

# Epidemiological and clinical characteristics of imported cases with COVID-19 infection: a multicentre study

**Jinjun Zhang** (✉ [zhang92560@163.com](mailto:zhang92560@163.com))

Beijing Emergency Medical Center

**Shixiong Yang**

Nanning Emergency Medical Center

**Yi Xu**

Chongqing Emergency Medical Center

**Jialiang Liu**

Jinan Emergency Medical Center

**Jinjun Guo**

Chongqing Emergency Medical Center

**Sijia Tian**

Beijing Emergency Medical Center

**Shaoping Wang**

Jinan Emergency Medical Center

**Kai Liao**

Nanning Emergency Medical Center

**Ying Zhang**

Chongqing Emergency Medical Center

**Yu Ma**

Chongqing Emergency Medical Center

**Yuguo Chen**

Shandong University Qilu Hospital

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## Research Article

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## **Abstract**

Objective: Numerous cases of COVID-19 were confirmed in the world in succession. We reported the epidemiological and clinical features of 478 confirmed cases from a multicentre study outside of Wuhan, China.

Methods : We collected patients who were transferred by Emergency Medical Service to the designated hospitals in four major cities including Beijing, Chongqing, Jinan and Nanning in China. We compared the characteristics between imported and indigenous cases, and calculated the fatality, and the rate of severe cases, mild and asymptomatic cases to generate the pyramid of COVID-19 infection.

Results : The mean age of patients was 46.9 years old and 49.8% were male. The most common symptoms at the onset of illness were fever (69.7%), cough (47.5%), fatigue (24.5%), dyspnea (8.4%) and headache (7.9%). In the study, most cases (313, 65.5%) were indigenous, while 165 (34.5%) were imported. During the early stage, the imported cases were dominant, which declined from Feb 1, when the indigenous cases rise sharply. Compared with the indigenous cases, the imported cases were significantly distinct concerning gender composition ( $P=0.002$ ), classification of severity ( $P=0.006$ ).

Conclusions : On the basis of this study, we suggest that preventing import from outside and controlling spread inside should be a basic principle for resisting COVID-19 infection. If not, the region or area will face chaos.

## **Introduction**

According to the World Health Organization (WHO) report, as of March 30, 2020, a total of 693282 cases with laboratory-confirmed with novel coronavirus (COVID-19) infection pneumonia have been detected in the world.[1–2] In mainland China, there have been 81518 accumulated confirmed cases of COVID-19 infections, of which 3305 patients have died, 76052 have been discharged and 2161 patients remained in hospital.[3] The confirmed cases were also reported in Italy, Thailand, Singapore, Vietnam, the US, and more than 200 countries or regions globally.[4–6] The recent published literatures on the epidemic and clinical features of COVID-19 mainly focused on Wuhan, China,[7–10] relatively few on outside of Wuhan. [11–12] A multicentre clinical study is more exceedingly rare. Furthermore, the data of most studies were obtained from the early stages of the outbreak in Wuhan, in which the reported cases might have been incomplete observed, which might be admitted to the intensive care unit afterward. Herein, COVID-19 is a new global health issue, it is understandable that its emergence and spread cause confusion, anxiety and fear among the general public. We provided a multicentre retrospective clinical study to analyze the epidemiological and clinical characteristics of imported patients with confirmed COVID-19 infection in four cities in China, and tried to unravel the proportion and relationship between the imported and indigenous cases.

## **Methods**

# **Study design and participants**

This is a multicentre retrospective study. We enrolled patients with COVID-19 infection who were transferred from the general hospitals to the designated hospitals for special treatment of infectious diseases by Emergency Medical Service (EMS) in Beijing, Chongqing, Jinan and Nanning outside of Wuhan, China, from Jan 20 to Feb 20, 2020. Patient was defined as a confirmed case with COVID-19 infection according to the new coronavirus pneumonia diagnosis and treatment program published by the National Health Commission of the People's Republic of China.[13] Only laboratory-confirmed COVID-19 infection was enrolled in this study, laboratory confirmation of COVID-19 was detected in the first admission hospital and verified by the local. The information including demographic, epidemiological, clinical, laboratory test for the COVID-19, diagnostic type, cluster case and outcome etc were collected in four major cities of China. Clinical outcomes were followed up to February 20, 2020. If the data missing from the medical records was needed, we obtained by direct communication with EMS providers.

An imported case was defined as a confirmed case who acquired COVID-19 infection outside the area where it was diagnosed referencing to the WHO definition on malaria.[14] The definition was done by investigation of patient's travel history to Hubei province, especially to Wuhan endemic area through epidemiological history. While an indigenous case was defined as a case infected in the local.

## **Statistical analysis**

Continuous variables were expressed as the means and standard deviations, and were compared with the Mann-Whitney U test. The categorical variables were presented as percentages in each category and analyzed by Wilcoxon test between imported and indigenous cases. All statistical analysis were performed with SPSS software version 22.0. P < 0.05 was the threshold for statistical significance.

## **Results**

By Feb 20, 2020, 478 patients who were identified as confirmed COVID-19 infection were included in this study, those patients were transferred from 89 hospitals in Beijing, Chongqing, Jinan and Nanning to the designated hospitals by the local EMS(figure 1) , of whom 328 (68.6%) patients were associated with clustering which had two confirmed cases at least in a family, hospital or other place closed contact within 14 days, 254 (53.1%) patients were familial clustering. The mean age of patients was 46.9 years, and 88 (18.4%) were older than 65 years, 238 (49.8%) were men. The most common symptoms of illness onset were fever (69.7% ), cough (47.5%), fatigue (24.5%), dyspnea (8.4%) and headache (7.9%). The mean time from contact symptomatic case to illness onset was 7.9 days, from illness onset to visit hospital was 2.6 days, from visit hospital to defined confirmed case was 1.6 days (table 1).

347 (72.6%) patients were mild cases, 48 (10%) were asymptomatic, it's one of the particular features of this study, and there were 83 (17.4%) severe patients, 4 (0.8%) patients died. The fatality, the severe rate and the mild and asymptomatic rate due to COVID-19 infection were 1 death, 17 severe and 82 mild or asymptomatic (per 100 patients) respectively (figure 2A). Compared with the data published by the

National Health Commission of the People's Republic of China, the rate of types of infection were no difference ( $Z=-1.027$   $P=0.304$ ). The pyramid ratio for all confirmed cases with COVID-19 infection was 1:4:28 in China (figure 2B). By the end of Feb 20, 2020, 198 (41.4%) of 478 patients were discharged and 276 (57.7%) remained in hospital, 4 (0.8%) patients died (table 1).

There were the first confirmed case on January 20, 2020 in Beijing and Chongqing, the first four confirmed case in four cities all have been to Wuhan before illness onset. Of 478 patients, most cases (313, 65.5%) were classified as the indigenous, and 165 (34.5%) cases were the imported cases. The daily new imported cases were increased during the early stage, exceeding the number of indigenous from Jan 20 to Jan 31, 2020, then declined afterwards, the number of accumulated cases both of imported and indigenous were same on Feb 3. The number of new daily cases and accumulated cases of indigenous exceeding imported after Feb 3, and declined quickly after Feb 4, 2020 (figure 3-4).

Compared with the indigenous, the imported was significantly different in gender composition ( $=9.295$ ,  $P=0.002$ ), degree of disease ( $=10.149$ ,  $P=0.006$ ), fever ( $=19.411$ ,  $P<0.001$ ), the highest body temperature ( $=23.665$ ,  $P<0.001$ ), family clustering ( $=39.258$ ,  $P<0.001$ ), history of contact ( $=24.908$ ,  $P<0.001$ ) and the primary outcome ( $=29.168$ ,  $P<0.001$ ) (table 1).

## Discussion

This multicentre study, to our best knowledge, is the series to explore the epidemiological and clinical characteristics of imported patients with COVID-19 infection outside of Wuhan, China, including data on 478 patients who were transferred by EMS to the designated hospitals for special treatment of infectious diseases in Beijing, Chongqing, Jinan and Nanning in China. According to prof. Wu et al forecasted, Chongqing and Beijing were the top two imported cities with high risk of epidemics of COVID-19, Jinan and Nanning relatively low, [15] therefore above four cities were enrolled. As of Feb 20, 2020, 198 (41.4%) of 478 patients were discharged and 276 (57.7%) remained in hospital, 4 (0.8%) patients died. The fatality of COVID-19 infection was 0.8%, significantly lower than other studies.[7, 9, 10, 11] The proportion of severe versus mild and asymptomatic cases were 1:5, and noteworthy, the rate of asymptomatic cases was higher than our previous study.[16] According to the results, we generated the pyramid of COVID-19 infection. The concept of the COVID-19 pyramid was firstly used by Munster VJ et al, in the study – A novel coronavirus emerging in China-key questions for impact assessment, published in the New English Journal of Medicine on February 20, 2020,[17] the pyramid showed the proportion of mild and asymptomatic cases versus severe cases and death cases directly, and could be used as an indicator that enables an intuitive understanding of the scope of each type of COVID-19 infection.[18] Asymptomatic cases (10%) were mainly found in close contacts during medical observation in this study, if can not found, asymptomatic can transmit from person to person, which has been proved.[19–20] Thus, identifying and controlling asymptomatic cases are the important measures to prevent transmission of COVID-19.

We observed that a greater number of patients were young and middle-aged, the mean age of patients was 46.9 years old, 18.4% were old than 65 years. 238 (49.8%) were men, there were no difference between male and female. As mentioned in previous studies, the most common symptoms of illness onset were fever, cough, fatigue, and headache, severe cases with dyspnea.

With globalization and increased international movement by convenient transportation, possible transmission of COVID-19 infection has become an important public health issue in the world, rigid prevention and control both for imported cases from epidemic area and exported to other places are vital. In this study, 34.5% cases were imported from Wuhan or other cities of Hubei province, and localization after a while. The daily new imported cases were increased during the early stage, exceeded the number of indigenous after about ten days, then declined, and the number of new daily and accumulated cases of indigenous exceeded imported. Both new daily imported and indigenous cases declined quickly after Feb 4, 2020. Therefore, the four cities were very successful in preventing and controlling the COVID-19 infection. It benefits from the correct leadership and experience of SARS in 2003 greatly.

Compared with indigenous, the imported cases were significantly different concerning gender composition, classification of severity, fever, the highest body temperature, family clustering, history of contact and the primary outcome. Most imported patients were men, maybe men traveled times more than women. While the rate of asymptomatic of indigenous cases were higher than imported, mainly for asymptomatic cases were found in close contacts during medical observation in this study, therefore, the close contacts should be quarantined and observed for 14 days at least. This leads to another difference, fever, which has significantly difference with the highest body temperature between indigenous and imported, 37.1% of indigenous patients were afebrile. Most indigenous patients cause by the clustering (78.3%), mainly were family clustering, members of family should be quarantined earlier.

This study has some limitations. First, only the COVID-19 confirmed cases transferred by EMS just in four cities were included, the first admission to the designated hospitals cases were not enrolled. It would be better to cover as wide population as possible. Second, the observation time of this study is 30 days, which is still short, many patients need time to further observed. However, this study represents characteristics of relatively middle stage of COVID-19 in four cities in China, which has certain value for future control and research for the world.

## Conclusion

In this paper, we presented the characteristics of imported patients with COVID-19 infection in four cities outside of Wuhan, which were obviously different from indigenous cases, with a lower fatality and higher discharge rate, new infected patients had shifted from the imported to local gradually, and have been declined to a low level. On the basis of this study, we suggest that preventing import from outside and controlling spread inside should be a basic principle for resisting COVID-19 infection. If not, the region or area will face chaos. We should pay more attention to other countries.

# **Abbreviations**

CDC: Center for Disease Control; COVID-19: Corona Virus Disease 2019; EMS: Emergency Medical Service; WHO:World Health Organization;

# **Declarations**

## **Acknowledgments**

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## **Authors' contributions**

JZ, YM and YC conceived and designed the study. SY, YX, JL, SW, KL, and YZ collected data. JZ, and ST analysed data. JZ and ST wrote the first draft. All authors read and approved the final manuscript.

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## **Availability of data and materials**

Not applicable.

## **Ethics approval and consent to participate**

The study was approved by Ethics Committee of Beijing Emergency Medical Center (No.2020-01) and the written informed consent was waived.

## **Consent for publication**

Not applicable.

## **Competing interests**

The authors declare that they have no competing interests.

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## Tables

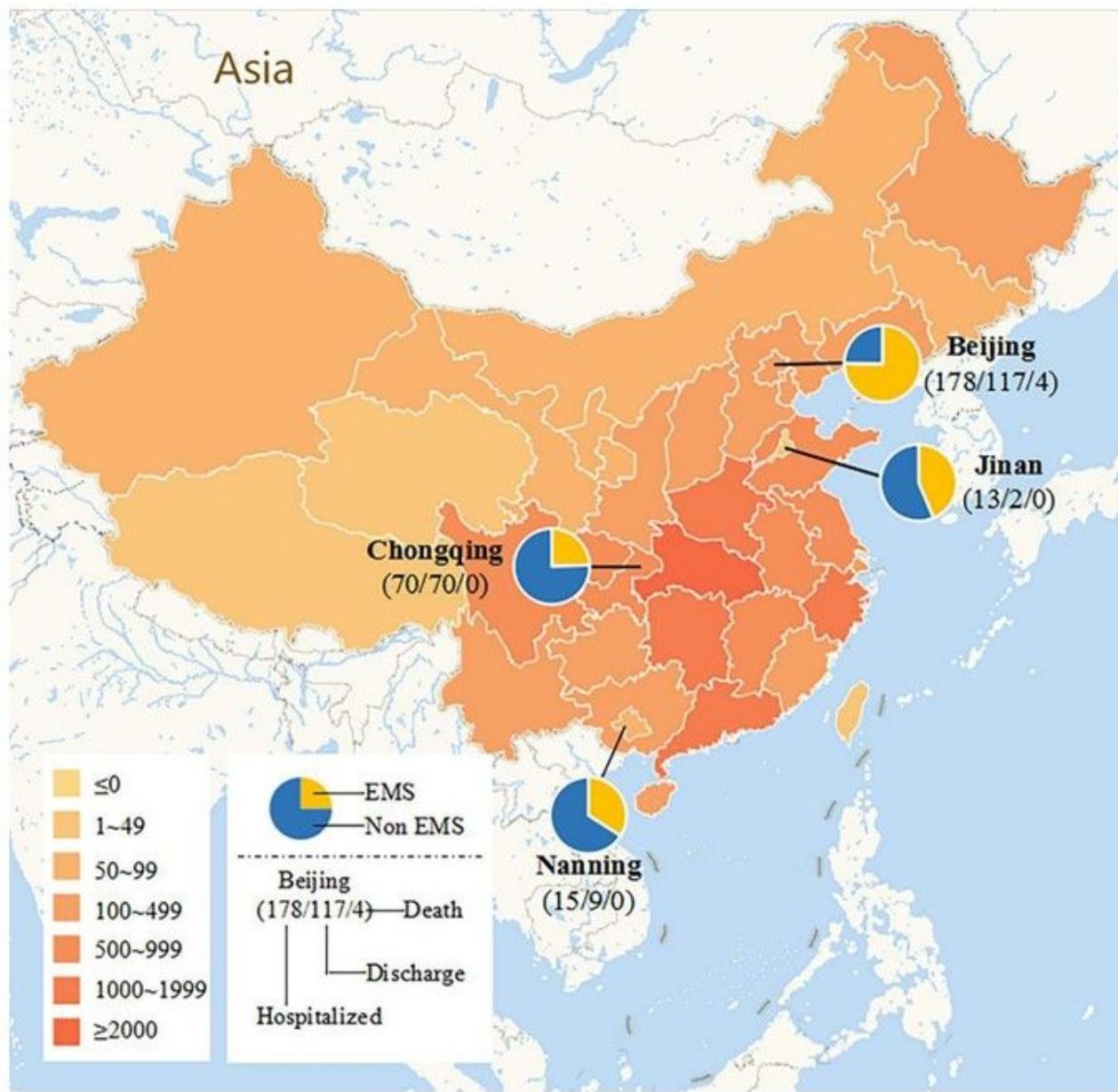
Table 1 Characteristics of the imported and indigenous cases with COVID-19

	All case (N=478)	Imported (N=165)	Indigenous (N=313)	Statistic value	P
Male(%)	238(49.8)	98(59.4)	140(44.7)	9.295	0.002
Age group				2.713	0.258
Median(range),y	46(1-94)	44(1-89)	47(1-94)		
<18	32(6.7)	9(5.5)	23(7.3)		
19-64	358(74.9)	131(79.4)	227(72.5)		
≥65	88(18.4)	25(15.2)	63(20.1)		
City				18.564	<0.001
Beijing	299(62.6)	123(74.5)	176(56.2)		
Chongqing	140(29.3)	33(20.0)	107(34.2)		
Jinan	15(3.1)	6(3.6)	9(2.9)		
Nanning	24(5.0)	3(1.8)	21(6.7)		
Degree of Disease				10.149	0.006
Asymptomatic	48(10)	8(4.8)	40(12.8)		
Mild	347(72.6)	133(80.6)	214(68.4)		
Severe	83(17.4)	24(14.5)	59(18.8)		
Symptoms					
Fever	333(69.7)	136(82.4)	197(62.9)	19.411	<0.001
Highest temperature				23.665	<0.001
<37.3	145(30.3)	29(17.6)	116(37.1)		
37.3-38.0	177(37.0)	74(44.8)	103(32.9)		
38.1-39.0	142(29.7)	53(32.19)	89(28.4)		
>39.0	14(2.9)	9(5.5)	5(1.6)		

Cough	227(47.5)	75(45.5)	152(48.6)	0.418	0.518
Fatigue	117(24.5)	45(27.3)	72(23.0)	1.065	0.302
Dyspnoea	40(8.4)	11(6.7)	29(9.3)	0.951	0.329
Headache	38(7.9)	12(7.3)	26(8.3)	0.158	0.691
Cluster	328(68.6)	83(50.3)	245(78.3)	39.258	<0.001
Family	254(53.1)	66(40.0)	188(60.1)		
Other	74(15.5)	17(10.3)	57(18.2)		
History of Contact	435(91.0)	165(100.0)	270(86.3)	24.908	<0.001
Have been to Wuhan in 14 days	136(28.5)	136(82.4)	0(0.0)	360.580	<0.001
Have contacted the confirmed case in 14 days	285(59.6)	30(18.2)	255(81.5)	179.761	<0.001
Outcome				29.168	<0.001
Hospitalized	276(58.8)	68(41.2)	208(66.5)		
Discharged	198(41.4)	96(58.2)	102(32.6)		
Death	4(0.8)	1(0.6)	3(1.0)		

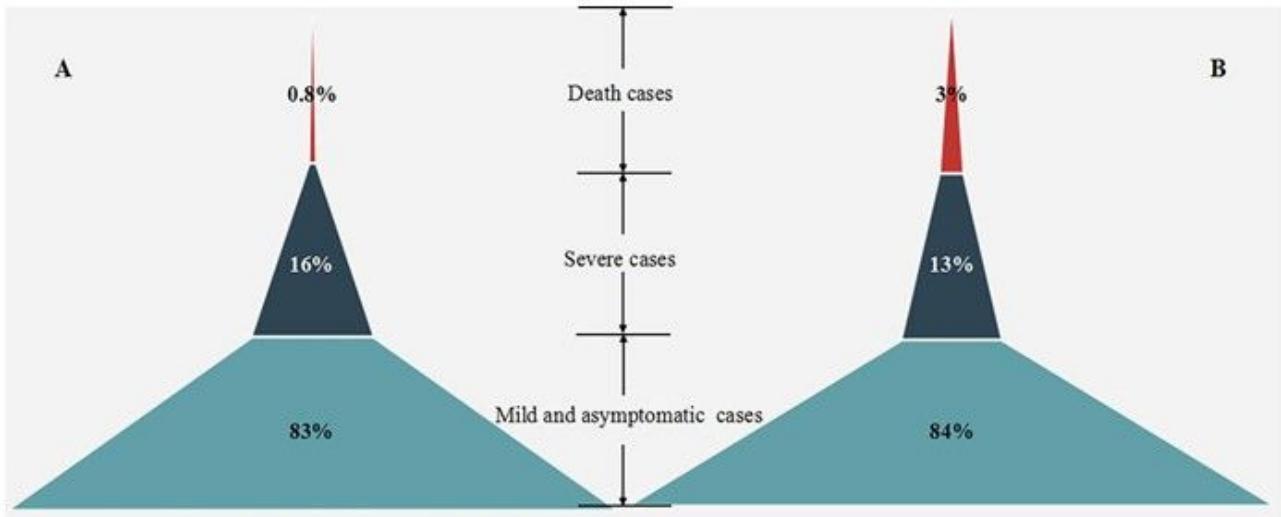
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## Figures



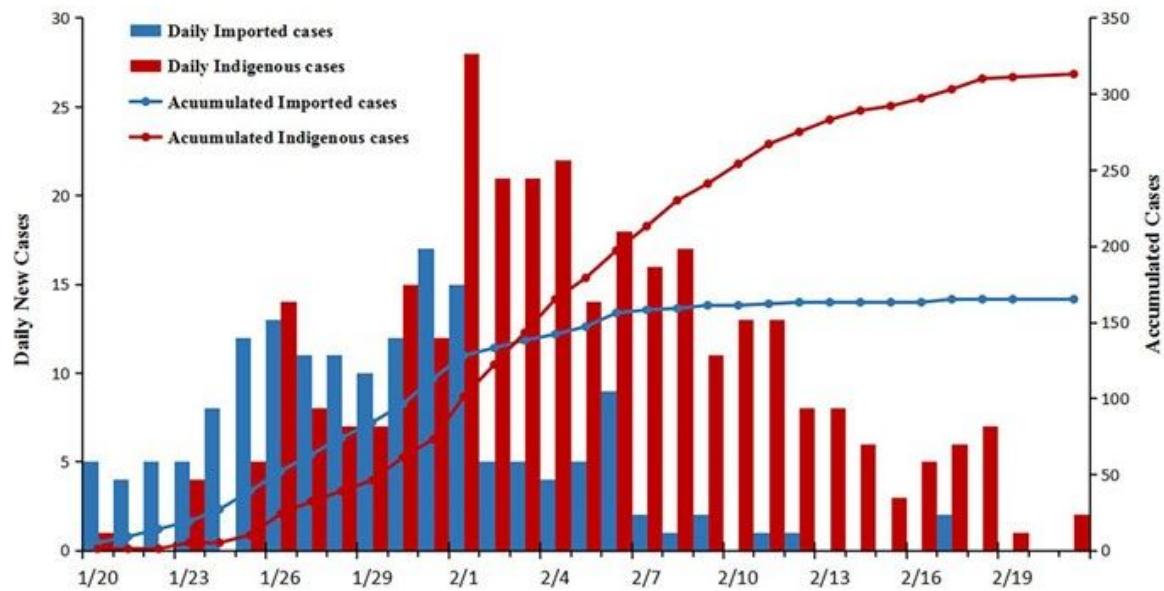
**Figure 1**

Geographic distribution of COVID-19 infection in China, as of February 21, 2020. EMS: Patient who was transferred by EMS from general hospital to the designated hospital. Non EMS: Patient who didn't transferred by EMS. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.



**Figure 2**

### Pyramid of COVID-19



**Figure 3**

### Change of imported cases

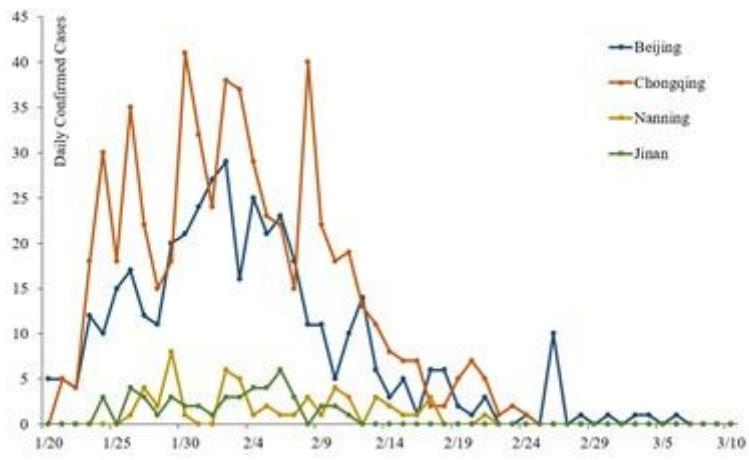
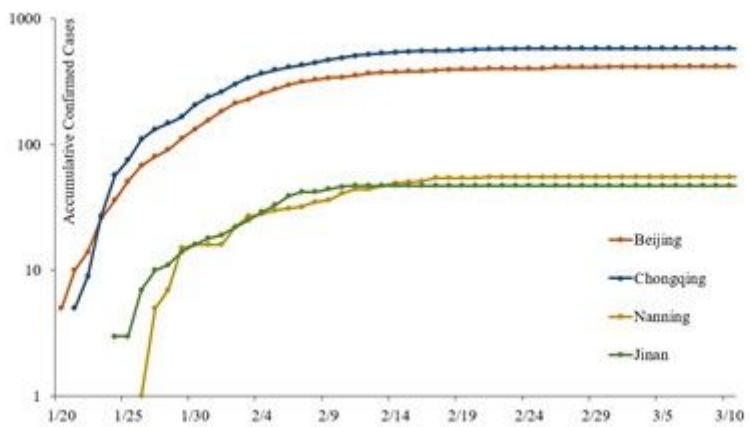


Figure 4A Daily new COVID-19 Cases reported



## Figure 4

4A Daily new COVID-19 Cases reported 4B Accumulative COVID-19 Cases reported