Epidemiological characteristics and incubation period of 7,015 confirmed cases with Coronavirus Disease 2019 outside Hubei Province in China

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Summary: Since the implementation of strict traffic restrictions in Hubei Province on January 23, the proportion of imported cases outside Hubei Province has gradually decreased, and the incubation period of imported cases has increased over time.

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Abstract

Background: Disease caused by SARS-CoV-2 broke out in Wuhan in December 2019. We utilized confirmed cases outside Hubei Province to analyze epidemiologic characteristics and evaluate the effect of traffic restrictions implemented in Hubei beginning on January 23, 2020.

Method: Information on 7,015 confirmed cases from January 19 to February 8, 2020, in all provinces outside Hubei was collected from the national and local health commissions in China. Incubation period and interval times were calculated using dates of the following events: contact with an infected person, onset, first visit and diagnosis. We evaluated changes in incubation period and interval times.

Results: The average age of all cases was 44.24 years old. The median incubation period was 5 days and extended from 2 days on January 23 to 15 days on February 8. The proportion of imported cases decreased from 85.71% to 33.19% after January 23. In addition, the lengths of the intervals between onset and diagnosis, onset and first visit, and first visit and diagnosis decreased over time.

Conclusion: Rapidly transmitting COVID-19 has a short incubation period. The onset mainly occurs among young to middle-aged adults. Traffic restrictions played an important role in the decreased number of imported cases outside Hubei.

Key words

SARS-CoV-2; Coronavirus disease 2019; Incubation period

Introduction

In December 2019, a cluster of pneumonia cases caused by novel coronavirus (SARS-CoV-2) was identified in Wuhan of Hubei Province, China's central transportation hub [1]. The viral data were rapidly determined through high-throughput sequencing on January 7 and identified as having homology with human severe acute respiratory syndrome (SARS), the zoonosis originating from wild animals [2,3]. The most reported initial pneumonia cases were geographically linked with the Huanan seafood market, which also sells wild animals in Wuhan [4].

To prevent widespread epidemic outbreaks, the government implemented isolation in Wuhan with traffic-blocking measures on January 23, 2020, and Hubei Province finished blocking trafficon January 26 [2,5]. However, millions of people had left Wuhan before isolation due to the high mobility of the population during the Spring Festival (a traditional festival in China when families are reunited), which contributed to the spread of SARS-CoV-2. On January 30, 2020, the epidemic was listed as a Public Health Emergency of International Concern (PHEIC) by the World Health Organization (WHO) and was later officially named coronavirus disease 2019 (COVID-19) [6,7]. As of February 8, 2020, a total of 27,100 cases were confirmed in Hubei Province and a total of 10,098 cases were confirmed in other parts of China [8,9].

Human-to-human transmission has been confirmed in early epidemiological analyses of COVID-19 [5]. Since SARS-CoV-2 could be transmitted via respiratory droplets and close contact [10], more evidence emerged to show positive PCR detection of the virus in various clinical specimens, such as blood, sputum, feces, urine, and nasal samples [11,12]. The live virus has even been detected in feces [12], implying the possibility of fecal-oral spread. In recent studies the basic reproduction number (R0) was calculated as 2.20~3.77, higher than those of SARS and Middle East respiratory syndrome (MERS) [3,5]. Due to the large number of cases of infection in Hubei Province, the details of the cases were not released, so we collected information on cases confirmed to be from outside of Hubei Province. In this study, our objectives were to analyze the epidemiological characteristics of confirmed cases and the length of the interval between contact with infected patients to the onset of symptoms and the diagnosis.

Method

Study population and source of data. This retrospective study was conducted with 7,015 COVID-19 cases from January 19 to February 8, 2020 in all provinces of China outside Hubei Province. The information of all participants was collected from the website of the National Health Commission of the People's Republic of China (NHCPRC) and health commission website of each province or city. Detailed data included age, gender, residence, history of contact confirmed cases or persons from

Hubei Province, travel history, initial symptoms, information on family clusters, and several crucial dates (such as onset date, first visit date, diagnosis date, hospitalization date and isolation date). We indicated the amount or number of cases using in the analysis when part of the information unable to be collected. A total of 3,294 cases with detailed clinical performance information were included in the analyses of clinical symptoms and 2,907 cases with contact history and date of onset or diagnosis were analyzed for incubation period in this study. To compare the characteristics of confirmed cases with that of the domestic population, latest demographic data (sex-stratified, age-stratified and province-stratified population data) were obtained from the National Bureau of Statistics of China [13].

Diagnosis and prognosis of COVID-19. A confirmed case with COVID-19 was defined as a case with epidemiological exposure, clinical symptoms and a positive result for nucleic acid detection in nasal and pharyngeal swab specimens by high-throughput sequencing or real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay according to the guidance from the NHCPRC [14,15].

The prognosis of disease (cure or death) was also collected. A cured case was defined as a case with body temperature that had returned to normal, markedly improved respiratory symptoms, significant inflammatory absorption shown in lung CT, and two consecutive nucleic acid detections that were negative, according to the guidance from the NHCPRC [14,15].

Definitions of variates. An imported case was defined as one with exposure to pathogens in other cities, such as Wuhan or other cities in Hubei Province, including cases with a history of travel or residence in other cities or contact with a diagnosed person in other cities before the onset of symptoms. A nonimported case was defined as one with no travel history to other cities before onset and only local exposure to pathogens.

We extracted the last contact date to estimate the incubation period. Collected contact history information through individual epidemiological questionnaire surveys by public health physician. The questionnaire information includes four types of contact: (1) contact with confirmed cases, (2) contact with suspicious cases or fever, (3) contact with people come from Hubei, (4) the travel or residence history of Hubei province. By comparing the date of each type of contact, the last date of contact was extracted. If there was only one, the time was the last contact date. Incubation period was defined as the duration between the last contact date and the onset date. The onset date was defined as the first day when symptoms developed, such as fever and cough. In addition, to evaluate the relationship among exposure, onset and diagnosis, we calculated several time intervals: (1) the time interval between onset and diagnosis, (2) the time interval between onset and first visit, (3) the time interval between first visit and diagnosis, and (4) the time-course, the time interval between onset and the censored date (cure date, death date or February 8, 2020).

Statistical analysis. To study the distribution of COVID-19 cases, we presented the case number by gender, age and province. Considering the variable distribution, age was presented as the mean and standard deviation, and the incubation period and time intervals mentioned above were presented as the median (25%Q, 75%Q). The difference between imported cases and nonimported cases was tested using the t-test or Wilcoxon rank-sum test. The chi-square test was used to compare the numerical difference between imported cases and nonimported cases. All analyses were performed using R software (version 3.6.2) or Excel (Microsoft). A two-sided $P<0.05$ was statistically significant.

Results

The distribution of 7,015 confirmed COVID-19 cases (3,695 males, 54.12%) is shown in Table 1. Henan Province (1,017) and Guangdong province (852) reported more cases than other provinces did (Table S1). The average age for all cases was 44.24 years, with a range from two months to 97 years old. Over 60% of confirmed cases were between 30 and 59 years old (21.81% for 30-39 years old, 21.07% for 40-49 years old, 19.24% for 50-59 years old). By comparing with the age-specific proportion of the national population, we found the proportion of cases under 20 years old (20,826 per 10^6) is much lower than that of other age groups (56,189 per 10^6). Up to 61.50% (3,802) of all cases were imported cases and 37.56% (1,428) of them came directly from Wuhan (Table 2). The proportion of imported cases in adjacent

provinces of Hubei was 55.77% (1,411 cases) and in non-adjacent provinces was 65.47% (2,391 cases).

As shown in Table 3, among 3,294 confirmed cases (53.94% male) with an average age of 44.71 years old, the most common symptoms were fever (83.00%) and cough (33.61%). Fatigue (9.96%) and pharyngalgia (6.68%) were common as well. A few cases also reported digestive tract symptoms such as diarrhea, nausea or vomiting. Compared with 533 cured cases, 21 deaths occurred among patients who were much older (71.9 vs 39.9 years old), and a much higher proportion of these deaths occurred among patients with other diseases (71.4% vs 0.9%).

We analyzed the variation in the age, gender and proportion of imported cases by diagnosis date (Figure 1). The average age of the cases was 66 years old on January 19 and 56.21 years old on January 20, and the average age gradually decreased to 43.73 years old on January 23. After January 23, the average age for confirmed cases remained near 44.18 ± 16.28 years old. The proportion of imported cases gradually decreased with later dates of diagnosis, especially after January 23. Before January 23, the proportion of imported cases was approximately 85.71% to 100%, and the proportion decreased to 33.19% on February 8. We did not observe any difference in the age or gender distribution between cases from provinces adjacent to Hubei Province and those from other provinces with the time of diagnosis.

The median incubation period for 2,907 COVID-19 cases was 5 days (2 days, 8 days), and the longest incubation period was 24 days for 1 case. The incubation period

for more than 95% of the COVID-19 cases was less than 13 days. We did not observe a significant difference in incubation period among males [5 days (2, 8)] and females [4 days (2, 8), *P*=0.22]. The incubation period in imported cases was 5 days, while it was 4 days in nonimported cases, with no significant difference (*P*=0.23). Interestingly, we observed that the median incubation period gradually extended over time (Figure 2 and Figure 3). We further analyzed the change in the incubation period between imported and nonimported cases (Figure 4). The extension of the incubation period was observed in imported cases, but no significant change was observed among nonimported cases.

The median time from disease onset to diagnosis, disease onset to first visit, first visit to diagnosis and disease onset to censoring was 4, 0, 2 and 12 days, respectively. We collect data in the early stages of the epidemic, so the outcome of many cases has not yet occurred. We used February 8 as censored time for confirmed cases, the cured time for cured cases and the death time for death cases. The time between disease onset and diagnosis for imported cases (4 days, 2-7days) was significantly shorter (*P*<0.01) than for nonimported cases (5 days, 2-8days) (Table 2). The median time from disease onset to diagnosis was decreased to zero over the onset time (Figure 3-a). Similar trends were observed in the median time from onset to first visit (Figure 3-c) and first visit to diagnosis (Figure 3-b). Over time, the median time from disease onset to diagnosis decreased rapidly, from 16 days on January 19 to 4 days on approximately January 23, and then stabilized to 4 to 5 days after January 23 (Figure 2-a). Similar trends were observed for both the time from onset to first visit (Figure 2-

c) and the time from first visit to diagnosis (Figure 2-b); these time intervals decreased rapidly before January 23 and then stabilized to 0 days and 2 days, respectively, after January 23. We did not observe a significant difference in the length of time from disease onset to the first visit or the length of time from the first visit to diagnosis between imported cases and nonimported cases.

Discussion

In this study, we collected information on 7,015 confirmed COVID-19 cases (over 50% male; average age of 44.24 years old). The most common symptoms were fever and cough. We observed a decreasing trend in the proportion of imported cases in provinces outside Hubei Province and decreasing trends in the time intervals between onset and diagnosis, onset and first visit, and first visit and diagnosis from January 19 to February 8. Based on 2,907 confirmed cases, the median incubation period of COVID-19 was 5 days, and more than 95% of cases had an incubation period of less than 13 days. An increasing trend in the incubation period with the time of diagnosis or onset was observed in this study, especially among imported cases.

We found that the median incubation period was slightly longer than that found in the 1,099-case report by Wei-jie Guan et al. (5 days vs. 3 days) [11] but similar to that reported by Qun Li et al. (5 days vs. 5.2 days) [5] and was supported by a reported family clustering case in which five family members experienced the onset of symptoms 3-6 days after exposure [16]. Moreover, the longest incubation period

was 24 days in this study, which is consistent with the longest incubation period reported by Wei-jie Guan et al. [11]. It should be noted that we extracted the date of last contact with infected persons as the date of contact to calculate the incubation period. When actual contact was earlier than this date, it may lead to an underestimation of the incubation period. In addition, it would appear equally likely that infection might have occurred through contact with some other infected but unidentified person at some time after contact with the known infected person, resulting in an overestimate of the incubation period.

Since the outbreak of the COVID-19, mandatory traffic restrictions have been adopted across China to prevent further spread of the epidemic. For example, Wuhan stopped all traffic inside and outside the city on January 23, and no residents could leave Wuhan unless they had very special circumstances. In the following days (January 24 to January 26), transportation in other cities and surrounding counties in Hubei Province also stopped. Our study showed that from January 23, the incubation period among imported confirmed cases outside Hubei Province showed a gradual upward trend, but this trend was not obvious in nonimported cases. We also observed that the proportion of imported cases decreased from 100% on January 19 to 33.19% on February 8. This situation suggested that imported cases started to decrease after traffic restrictions were imposed. After the closure of Hubei Province, new imported cases would no longer increase, and cases that had been imported into other provinces outside Hubei Province gradually developed, thus prolonging the incubation period. On the other hand, the main transmission routes of COVID-19 that have been

confirmed thus far are respiratory droplets and contact transmission [5,11,16,17], while other possible transmission routes (such as aerosol and digestive tract transmission) have not been confirmed [10,15]. Therefore, the opportunities for infection with 2019-nCoV did not change, which might partly explain the relatively stable incubation period among nonimported cases.

In the present study, we observed that the median time from disease onset to diagnosis decreased very rapidly, from 16 days on January 19 to 4 days on and after January 23. This phenomenon should be attributed to the gradual recognition of COVID-19 and the rapid application of nucleic acid antibody detection. Our results also found that the time between disease onset and diagnosis for imported cases was significantly shorter than that for nonimported cases. This indicated that physicians were more likely to consider the possibility of COVID-19 among pneumonia cases from Wuhan or Hubei Province. In addition, the rapidly decreasing time interval from onset to the first visit and from the first visit to diagnosis, especially after January 23, also illustrated the effectiveness of the traffic restriction measures in Hubei Province and the improvement in diagnostic capacities.

In summary, our analysis provided evidence that the various policies and isolation measures taken by Hubei Province have been effective since the outbreak of COVID-19. Imported cases started to decrease after traffic restrictions were imposed, and the incubation period gradually increased.

Author's contribution

WC, XN, MZ, GM participated in study design; XN, GM, LF, MW performed data analysis; all authors assisted in collecting the data; XN, GM, QT, LF, MW, YX, WC drafted the manuscript; all authors provided critical review of the manuscript and approved the final draft for publication.

Declaration of interests

All authors declare no competing interests.

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Footnote page

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Figure 1. The variation of age (A), gender (B) and proportion of imported cases (C) with diagnosis date.

Figure 2. The variation of time interval with diagnosis date

a The variation of time between onset and diagnosis with diagnosed date

bThe variation of time between first visit and diagnosis with diagnosed date

c The variation of time between onset and first visit with diagnosed date

d The variation of time between Incubation period with diagnosed date

Figure 3. The variation of time interval with onset date

a The variation of time between onset and diagnosis with onset date

b The variation of time between first visit and diagnosis with onset date

c The variation of time between onset and first visit with onset date

d The variation of time between Incubation period with onset date

Figure 4. The association between the incubation period and diagnosis date or onset date in imported or non-imported cases.

a The variation of incubation period with diagnosis date in non-imported cases

b The variation of incubation period with diagnosis date in imported cases

c The variation of incubation period with onset date in non-imported cases

d The variation of incubation period with onset date in imported cases

Table 1 Epidemiological characteristics of 7,015 confirmed cases with COVID-19

Characteristics	Confirmed cases (n, %)	Cured cases (n, %)	Death cases (n, %)	Domestic population distribution (%) *
Gender				
Male	3695 (54.12)	272 (56.20)	12 (60.00)	51.13
Female	3132 (45.88)	212 (43.80)	8 (40.00)	48.87
Age				
< 20 yr	640 (9.12)	98 (18.39)	1 (4.76)	21.95
20-≤29 yr	831 (11.85)	86 (16.14)	—	14.07
30-≤39 yr	1530 (21.81)	136(25.52)	2 (9.52)	15.29
40-≤49 yr	1478 (21.07)	95 (17.82)	—	16.24
50-≤59 yr	1350 (19.24)	68 (12.76)	3 (14.29)	14.56
60-≤69 yr	787 (11.22)	37 (6.94)	2 (9.52)	10.73
≥70 yr	399 (5.69)	13 (2.44)	13 (61.90)	7.15
Province †				
Adjacent provinces	2964 (42.25)	179 (33.58)	6 (28.57)	24.68
Non-adjacent provinces	4051 (57.75)	354 (66.42)	15 (71.43)	75.32

* Domestic population distribution data were extracted from China Statistical Yearbook 2019.

† Classified by adjacent of Hubei province.

Table 2. Epidemiological characteristics of imported and non-imported COVID-19 cases

Characteristics	All confirmed Cases	Number #	Imported COVID-19 Cases	Number#	Non-imported COVID-19 Cases Number#		*P* value
Imported cases, n (%)	3802 (61.50)	6182					
Male, n (%)	3695 (54.12)	6827	2155 (58.01)	3715	1119 (48.80)	2341	<0.001 ‡
Age, year (mean±SD)	44.24±16.24	6728	42.06±15.22	3703	47.37±17.33	2338	<0.001 §
Adjacent provinces, n (%)	2530 (40.93)	6182	1411 (37.11)	3802	1119 (47.02)	2380	<0.000 ‡
Wuhan permanent resident cases, n (%)	1428 (26.36)	5446	1417 (48.66)	2912	11 (0.47)	2352	<0.001 ‡
Time between onset and diagnosis, day M (25Q, 75Q)	4 (2, 7)	5864	4 (2, 7)	3250	5 (2, 8)	1957	<0.001 †

Time between onset and first visit, day M (25Q, 75Q)	0 (0, 3)	2723	0 (0, 3)	1739	0 (0, 3)	827	0.484†
Time between first visit and diagnosis, day M (25Q, 75Q)	2 (1, 4)	2714	2 (1, 4)	1734	2 (1, 4)	823	0.054†
Time between onset and censored, day M (25Q, 75Q) *	12 (9, 16)	5930	14 (10, 17)	3276	7 (11, 14)	1988	<0.001 †
Incubation period, day M (25Q, 75Q)	5 (2, 8)	2907	5 (2, 8)	2412	4 (1, 8)	473	0.225†

The number of each item is different due to lack of data.

* Censored time for confirmed cases is 2020/2/8, for cured cases is the cured time and death cases is the death time.

† Wilcox rank sum test was used to compare medians of the continuous variables between the two groups.

§ Student's t-test was used to compare means of the continuous variables between the two groups.

‡ Chi-square test was used to compare distributions of category variables between the two groups.

Table 3. Symptoms of 3,294 confirmed cases, 292 cured cases and 14 death cases with COVID-19

Symptoms	confirmed cases	cured cases	death cases
Fever, n(%)	2734 (83.00)	242 (82.88)	9 (64.29)
Cough, n(%)	1107 (33.61)	149 (51.03)	7 (50.00)
Fatigue, n(%)	328 (9.96)	51 (17.47)	0 (0.0)
Pharyngalgia, n(%)	220 (6.68)	19 (6.51)	0 (0.0)
Expectoration, n(%)	167 (5.07)	19 (6.51)	3 (21.43)
Chill, n(%)	166 (5.04)	9 (3.08)	0 (0.0)
Myalgia, n(%)	147 (4.46)	14 (4.79)	2 (14.29)
Headache, n(%)	132 (4.01)	11 (3.77)	0 (0.0)
Rhinorrhoea, n(%)	80 (2.43)	10 (3.42)	0 (0.0)
Chest distress, n(%)	74 (2.25)	7 (2.40)	4 (28.57)
Nasal congestion, n(%)	68 (2.06)	6 (2.05)	0 (0.0)
Dizziness, n(%)	62 (1.88)	8 (2.74)	0 (0.0)

Diarrhea, n(%)	57 (1.73)	4 (1.37)	0 (0.0)
Shortness of breath, n(%)	51 (1.55)	9 (3.08)	8 (57.14)
Nausea or vomiting, n(%)	24 (0.73)	2 (0.68)	0 (0.0)
Anorexia, n(%)	23 (0.70)	0 (0.0)	0 (0.0)
Abdominal pain, n(%)	20 (0.61)	0 (0.0)	0 (0.0)
Chest pain, n(%)	11 (0.33)	4 (1.37)	0 (0.0)

Figure 1

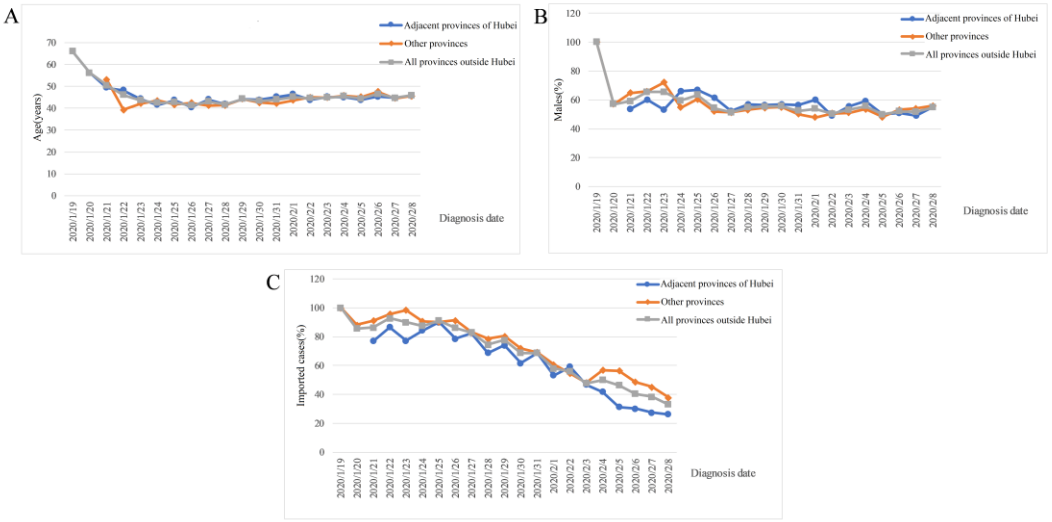

Figure 2

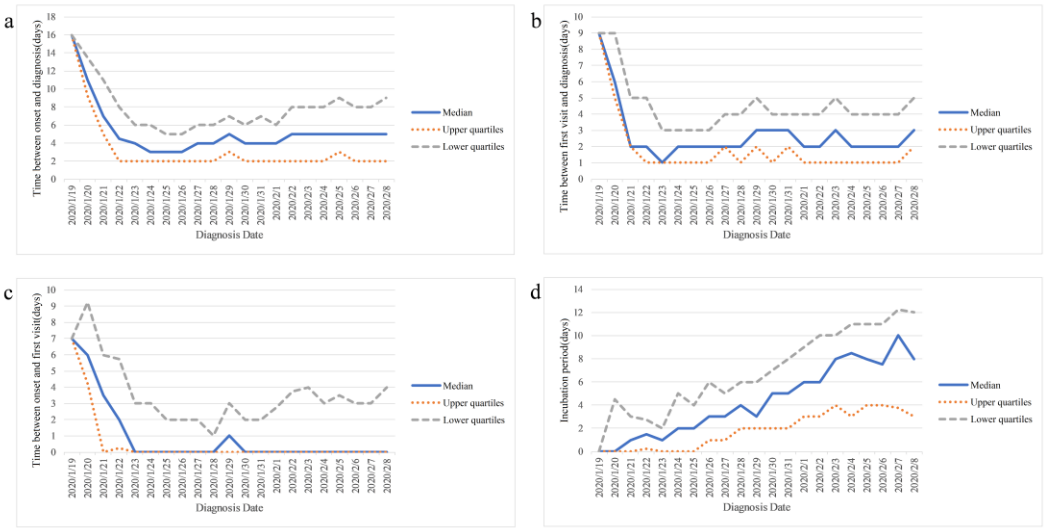

Figure 3

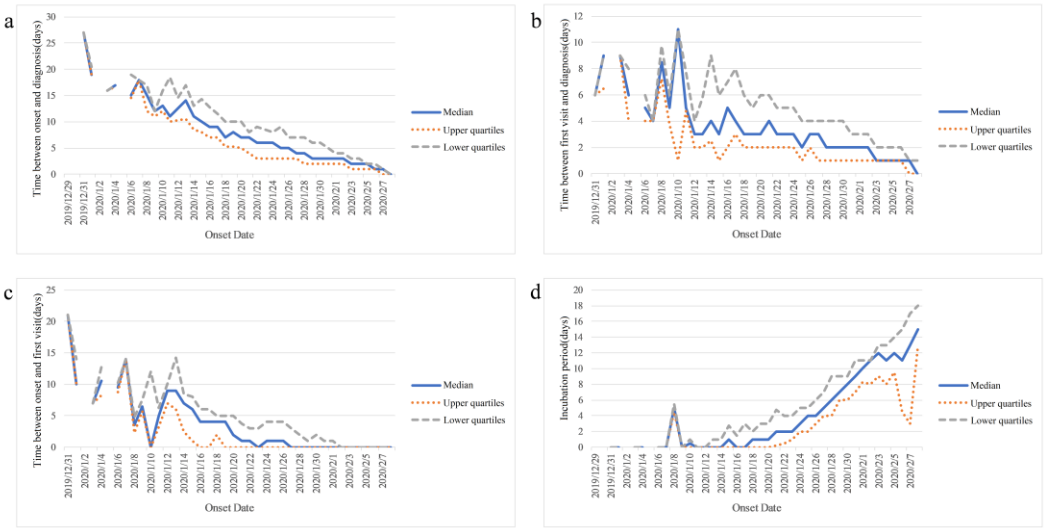

Figure 4