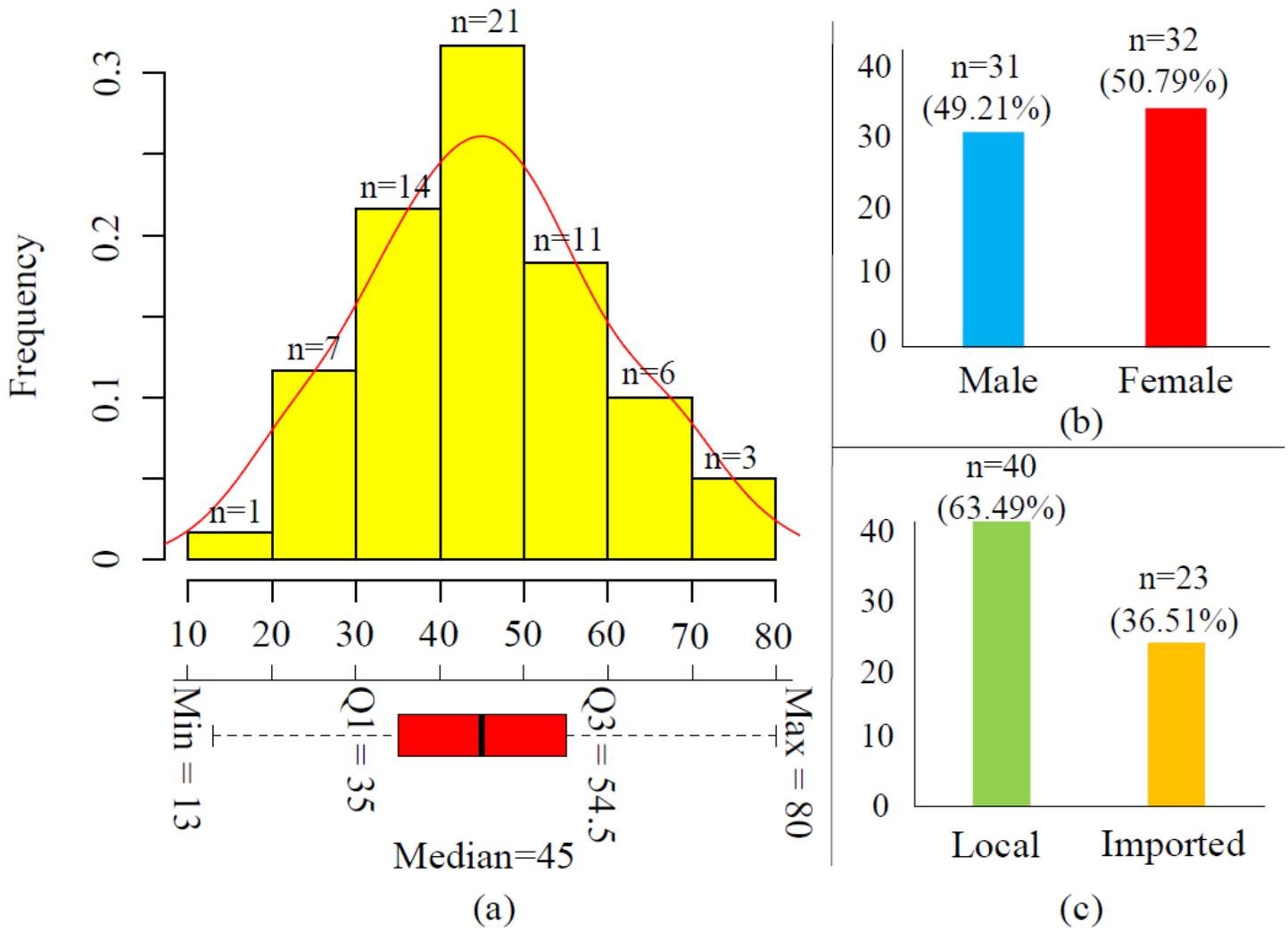


Figure 4

Demographic analysis of 63 confirmed COVID-19 cases in Xuzhou in terms of age, gender, and transmission routes: (a) age distribution; (b) sex ratio; (c) number of local and imported cases.

A representative Familial Cluster of 6 Cases in Pizhou City, Xuzhou

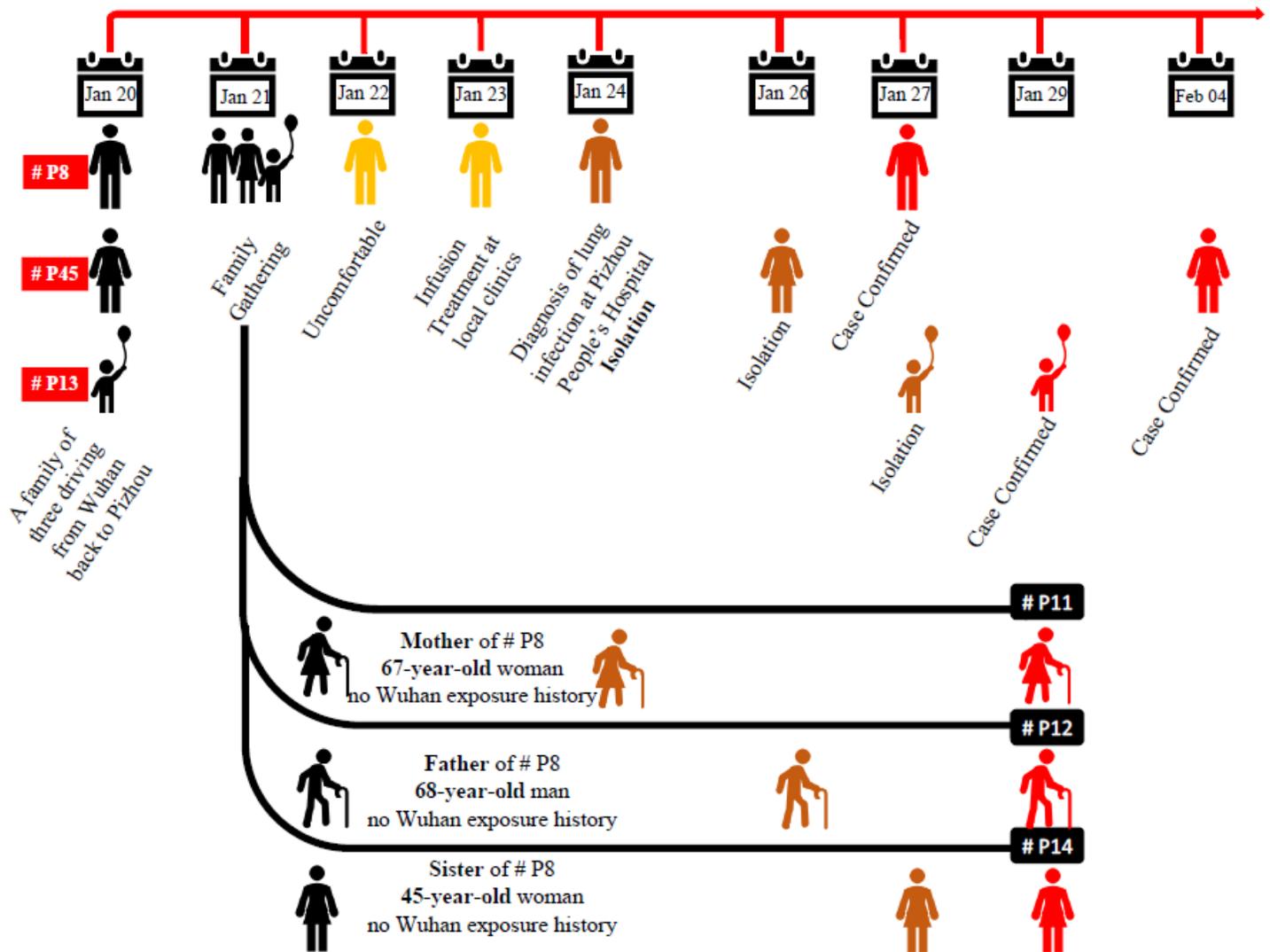


Figure 5

Illustration of the contact history in a representative familial cluster with 6 cases at Pizhou City in Xuzhou. Normal state: black body icon. Initial symptom: yellow body icon. Isolation: brown body icon. Confirmation: red body icon.

Supplementary Files

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