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Estimation of the Incubation Period and the Serial Interval of COVID-19 in Chongqing, China

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Abstract: In December 2019, the initial case of COVID-19's disease appeared in Wuhan, Hubei Province, China. But it soon caused an outbreak in Chongqing as well. Reasonable estimates for the incubation period distribution and the serial interval distribution would provide timely information to guide intervention policy for the government of Chongqing. We collect individual information from Chongqing Center for Disease Control and Prevention(CQCDC). We use doubly interval-censored data to estimate the incubation period and the serial interval for confirmed cases exposed to COVID-19 during incubation period,the mean incubation period is estimated to be 7.5(6.6-8.6,95% CI) days and the mean serial interval is estimated to be 6.1 (5.0-7.5,95% CI) days. The analysis result show that COVID-19 could spread in the incubation period,which may complicate quarantine work. The implementation of control measures is indispensable in reducing the spread of asymptomatic incubation period in high-risk population.

Keywords: COVID-19; Incubation Period; Serial Interval; Chongqing; Coronavirus

Key Massages:

1.To estimate the incubation period and the serial interval for confirmed cases exposed to COVID-19 during both the incubation period and symptomatic period.

2.To verify that COVID-19 could spread in the incubation period.

3.To compare the differences of incubation period and serial interval among patients with different contact periods.

Introduction

In December,2019,an outbreak of novel coronavirus disease COVID-19 broke out in Wuhan, Hubei Province of China[1].The novel coronavirus SARS-CoV-2,dubbed COVID-19 (coronavirus disease 2019) by the World Health Organization (WHO) is characterized by fever,cough,fatigue, shortness of breath,pneumonia,and other respiratory tract symptoms[2–4],and in many cases will develop to death. Due to the migration of the annual Spring Festival,the epidemic spread rapidly.As a close neighbor of Wuhan,Chongqing has become one of the cities which was most affected by the coronavirus disease COVID-19 epidemic, during the early stage. As of January 21st, Chongqing has reported 5 cases of coronavirus COVID-19,including 2 cases in Wushan, 2 cases in Wanzhou and 1 case in Changshou[5]. All of the imported cases have lived experience of working in Wuhan. Fortunately, the officials have taken effective measures to control them.

As of February 24st,there were no newly confirmed cases in 13 districts and counties in Chongqing for 14 consecutive days,and there were no newly confirmed cases in 26 districts and counties for 7 consecutive days[6]. At the same time,the global epidemic is getting more and more serious.Key aspects of novel coronavirus disease (COVID-19) transmission dynamics in 2019 are still unclear [7].

Due to the lack of understanding of the key epidemiological and transmission characteristics of new pathogens,especially the limited understanding of their transmission ability and toxicity in the population.

Through the estimation of incubation period and serial interval and exposure type analysis, we provide the infection characteristics of COVID-19, that is, incubation period and serial interval, in order to provide clues to containment measures and reduce the spread of infection.

1. Method

1.1 Case definitions

According to standard clinical guidelines,COVID-19 suspected cases are defined as the combination of clinical characteristics and epidemiological histories. Clinical characteristics of suspected case must fit at least 2 of 3 following criteria: “fever and/or symptoms in respiratory system; radiographic evidence of pneumonia[8]; The white blood cell count is low or normal, or the lymphocyte count is low. ” Epidemiologic histories must fit at least 1 of 4 following criteria: “a history of traveling in Hubei Province or other districts that has confirmed cases reported within 14 days of symptom onset; Previous contact with a patient with fever or respiratory symptoms from Hubei Province or elsewhere who reported a confirmed case within 14 days of the onset of symptoms;Anyone who has close contact with confirmed case; cluster cases[8].” A confirmed case was defined as a case with respiratory specimens that tested positive for the COVID-19 by at least one of the following two methods:positive result by real-time Reverse-Transcription-Polymerase-Chain-Reaction (RT-PCR) assay for COVID-19 or a genetic sequence that matches COVID-19.

1.2 Data sources

The COVID-19 infectious disease report card and close contacts survey were obtained from the China Disease Control and Prevention Information System.The COVID-19 cases reported in Chongqing from January 21,2020 to March 31st were investigated and collected according to the notice of the "Notifications of the Sero-epidemiological Survey Plan for the Issuance of COVID-19 Asymptomatic Infectious Diseases" (National Office of inventions [2020] 14).We collect individual information including age, gender, source of infection, onset time of symptoms, diagnosis time, the left and right endpoints on the possible exposure interval.

We divide patients into three categories:

1. Incubation period exposure:When the patient comes into contact with infectious people,the infectious people are in the incubation period without any symptoms;
2. Symptomatic period exposure: When the patient contacts the infectious person,the infectious person has developed symptoms;
3. Unsure: the patient has contacted the infectious person who has not yet come into contact with the infectious person who has already developed the disease,but is not sure which kind of infectious person is infected.

The incubation period,that is,the time between infection to onset,is very important in the monitoring and control of infectious diseases,but it is usually only a rough observation[9].To estimate the incubation period,we delete the data of asymptomatic patients. We estimate the incubation period with doubly interval-censored data[10].

The serial interval of COVID-19 is defined as the time duration between a primary case-patient injector) having symptom onset and a secondary case-patient (infected) having symptom onset [11-12]. As for the serial interval,we use the time to diagnose the source of infection and the infected person instead of the onset time of symptoms.

1.3 Statistical Analysis

The incubation period is calculated with doubly interval-censored data by using Survival Analysis and the doubly interval-censored analyses[13].We use Survival Analysis for estimating the serial interval.In order to estimate the incubation period and the serial interval accurately,only confirmed cases are retained.

2. Result

Up to March 30th,2020,576 cases of COVID-19 have been reported in Chongqing,and we collect personal information on 552 confirmed cases.Among the 552 confirmed cases,the median age is 48 years (38-56) and 283 cases(51.2%) are female.In addition, we also analyzed the time interval from symptoms to diagnosis. The mean interval of 4.3 days.

2.1 Estimation of incubation period

For confirmed cases infected with COVID-19 during the incubation period,the Lognormal distribution provides the best

match with the data by using Survival Analysis (Tab. 1). We estimate that the mean incubation period in Chongqing is 7.5 (6.6-8.6,95% CI) days. The incubation period in Chongqing ranged from 1.1 to 23.4 days (2.5^{th} to 97.5^{th} percentile).Then we used the Lognormal distribution to fit the coarse data for estimating the incubation period. This time,the mean incubation period was estimated at 7.5 days (6.3-8.7 days, 95% CI).

For confirmed cases infected with COVID-19 during symptomatic period,the Gamma distribution provides the best fit to the data by using Survival Analysis(Tab. 2). The mean incubation period in Chongqing was estimated to be 6.0(4.9-7.2,95% 95% CI) days. The incubation period in Chongqing ranged from 0.9 to 19.3 days (2.5^{th} to 97.5^{th} percentile).Then we used the Gamma distribution to fit the coarse data for estimating the incubation period.The mean incubation period in Chongqing was estimated to be 6.0 (5.0-7.2,95% CI) days.

Tab. 1 Estimated incubation period for confirmed cases[a]

	Mean (Days)		
Distribution	Estimate	(95% CI)	AIC*
Lognormal	7.5	(6.6,8.6)	356.9
Weibull	8.4	(3.5,17.9)	359.1
Gamma	8.1	(7.0.9.3)	357.0

AIC*:Short for Akaike information criterion; this indicates the goodness-of-fit,where lower values indicate a better fit.
confirmed cases[a]:The confirmed cases exposed to COVID-19 during incubation period.

Tab. 2 Estimated incubation period for confirmed cases[b]

	Mean (Days)		
Distribution	Estimate	(95% CI)	AIC*
Lognormal	5.4	(4.4,6.6)	244.3
Weibull	6.1	(4.7,8.1)	243.5
Gamma	6.0	(4.9,7.2)	241.7

AIC*: Short for Akaike information criterion; this indicates the goodness-of-fit,where lower values indicate a better fit.
confirmed cases[b]:The confirmed cases exposed to COVID-19 during symptomatic period.

2.2 Estimation of serial interval

For confirmed cases infected with COVID-19 during the incubation period,the Lognormal distribution provides the best fit to the data by using Survival Analysis (Tab. 3). The mean serial interval in Chongqing was estimated to be 6.1 (5.0-7.5,95% CI) days. The incubation period in Chongqing ranged from 1.9 to 20.1 days (2.5^{th} to 97.5^{th} percentile).For confirmed cases infected with COVID-19 during symptomatic period,the Weibull distribution provides the best fit to the data by using Survival Analysis(Tab. 4). The mean serial interval in Chongqing was estimated to be 4.9(3.9-6.0,95% CI) days. The incubation period in Chongqing ranged from 0.4to 17.8 days (2.5^{th} to 97.5^{th} percentile).

Tab. 3 Estimated serial interval for confirmed cases[a]

	Mean (Days)		
Distribution	Estimate	(95% CI)	AIC*
Lognormal	6.1	(5.0,7.5)	189.9
Weibull	6.7	(5.4,8.3)	194.8
Gamma	6.5	(5.3,8.0)	192.1

AIC*: Short for Akaike information criterion; this indicates the goodness-of-fit,where lower values indicate a better fit.
confirmed cases[a]:The confirmed cases infected with COVID-19 during incubation period.

Tab. 4 Estimated serial interval for confirmed cases[b]

	Mean (Days)		
Distribution	Estimate	(95% CI)	AIC*
Lognormal	4.1	(3.3,5.2)	382.4
Weibull	4.9	(3.9,6.0)	377.6
Gamma	4.7	(3.8,5.6)	378.3

AIC*: Short for Akaike information criterion; this indicates the goodness-of-fit,where lower values indicate a better fit.

confirmed cases[b]:The confirmed cases infected with COVID-19 during symptomatic period.

2.3 Comparison of COVID-19 incubation period to other study

A comparison to the estimated incubation period distribution for COVID-19(Tab. 5) shows that there are difference between these values, but the differences are not significant.The estimated mean incubation periods for COVID-19 in Chongqing are slightly longer.

Tab. 5 Estimated incubation periods for coronaviruses from different studies

		Mean (Days)	
Study	Distribution	Estimate	(95% CI)
This study(Incubation period contact)	Lognormal	7.5	(6.6,8.6)
This study(Incubation period contact)	Weibull	8.4	(3.5,17.9)
This study(Incubation period contact)	Gamma	8.1	(7.0.9.3)
This study(Symptomatic period contact)	Lognormal	5.4	(4.4,6.6)
This study(Symptomatic period contact)	Weibull	6.1	(4.7,8.1)
This study(Symptomatic period contact)	Gamma	6.0	(4.9,7.2)
This study(Unsure)	Lognormal	5.7	(4.9,6.5)
This study(Unsure)	Weibull	6.4	(5.0,8.3)
This study(Unsure)	Gamma	6.2	(5.4,7.1)
Li Q[8]	Lognormal	5.2	(4.1,7.0)
Chun,J. Y. [14]	Lognormal	2.87	(2.33,3.50)
Ren,X. [15]	Lognormal	5.3	(4.6,6.0)
Du Z C [16]	Lognormal	4.958	(3.472,7.318)
Du Z C [16]	Gamma	5.083	(3.511,7.314)
Du Z C [16]	Weibull	5.695	(3.675,7.674)
Yang,L. [17]	Weibull	5.5	(4.8,6.0)

3. Discussion

This study provides an initial analysis among epidemiologic characteristics and two typical transmission phenomena of COVID-19 in Chongqing. The mean incubation period in Chongqing was estimated to be 7.5(6.6-8.6,95% CI)and 6.0(4.9-7.2,95% CI) days and the mean serial interval is estimated to be 6.1 (5.0-7.5,95% CI)and 4.9(3.9-6.0,95% CI) days.It can be seen from the results that both the estimation of incubation period and the estimation of serial interval,the cases exposed to infection in the incubation period were slightly longer than those in the symptomatic period. When collecting data,the exposure time range filled in by confirmed patients exposed to infected individual during the incubation period may be longer than the actual one,and it is difficult to recall the exact date. As for the serial interval,we replace the onset time of symptoms with the time of diagnosis of the source of infection and the infected person,because we found that the interval between the onset time and the diagnosis time of most patients is too long. Considering the imperfection of medical examination methods in the early stage of the epidemic and the patients' lack of active seeking medical treatment,we finally decided to use the diagnosis time to estimate the serial interval. In any case, there may be some unreasonable aspects in our way of

processing data in this way, but whether there is a more sensible way of data processing remains to be considered. The incubation period that we calculate is slightly longer according to other studies(Tab. 5).

It's not hard to find out that the estimated values of serial interval is shorter than the incubation period.This result can preliminarily prove the possibility of COVID-19 spreading in the incubation period.The infectivity of incubation period increases the difficulty of control and the risk of infection,which indicates that personal protective measures are necessary.

We estimate a mean serial interval for COVID-19 of 4.9 (3.9-6.0,95% CI) days and 6.1 (5.1-9.2,95% CI) days. Li et al. [8] estimated the serial interval distribution to have a mean of 7.5 days (5.5-19,95% CI) based on 6 observations,and the incubation period distribution has a mean of 5.2 days (4.1-7.0,95% CI) based on 10 observations. Other studies estimate the incubation period distribution to have a mean of 6.4 days (5.6-7.7 95% CI) [18],median of 5 days (4.0-5.8 95% CI)[19],mean of 5.2 days (range 1.8-12.4 days) [20],and a mean of 4.8 days (range 2-11 days) [21]. After comparison,our estimated results are close to those of other studies.It indicates that our estimation results have a certain reference value.

Although many scholars have found novel coronavirus pneumonia epidemiological characteristics,many countries have not effectively controlled the epidemic situation. Even after the successful control of the epidemic in China,some countries are still dissatisfied with such important measures as wearing masks and isolation,which is also the reason why it is difficult to effectively control the epidemic abroad.

In recent years,mankind has been faced with new crises,such as SARS,H1N1,Ebola COVID-19 pneumonia etc. The reason why we can control the epidemic so quickly is that we have studied SARS and gained experience before.Although the new epidemic in the future may be different from the COVID-19 pneumonia,it has left us with experience and knowledge on how to deal with sudden epidemic again.

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