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Coronavirus Pandemic

Epidemiologic Characteristics of COVID-19 in Guizhou Province, China

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Abstract

Introduction: At the end of 2019, the COVID-19 broke out, and spread to Guizhou province in January of 2020.

Methodology: To acquire the epidemiologic characteristics of COVID-19 in Guizhou province, we collected data from 169 laboratory-confirmed COVID-19 related cases. We described the demographic characteristics of the cases and estimated the incubation period, serial interval and the effective reproduction number. We also presented two representative case studies in Guizhou province: Case Study 1 was an example of the asymptomatic carrier; while Case Study 2 was an example of a large and complex infection chain that involved four different regions, spanning three provinces and eight families.

Results: Two peaks in the incidence distribution associated with COVID-19 in Guizhou province were related to the 6.04 days (95% CI: 5.00 – 7.10) of incubation period and 6.14±2.21 days of serial interval. We also discussed the effectiveness of the control measures based on the instantaneous effective reproduction number that was a constantly declining curve.

Conclusions: As of February 2, 2020, the estimated effective reproduction number was below 1, and no new cases were reported since February 26. These showed that Guizhou Province had achieved significant progress in preventing the spread of the epidemic. The medical isolation of close contacts was consequential. Meanwhile, the asymptomatic carriers and the super-spreaders must be isolated in time, who would cause a widespread infection.

Key words: SARS-Associated Coronavirus; Incubation Period; Infectious Disease; Asymptomatic Infections.

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Introduction

At the end of 2019, a novel coronavirus SARS-CoV-2 outbroke. The disease caused by this virus strain was named COVID-19 by World Health Organization (WHO) officially [1]. As of 8 April 2020, 1,282,931 confirmed cases and 72,774 deaths had been reported globally [2]. Guizhou province is in the southwest of China, close (~1,000 km) to Wuhan. With the increasing number of COVID-19 patients in mainland China, Guizhou CDC detected its first confirmed case on January 21, 2020, who was officially confirmed by the Chinese Center for Disease Control and Prevention (China CDC) on January 23. Before the confirmation of the first case, Guizhou CDC identified and screened suspected COVID-19 cases by "pneumonia of unknown etiology" surveillance mechanism [3]. It was developed after SARS in 2003, to monitor cases with pneumonia in case they were infected by any novel pathogen. As of February 29, 2020, over 140 laboratory-confirmed cases were officially reported by Guizhou Health Commission [4]. In this study, considering that most cases were imported from other locations and the impact of control measures during the epidemic, we analyzed the data of the 169 laboratory-confirmed cases (23 cases without symptoms included) in Guizhou province to demonstrate the epidemiologic characteristics of COVID-19. Epidemiological investigations throughout the epidemic often provide valuable data. Here, we also described two representative case studies in Guizhou province: Case Study 1 refers to 6 cases of infection in 3 families by index cases with no symptoms; Case Study 2 is an example of a large and complex infection chain that involves 4 different regions spanning 3 provinces and 8 families.

Methodology

Case Definitions

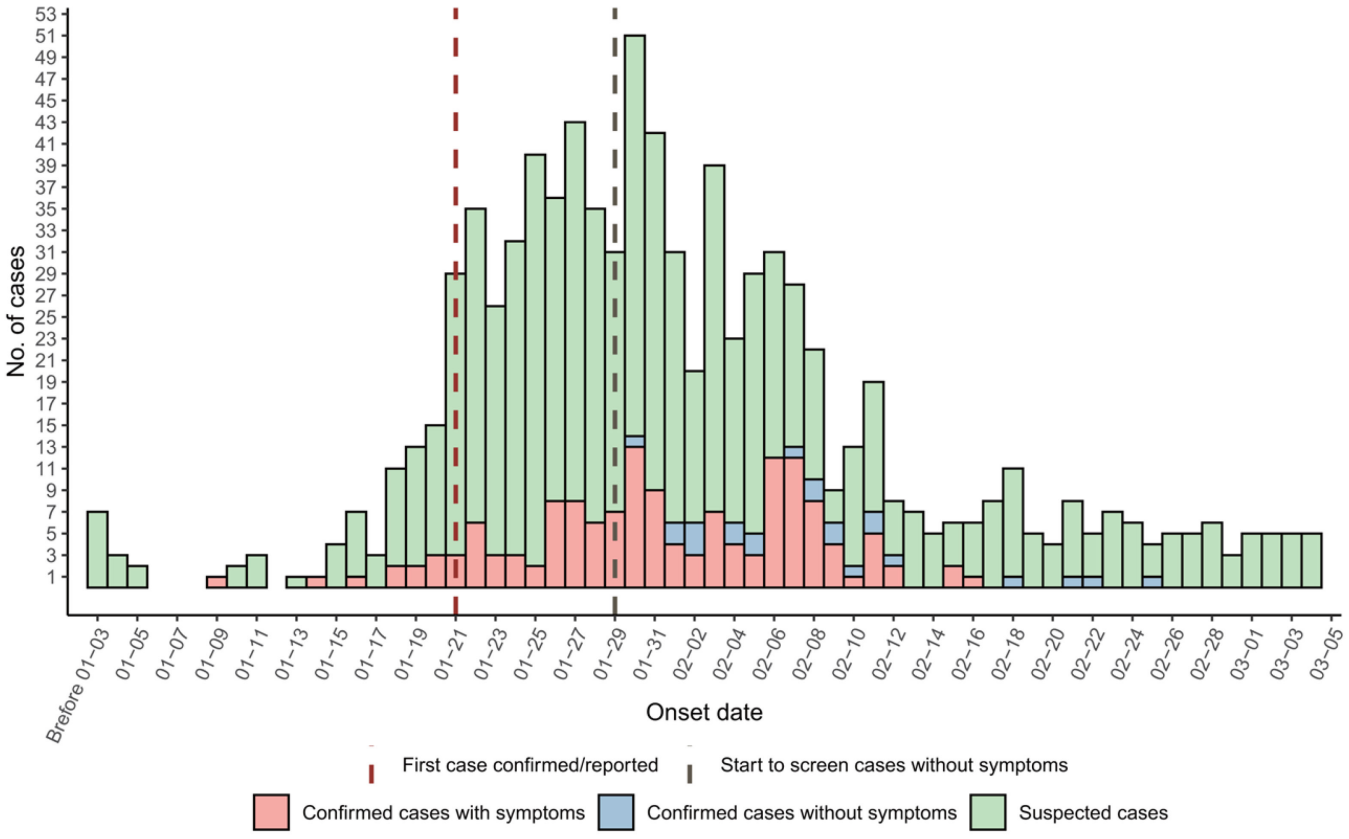
According to standard clinical guidelines, suspected COVID-19 cases were defined by a combination of clinical characteristics and epidemiologic histories. Clinical characteristics of suspected cases must fit at least 2 of the 3 following criteria: "fever and/or symptoms in the respiratory system; radiographic

evidence of pneumonia; low or normal white-cell count or low lymphocyte count" [5]. Epidemiologic histories must fit at least 1 of the 4 following criteria: "A history of traveling Hubei Province or other districts that has confirmed cases reported within 14 days of symptom onset; A history of contacting with a patient who has fever or symptoms in respiratory system from Hubei Province or other districts that has confirmed cases reported within 14 days of symptom onset; Any person who has had close contact with confirmed cases; cluster cases" [5]. Guizhou Health Commission adopted a stricter definition than that from the guidelines and reported all cases that fit clinical characteristics criteria regardless of epidemiologic histories described above as suspected cases. Confirmed cases were defined as those whose respiratory specimens testing positive for SARS-CoV-2, using at least one of the following two methods: positive result by real-time reverse-transcription–polymerase-chain-reaction (RT-PCR) assay for SARS-CoV-2 or a genetic sequence that matches SARS-CoV-2. Close contacts referred to persons who had not taken effective protections and had close contact with suspected and confirmed cases since 2 days before the onset of symptoms or 2 days before the sampling of specimens of the asymptomatic carrier.

Sources of Data

The suspected case was screened by a local hospital or local Center for Disease Control and Prevention (CDC). Once the patient was identified as a confirmed case by the laboratory, a joint field epidemiology team comprising members from Guizhou CDC and the local CDC would open a detailed field investigation on demography information, epidemiologic histories, timelines of key events, and close contacts. Data from all epidemiological reports were inputted into a standardized form according to technical protocols designed by the China CDC. At least two team members independently review the full report of each case report to ensure that the data was input correctly.

Figure 1. Distribution of the onset date of confirmed and suspected cases of COVID-19 in Guizhou province, China.



The horizontal axis represents the onset date of confirmed cases or suspected cases. The onset date was defined as the self-reported date of the first onset of COVID-19 related symptoms. The date for confirmed cases without symptoms was depicted as their confirmation date. On January 21, the first case was officially confirmed and reported by the Guiyang (the capital city of Guizhou province) CDC, whose onset date was on January 9th when the case was still in Wuhan. On January 29th, we started to identify and screen close contacts of confirmed cases and those who had a positive result by real-time reverse-transcription–polymerase-chain-reaction (RT-PCR) yet without symptoms were labeled as "Confirmed cases without symptoms" in the figure.

Epidemiological investigation

Once a suspected case was found, the local CDC would finish an initial investigation report within 24 hours and collect respiratory specimens for centralized laboratory testing. When the case was confirmed as positive to COVID-19, province CDC would send a special epidemiology team to investigate with local CDC, to acquire more detailed information. Information on epidemiologic characteristics was collected from infected individuals, family members, medical workers, close contacts, GPS-info, and CCTV cameras, etc. The information included basic demography data, detailed life trace and all close contacts, clinical characteristics, exposure history, etc.

Laboratory confirmation

According to the World Health Organization (WHO) guidelines, professional medical workers from the CDC or hospitals collected specimens from the upper and lower respiratory tracts of suspected cases for RT-PCR tests [6]. RNA was extracted and tested by RT-PCR with primers and probes for SARS-CoV-2. Cross-reactivity with other known respiratory viruses and bacteria such as Influenza A (H1N1, H3N2, H5N1, or H7N9), Influenza B (Victoria or Yamagata), MERS-CoV, Adenovirus, were also be tested.

Statistical analysis

The onset date was defined as the self-reported date of the first onset of symptoms associated with COVID-19 or the date of visiting the clinical facility in the absence of an accurate onset date. When plotting the distribution of the onset date (Figure 1), we depicted the confirmation date for confirmed cases without symptoms as their onset date. As the date of infecting exposure for a given individual falls within a finite interval, an exposure window was clarified to denote this interval. Frequencies of categorical variables were compared using the Pearson χ^2 test. The incubation period was estimated by fitting a parametric accelerated failure time model with the log-normal distribution of cases with detailed exposure window data. This was performed by R package *coarseDataTools* [10]. The serial interval distribution (i.e. the duration between symptom onset of a primary/index case and symptom onset of its secondary cases) was fitted by a log-normal distribution with infector/infectee pairs. The effective reproduction number (R) was defined as the average number of cases directly generated by one case in a population where all individuals were susceptible to infection over a predefined time window. This value was typically smaller than the value of the basic reproduction number, and it reflected the impact of control measures and the depletion of susceptible persons during the epidemic. With the Wallinga and Teunis method, the assumption that an exponential increase in the number of cases over time could be avoided by using a likelihood-based estimation procedure [8,9]. This model was applied by the R package *EpiEstim* [11].

All analyses and statistical graphs were conducted with R software version 3.6.3 (R Foundation for Statistical Computing).

Table 1. Demographic Characteristics of Cases with COVID-19 in Guizhou Province.

Characteristics	Value
Sample size	169
Cases with symptoms	146
Cases without symptoms	23
Median age (range) — year	37 (1 month - 91)
Age group — no. (%)	
< 15 year,	17 (10.06%)
15–44 year,	93 (55.03%)
45–64 year,	46 (27.22%)
≥ 65 yesr	13 (7.69%)
Gender	
Male	87 (51.47%)
Female	82 (48.53%)
Exposure info — no. (%)	
Detailed exposure window	105 (62.13%)
Only right bound of exposure window known	56 (33.13%)
Exposure window unknown	8 (4.73%)
Exposure in Wuhan or other districts outside Guizhou— no. (%)	82 (48.53%)

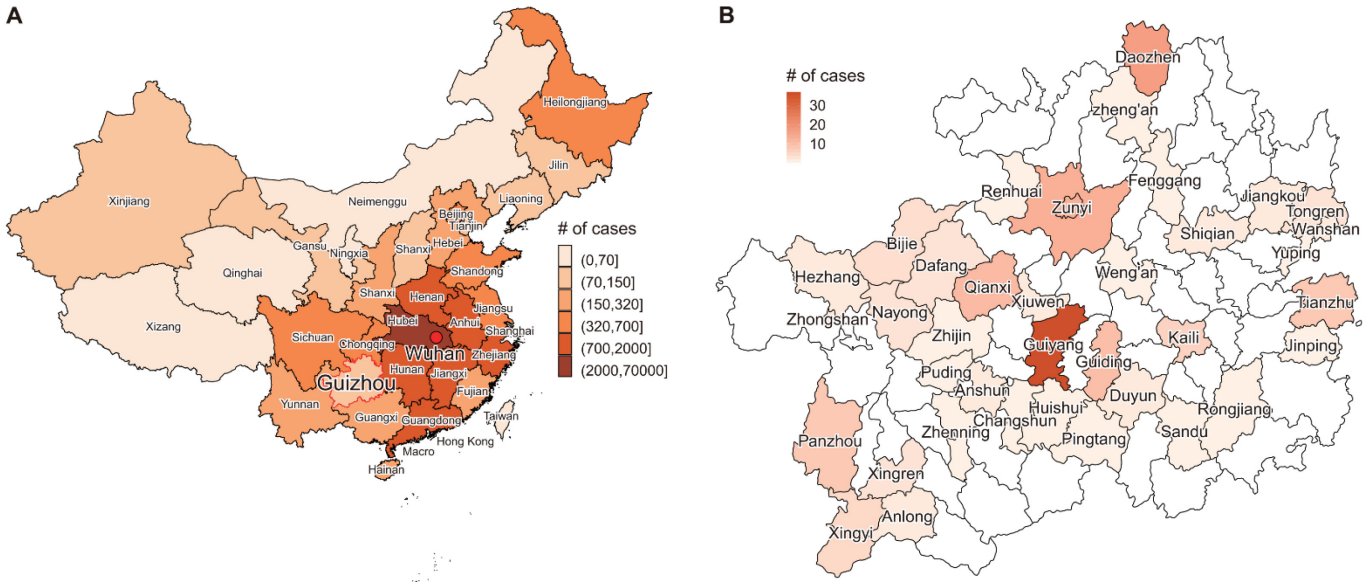
Ethics approval

Data collection, analysis of cases and their close contacts were determined by Guizhou Health Commission of the People's Republic of China. It was part of a continuing public health outbreak investigation and exempted from institutional review board assessment.

Results

Data of 866 cases were collected in total. Among all cases, 146 (16.86%) patients were symptomatic, 23 (2.66% of all 866 cases, 13.61% of all 169 confirmed cases) cases were confirmed as cases without symptoms throughout isolation/hospitalization, the other 697 (80.48%) cases were diagnosed as other diseases. Figure 2 shows the geographic distribution of confirmed cases throughout China and Guizhou province. The median age of all confirmed cases was 37 years (ranges from 1 month to 91 years), 87 (51.47%)

Figure 2. The geographic distribution of confirmed cases in China and Guizhou.



(A) Geographic distribution and statistics of all confirmed cases in China as of March 8. Data were collected from the National Health Commission [13]. Of the total 80,651 cases that were confirmed throughout China, 146 cases were in Guizhou province. **(B)** Geographic distribution and statistics in Guizhou province as of March 8. In addition to confirmed cases with symptoms, 23 cases without symptoms were also included, leading to 169 cases shown in the figure. Guiyang, located in the center of Guizhou province, the capital and largest city of the province, where 42 cases were reported. Throughout Guizhou province, 46 out of 88 administrative districts had reported confirmed cases.

were male, 82 (48.53%) were exposed to Wuhan or other districts outside Guizhou province, the detailed demographic data are shown in Table 1.

The first case was detected on January 21 and was officially confirmed by China CDC on January 23. It was reported by Guiyang (the capital city of Guizhou province) CDC. This case was a 51-year-old male, who was infected in Wuhan during his business trip. His onset date was on January 9 when he was still in Wuhan. After returning to Guizhou province on January 14, he made several visits to local hospitals before being quarantined on January 17. Figure 1 shows the distribution of the onset date of all cases overtime related to COVID-19. It was notable that unlike other provinces, the epidemic curve of COVID-19 in Guizhou province was not a bell curve that peaked between January 14 and January 27 [15,16]. In Guizhou, there was a gap between January 31 and February 5, which resulted in two waves of incidence around January 30 and February 6 (shown in Figure 1 and Figure 3D). There were 78 (53.42%) confirmed cases with symptoms had an onset date before February. Of cases whose onset date were before February, 22 cases were locally acquired (infected in Guizhou Province), and 56 cases were imported. However, of cases whose onset date were after February, 45 cases were locally acquired and 23 were imported ($p < 0.001$).

There were 90 confirmed cases who had detailed exposure window and onset date information were included to estimate the incubation period. (Figure 3 A-B). The median incubation period was 6.047 days (95% confidence interval [CI]: 5.000 – 7.095). The 95% percentile was 18.624 days (95% CI: 14.089 – 23.158) (Table 2). We obtained 52 infector/infectee pairs from cluster cases and estimated the serial interval

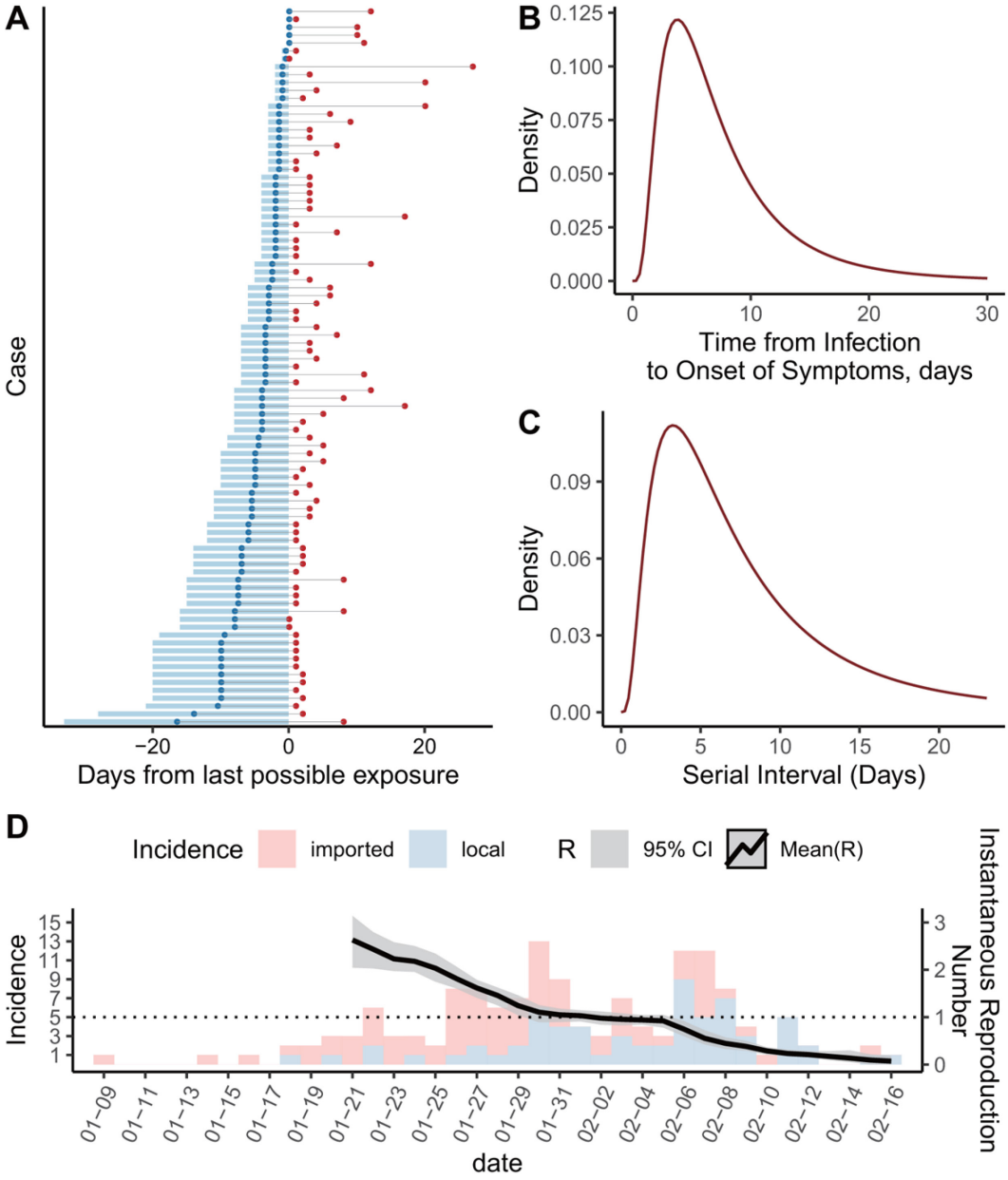
Table 2. Percentiles of the incubation period.

	Estimates	95%CI Low	95%CI High	Standard Error
P2.5	1.583	1.086	2.080	0.250
P5	1.964	1.408	2.519	0.280
P25	3.813	3.041	4.584	0.388
P50	6.047	5.000	7.095	0.527
P75	9.591	7.864	11.318	0.869
P95	18.624	14.089	23.158	2.282
P97.5	23.102	16.820	29.384	3.162

-2*Log Likelihood = 214.5.

distribution (Figure 3C) with the mean (± SD) of 6.14 ± 2.21 days. With this serial interval distribution, the estimated instantaneous effective reproduction number was shown in Figure 3D. It was notable that since February 2, 2020, the effective reproduction number was below 1.

Figure 3. Key time-to-event distributions.



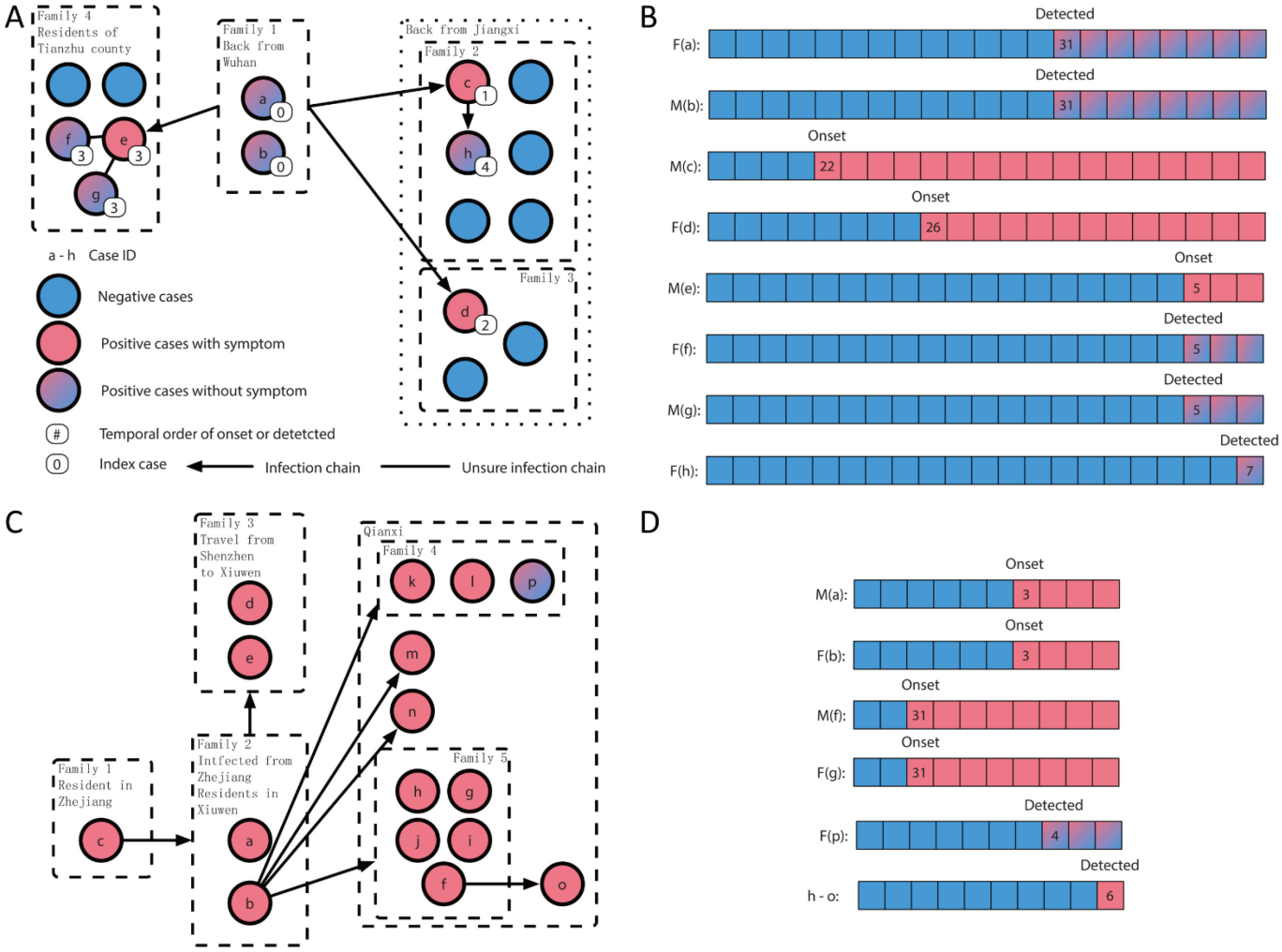
(A) The time windows of exposure and onset points of symptoms for 90 cases (44 females, 48.89%; 46 males, 51.11%; median age 41.5, IQR: 26.25-55) that have detailed information of exposure and onset dates. Blue shaded regions indicate the exposure windows, and blue points represent the midpoint within the region. Exposures were defined as travel histories to Wuhan or close contact with other infectious individuals. **(B)** The estimated incubation period distribution using a log-normal model. The estimated median incubation period in Guizhou province was 6.047 days (95% CI: 5.000 – 7.095). It was estimated that approximately 2.5% of the individuals had symptoms in 1.583 days (95% CI: 1.086 – 2.080) after the infection, and 97.5% of that showed symptoms within 23.102 days (95% CI: 16.820 – 29.384) after the infection. **(C)** The estimated serial interval distribution -- the duration between symptom onset of a primary case and symptom onset of its secondary cases -- fitted via the log-normal distribution, with a mean (±SD) of 6.14±2.21 days. **(D)** The estimation of effective reproduction number. The left y-axis was the incidence frequency grouped by local and imported cases, while the right y-axis was the value of the effective reproduction number. R was the abbreviation for the effective reproduction number.

Typical Case Study

Figure 4 showed two typical Case Studies in this outbreak of COVID-19 in Guizhou province. Case Study 1 was intended to demonstrate the infection chain among asymptomatic carriers, while Case Study 2 was an example of a trans-regional transmission chain.

As mentioned above, reports from different sources confirm the presence of asymptomatic carriers, which makes it more difficult to identify infected cases with mild symptoms [12,14]. In Case Study 1, the index cases (female *case a,* and male *case b*) were residents in Wuhan, whose hometown is Tianzhu county, Guizhou. On January 15, the brother (male *case c*) and sister (female *case d*) of *case a*, belong to Family 2 and Family 3, drove back together to Tianzhu from Jiangxi province. To celebrate the Chinese New Year, *case a* and *case b* came back to Tianzhu from Wuhan on January 17 and lived with Family 2. On January 18,

Figure 4. Detailed information on exposures and dates of illness onset of Case Study 1 and Case Study 2.



Panel A and B are Case Study 1, it was an example where the index cases did not show any symptom and had led to the infections of 6 cases from 3 families. **(A)** Network visualization of contacts among cases with COVID-19. Each circle represents a case. Lines with an arrow connecting the circle represented the infection chain. Lines without arrow represented the directions of the infection were unsure. **(B)** Four families with 16 cases were involved in Case Study 1, and 8 cases were infected out of which 5 were without symptoms. On January 17, the two index cases, *case a* (female) and *case b* (male) from Family 1, returned to Tianzhu, Guizhou from Wuhan. However, they did not show any symptoms and were not identified as positive cases. Since *case c* (male) from Family 2 showed symptoms on January 22, the index cases (Family 1) were identified and confirmed as positive cases.

Panel C and D are Case Study 2, it was an example of a large and complex infection chain that involved four different districts spanning three provinces and eight families. **(C)** Network visualization of contacts among cases with COVID-19. Each circle represented a case. Lines with an arrow connecting the circle represented the infection chain. The hypothesis index case was *case c*, the daughter of the *case a* and *b*, who were the residents of Taizhou, Zhejiang province. She infected *case a* and *b* at Taizhou from January 25 to 28 and was confirmed by the Zhejiang CDC on February 2. From January 29 to February 1, *case d* and *e*, the son and grandson of *case a* and *b*, came back from Shenzhen, Guangdong was infected by *case a* and *b* at Xiuwen county, Guizhou. On January 31, *case b* and *case f* (male, brother of *case b*) came back to their hometown, Qianxi County, Guizhou, and then infected the other 5 families, 11 individuals. **(D)** The timeline of onset in Study Case 2.

along with Family 4, four families had dinner together in *case d's house*. On the next day, *case a, b, c*, and *h* (wife of *case c*) took a trip to Leishan county (127 kilometers away from Tianzhu) where there were no confirmed cases reported until February 15. They also claimed that they did not contact any others during the trip. As of January 21, none of these cases showed any symptoms. On January 22, *case c* had cough and fatigue. On January 26, *case d* showed symptoms too. On January 29, *case c* was detected as a confirmed case by RT-PCR of the local CDC laboratory, and he was also both the first onset and first detected individual. The next day, all his close contacts were isolated by local medical affairs. In the following days, there were another 7 cases were confirmed as positive.

Four different districts spanning three provinces and eight families were involved in Case Study 2. It was a large and complex infection chain. The hypothetical index case was *case c*, daughter of *case a* and *b*, who was confirmed in Zhejiang province on February 2. On the same day, the Guizhou CDC received a notification from the Zhejiang CDC, which reported that *case a* and *b* were the close contacts to *case c*, as they had taken a trip together in Taizhou, Zhejiang for 3 days from January 25 to 28. After the epidemiological investigation by the Guizhou CDC, *case a* and *b* were found having close contacts with *case d* and *e*, the son and grandson of them, respectively. *Case d* and *e* were the residents of Shenzhen, Guangdong province, and they have been with *case a* and *b* for 4 days in Xiuwen county, Guizhou, from January 29 to February 1. Through the communications with the Guangdong CDC, the Guizhou CDC was told that *case d* and *e* were positive to SARS-CoV-2. On January 31, *case b* and *f* (male, brother of *case b*) came back to their hometown, Qianxi County, Guizhou, and infected other 5 families, 11 individuals.

Discussion

In this study, we analyzed epidemiological characteristics and two typical transmission phenomena of COVID-19 in Guizhou. Predominantly, as of February 2, 2020, the estimated effective reproduction number was below 1, and no new cases were reported since February 26. These showed that Guizhou Province had achieved significant progress in preventing the spread of the epidemic due to timely control measures such as community screening, isolation of close contacts, restriction of public transportation, expanding the population who receive the RT-PCR testing, strengthening of disinfection and health education, and so on.

Throughout the outbreak, unlike national incidence data outside Hubei province in China, the epidemic curve of COVID-19 in Guizhou province was a two-peak curve instead of a bell curve [15,16]. This was because the Guizhou CDC adopted strict measures to prevent imported cases in the early stage of the epidemic. More specifically, on January 23, a quarantine was announced in Wuhan, banning all travel in and out of the city. Since then, anyone traveling to Guizhou province with symptoms was quarantined and isolated under the management of professional medical institutions. With a 6.047 days median incubation period, cases who left from Wuhan to Guizhou province before January 23 would show symptoms around January 30, which led to the first peak in the distribution. Then, with a 6.14 days of serial interval, local cases who were infected by imported cases started to show symptoms around February 6, since local cases were in the majority after February ($\chi^2 = 19.593$, df = 1, $p < 0.001$), leading the second peak in the distribution. These indicated that the control of community transmission cannot be lax even if the imported cases were under control.

The median and 95% percentile incubation period were 6.047 days (95%CI: 5.000 – 7.095) and 18.624 days (95% CI: 14.089 – 23.158) respectively in this study, which was 0.8 and 6.1 days longer than a recent report of 425 patients (6.0 days vs. 5.2 days and 18.6 days vs. 12.5 days), this might be the result of recall bias [5]. During the epidemiological investigation, we found that some cases have had shown mild symptoms several days before the reporting date. For some cases without symptoms, after being informed they had positive for SARS-CoV-2, they would self-reported that they showed symptoms immediately. As a matter of fact, these patients may already show mild symptoms without being noticed. These recall biases would affect the estimation of results. The 95% percentile indicated that the tracking and observations of close contacts were rather important for cases with long incubation periods.

The effective reproduction number of Guizhou province was a constantly declining curve, which supported that our strict prevention and control measures were effective. Considering the effectiveness of control measures, the Guizhou CDC took the initiative to quarantine all people traveling from Hubei province, and isolated all those with symptoms between 20 and 27 January 2020. The effective reproduction number was dropped from 2.6 to 1.6 during that time. Since February 2, all close contacts were isolated regardless of whether they had any symptoms. The

effective reproduction number was below 1 since that day. Finally, on February 7, Guizhou CDC expanded the population who receive the RT-PCR testing to anyone from Hubei province, which made the effective reproduction number decreased from 0.75 to 0.55. These showed that strict surveillance of close contacts has important preventive effects on potential outbreaks. The medical isolation of close contacts was consequential. Since the Guizhou CDC began to screen cases without symptoms on 29 January, 91% presymptomatic cases were screened from close contacts of confirmed patients, which partially suggested that the RT-PCR testing of close contacts is essential. Notably, by analyzing the infection chain of Case Study 1, we provided evidence of asymptomatic transmission of COVID-19. This suggested that the asymptomatic carriers can also cause transmission and should be considered as a source of infection in epidemiological investigations. By Case Study 2, we demonstrated the ability of super-spreaders to spread the disease. If these cases were not isolated in time, they would cause a widespread infection. With the deepening of the investigation, Guizhou CDC found that there existed index cases who showed symptoms after their secondary cases. As discussed in the section Typical Case Study, in addition to the evidence of the human-to-human transmission, transmission might occur before symptom appear, as well as the presence of "super-spreaders". Secondly, there might still be missing carriers in the epidemiological investigation of some complex events, and the Case Study 1 mentioned above was one of the few events where the infection chain was very clear. Therefore, more large-scale multicenter studies were needed to verify our findings.

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