Early warning signs for severe patients with Coronavirus Disease 2019 and its epidemi Biological significance

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Research

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Abstract

Background Since December 2019 coronavirus disease 2019 (COVID-19) emerged in Wuhan city and rapidly spread throughout China. However, early warning signs for severe patients with COVID-19 were not fully known.

Methods Information on admission was collected through a standard questionnaire. We described the epidemiological characteristics of the patients with COVID-19, analyzed the risk factors associated with severe illness, and estimated the key epidemiologic time-delay distributions.

Results A total of 631 patients with laboratory-confirmed COVID-19 were identified. The proportion of severe cases was 8.4%. The epidemic of COVID-19 experienced four stages: sporadic phase, exponential growth phase, peak plateau phase, and declining phase. The proportion of severe cases was significantly different in four stages and 13 municipal prefectures (P < 0.001). Factors including elderly more than 65 years (yrs) old, underlying medical conditions, fever patient whose highest temperature beyond 39.0°C, dyspnea, and lymphocytopenia(< 1.0 × 10⁹/L) could possibly become the early warning signs for severe patients of COVID-19. In contrast, earlier visit to the clinic could reduce the severe risk. Besides, the viral load may be a potentially useful marker associated with disease severity of COVID-19 infection.

Conclusions The epidemic experienced four stages with obviously areas difference. People aged beyond 65 yrs or underlying medical conditions once appear symptoms like fever beyond 39.0°C and/or dyspnea should immediately visit health care.

Background

The World Health Organization (WHO) has recently declared COVID-19 a public health emergency required international concern[1]. China has incorporated COVID-19 as a national notifiable disease since January 20, 2020. As of March 9, 2020, a total of 80859 laboratory-confirmed cases and 3100 deaths had been documented in China[2]. Much effort has been devoted to rapidly understand the epidemiology, severity, and impact of COVID-19[3].

Since COVID-19 was first identified in Wuhan[4], it has been shown to have a wide spectrum of severity[3]. To better describe epidemiological characteristics and identify early warning signs for severe cases of COVID-19, we performed an analysis of all laboratory-confirmed cases in Jiangsu Province between 1 January, 2019 and March 9, 2020.

Methods

Case definitions

A laboratory-confirmed confirmed case of COVID-19 was defined as positive results of both ORF1ab and N gene (BioGerm) by Real-time reverse transcriptase polymerase chain reaction (RT-PCR). Sputum and throat swab specimens collected from all patients on admission. Laboratory confirmation of severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) was performed at the Jiangsu Center for Disease Control and Prevention
(JSCDC) before February 2, 2020, and subsequently in 13 certified municipal labs in each city of Jiangsu Province. RT-PCR were performed in accordance with the protocol established by the WHO[5].

We defined the degree of severity of COVID-19 (severe vs. non-severe) according to the COVID-19 diagnosis and treatment guideline published by the National Health Commission of China[6].

Data collection

A total of 631 laboratory-confirmed COVID-19 cases were reported to the Jiangsu National Health Commission between January 1 and March 9, 2020. The epidemiological investigation reports of confirmed cases were received and reviewed by Data Processing Center of JSCDC, and the formatted case questionnaires were uploaded to the China Information System for Disease Control and Prevention (CISDC) simultaneously. Key information was extracted from epidemiological investigation reports and cross-checked from the formatted case questionnaires in the CISDC to ensure the consistency and reliability. If the core information was lost or there was a logic error, the query form would be sent to the local CDC, where the case located, and the staff of local CDC would be responsible for checking the information again, correcting and resubmitting the data to CISDC and JSCDC.

Statistical Analysis

Continuous variables were expressed as median and interquartile ranges (IQR) or simple ranges, as appropriate. Categorical variables were summarized as counts and percentages. No imputation was made for missing data. 631 cases were divided into severe and non-severe groups, and the key time distribution was calculated respectively. We performed stepwise logistic regression to identify predictors for severe outcomes according to the exclusion criteria of p value $\geq 0.10$ and chi-square ($\chi^2$) test. The relationship between the severity of the disease and viral load was also analyzed. The time-dependent reproductive number ($R_t$) was calculated using the method developed by Thompson et al[7]. The daily number of reported COVID-19 cases and the serial interval (mean, 7.5 days [SD, 3.4 days]; constant across periods), derived from a previous epidemiological survey of the first 425 cases in Wuhan [8] were used to estimate $R_t$ and its 95% credible interval on each day via a 5-day moving average. All the analyses were performed with R software (3.6.2, R Foundation for Statistical Computing). We also created hierarchical color map and point density map to illustrate the regional distribution by ArcGIS software version 10.0 (ESRI, Redlands, CA, USA).

Results

Epidemiological characteristics of COVID-19 confirmed cases

A total of 631 laboratory-confirmed COVID-19 cases were identified. The median age of the patients was 46 yrs. Male patients accounted for 54.52%. The case-severity rate was 8.46%. 68.30% patients met at least one of the following conditions: 1) had the history of travel and residence in Wuhan city and surrounding areas, or other communities with reported cases (the first generation infections); 2) had contact with people from Wuhan city and surrounding areas, or other communities with reported cases (the second generation infections). The onset of the first case was on January 4, 2020, who had a recent travel history to Wuhan before symptoms appeared.
The epidemic of COVID-19 had undergone four stages (Figure 1). The first stage was for patients with illness onset between January 3 and January 17 where 3.32% of cases occurred sporadically, of which 71.43% was the first-generation infections and 23.81% was the second-generation infections. Only 4.76% patient contacted a locally confirmed or probable COVID-19 case (the third-generation infections). The second stage was between January 18 and January 26, during which the development of the epidemic curve followed an exponential growth, and peaked on January 26. 37.40% patients were reported during the stage, where the proportion of the first-generation infection (64.41%) has dropped slightly. Between January 27 and February 1, the epidemic arrived to the peak and entered to the third stage of the platform period, during which a continuous human-to-human transmission occurred. Still, 37.40% patients were identified, and the proportion of first- and third-generation infections was relatively similar (36.02% vs. 35.17%). The fourth stage was after February 2, during which 21.88% patients were identified, and the proportion of the third-generation infections (55.80%) increased sharply. The cases gradually declined over time in the last stage which had been 24 consecutive days since February 14 without any new confirmed cases reported (Figure 1-A, Table S1). The $R_t$ declined with the four stages, and was less than 1 after February 1 (Figure 1-B). Furthermore, there was a statistical difference in the occurrence of severe diseases in the four stages of the epidemic, and the proportion of severe diseases showed a decreasing trend (Table 1). We found that COVID-19 circulated in all of the cities of Jiangsu Province. Most cases came from Nanjing(93), capital of Jiangsu Province, Suzhou(87), which was adjacent to Shanghai and Zhejiang Province, and Xuzhou(79), where was national comprehensive transportation hub. The proportion of severe cases from 13 municipal prefectures in Jiangsu Province were significantly different ($\chi^2 =25.09, P=0.014$) (Figure 2).

**Clinical characteristics of COVID-19 confirmed cases**

30.90% patients had underlying medical conditions including 15.53% with hypotension, 6.02% with diabetes, 5.39% with cerebrovascular disease, 3.33% with chronic obstructive pulmonary disease or renal/liver disease, respectively, and 0.48% with pregnancy. Fever was most common in confirmed cases, which accounted for 77.02%. Dry cough ranked the second (33.60%), then the expectoration, fatigue, myalgia/arthralgia, and headache accounted for more than 10.00%. Symptoms like diarrhea, shortness of breath, dyspnea, and vomit were less common. Lymphocytopenia was present in 28.88%, and leukopenia in 24.03% (Table 1).

By March 9, 98.57% patients had been cured and discharge. The median time from illness onset to first hospital visit was 1.00 days (IQR: 0.00–4.00), to diagnosis was 7.00 days (IQR:4.00–10.00), to hospitalization was 3.00 days (IQR:1.00-6.00) respectively. The median time from hospitalization to discharge was 17.00 days (IQR:14.00-20.00). The probability density distributions of the onset-to-first hospital visit, onset-to-diagnosis, onset-to-hospitalization, and hospitalization to discharge intervals were relatively longer in severe cases than non-severe cases of COVID-19 (Figure 2), and these time intervals with the different epidemic phase gradually reduced (Table S1).

**Risk factors associated with confirmed severe COVID-19**

The severity of the disease was inversely related to age. The median age of severe COVID-19 patients was 56yrs which was statistically higher than that of non-severe cases with a median age of 44yrs ($p<0.001$). Moreover, elderly more than 65yrs also confronted with the higher risk of progressing to severe cases (33.96%
The underlying medical condition included hypertension, diabetes, and cerebrovascular disease were more common among severe cases than non-severe cases (62.26% vs. 28.03%). The first and second stages of epidemics, and urban spaces were also risk factors for severe outcome. While seek healthcare within 1 day after illness onset, and to hospitalization within 3 days after illness onset were protective factors avoiding severe cases. In addition, fever, especially high fever (the highest temperature ≥ 39.0℃), chill, shortness of breath, dyspnea, and chest tightness were all significantly more frequent in severe group (P<0.05). Notably, the presence of lymphocytopenia (<1.0×10^9) was statistically higher in severe group, which suggested an important predictor for risk of severe (p<0.001) (Table 1).

With multivariate backward logistic regression for 15 predictors identified by univariate analysis, we identified elderly more than 65yrs, underlying medical conditions, high fever (highest temperature ≥ 39.0℃), dyspnea and lymphocytopenia(<1.0×10^9/L) significantly elevated risk of severe disease, and possibly became the important early warning signs for severe patients of COVID-19 (P<0.05). In contrast, earlier visit to the clinic may reduce the risk of progression to severe cases. (Table2).

The association between viral load and disease severity

We obtained viral load information on 311 cases, including 31 severe cases and 280 non-severe cases. The time from onset to samples collection was 4.00 days (IQR:1.00-8.00days) for severe cases and 3.00 days (IQR:1.0-6.0days) for non-severe cases respectively. We analyzed the relationship between viral load and disease severity and found that there existed correlation. The median cycle threshold (Ct) values of ORF segment with severe cases was 26.90(IQR:22.00-32.20), which was significantly lower than that of non-severe cases (29.20, IQR:26.00-32.20). Similarly, the Ct values of N gene segments was lower in severe cases (27.60 VS 30.30).(Figure S1).

Discussion

We describe the detailed epidemiology and clinical features on admission of 631 laboratory conrmed COVID-19 cases identified during the study period, which will be important to better understand the evolving epidemiology of COVID-19 and the clinical spectrum. Moreover, we identified a number of important risk factors for severe outcome such as older age, coexisting disorder, the symptoms of fever beyond 39.0℃, dyspnea,and lymphocytopenia. Notably, earlier visit to clinical medical could reduce the risk of progression to severe, which will not only benefit for public health professionals, but also for clinicians who are in the forefront and are responsible for recognition and report of COVID-19. Additionally, severe cases with high viral loads may play a greater role in the spread of the disease, which may be highly infectious. Our findings provide important and valuable results for COVID-19, especially severe cases could identity and control[9].

The epidemic intensity of COVID-19 was significantly lower than that reported in Wuhan[8]. The development of the epidemic followed an exponential growth in the second stage, during which a massive human migration took place as individuals travelled back to Jiangsu Province to have the Chinese Lunar New Year holiday. In the third stage, the epidemic curve showed a continuous human-to-human transmission mode, which was largely due to the first generation of infected people spread the virus. During the above period, China’s decision to lock down the city of Wuhan,and implementation of nationwide control measures efficiently prevented the
exponential growth of case number\textsuperscript{10-12}. Jiangsu Province had also launched a series of measures to prevent outside imports and local diffusion, including restricting urban public transport systems and all cross-province bus routes, keeping social distancing, encouraging people to stay at home to limit social contacts and so on. More importantly, Jiangsu province used information technologies such as the mobile Internet and big data to investigate the exposure of patients and track close contacts, which has been powerful to control the local transmission of COVID-19. As a result of these effective implementation of these measures, the number of cases in the fourth stage, where were mainly local transmission kept decreasing and didn't enter the local outbreak phase. Geographical difference was also found in our study, which showed transportation developed and relatively frequent exchanges with Wuhan increased the infection of COVID-19 in Jiangsu Province.

For COVID-19, existing publications suggested that 80\% of infections were mild or asymptomatic, 15\% were severe infection requiring oxygen, and 5\% were critical infections requiring ventilation\textsuperscript{2}. Our study found the case-severity rate was 8.4\%, the data we have so far indicate that the crude case fatality rate was between 3-4\%, while the high may reach 6.8\% in Italy and 4.6\% in Wuhan\textsuperscript{13}. However, no death was found in Jiangsu Province, which was benefit from good medical resources and earlier seek healthcare. Of course, these fractions of severe and critical infection would be higher than what was observed for influenza virus infection\textsuperscript{14}, but would be lower than severe acute respiratory syndrome (SARS) and middle east respiratory syndrome coronavirus (MERS-CoV)\textsuperscript{15, 16}.

The majority of people infected were male, and the age range of patients was wide, which was consistent with the results of the recent reports\textsuperscript{17}. Most of the patients had mild to moderate symptoms, and only 2.1\% had dyspnea, which was consistent with previous reports\textsuperscript{18}. In concern with recent studies, fever and dry cough were the dominant symptoms, while gastrointestinal symptoms were uncommon\textsuperscript{3, 18}. The presence of fever in COVID-19 was relatively lower than that in SARS-CoV and MERS-CoV infection on admission\textsuperscript{19}, which was also revealed by our study that fever was identified in 77.02\% of the patients on presentation. As a result of that, temperature screening alone, no matter at exit or entry, was not an effective way to screen out suspicious patients. More sensitive screening methods such as 'drive-thru' coronavirus testing for populations at risk should be urgently implemented\textsuperscript{20}.

Those at most risk for severe influenza infection are children, pregnant women, elderly people, with underlying chronic medical conditions and those who are immunosuppressed\textsuperscript{21-23}. For COVID-19, our study found that severe patients were older and had a greater number of coexisting conditions than those non-severe patients, which suggested that older age and underlying conditions increase the risk for severe infection, which was consistent with the results of the recent reports\textsuperscript{3, 24}. Compared with non-severe cases with COVID-19, symptoms were more common in severe patients on admission, including fever (highest temperature $\geq 39.0^\circ\text{C}$), dyspnea and lymphocytopenia. These symptoms on admission may help physicians identify the patients with poor prognosis. It was also worth mentioning that we had three pregnant women, one of them was very seriously ill. We didn't get any valuable results for either single or multiple risk factors of pregnant patient. Although one study also showed that the clinical characteristics of COVID-19 pneumonia in pregnant women were similar to those reported for non-pregnant adult patients who developed COVID-19 pneumonia, the conclusions were limited by the small sample size\textsuperscript{25}. Whether pregnant women were more likely to
become severe cases require further observation. Our severity data also found one independent protective factor which was earlier visit to first medical care, suggesting that elderly or people with underlying medical conditions should immediately contact their health care as long as any symptoms consistent with COVID-19 appear\[17, 26\]. Besides, the viral load was a potentially useful marker associated with disease severity of COVID-19 in our study. So it was important to pay special attention to patients with the above-mentioned severe predisposition factors at the time of admission, of whom may be more highly infectious and even may become super spreaders.

Our study has some notable limitations. First, we did not collect sufficient information from all patients on laboratory results at early stage, which limited in identifying and comparing the difference. Second, we focused on patients who had obvious clinical symptoms and went to the hospital for treatment, might missing patients without symptoms or had mild symptoms, or those did not go to the hospital for treatment. Third, nine people were not discharged from the hospital during the study period, and their severity may change.

**Conclusion**

In conclusion, our data could help us to better understand the evolving epidemiology of COVID-19 in the local region and the clinical spectrum of disease. Moreover, a number of important risk factors for severe outcomes including older age, coexisting disorder, the symptoms of fever beyond 39.0°C, dyspnea, and lymphocytopenia were identified. However, there are still many unknowns. Expanded and enhanced surveillance will help in the early detection and diagnosis of suspected cases, thereby reducing severe cases and deaths.

**Abbreviations**

COVID-19: Coronavirus disease 2019; WHO: World Health Organization; RT-PCR: Reverse transcriptase polymerase chain reaction; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; JSCDC: Jiangsu Center for Disease Control and Prevention; CISDC: China Information System for Disease Control and Prevention; Rt: Time-dependent reproductive number; IQR: Interquartileranges; Ct: Cycle threshold; SARS: Severe acute respiratory syndrome; MERS-CoV: Middle east respiratory syndrome coronavirus. NDRS: National Notifiable Disease Reporting System.

**Declarations**

**Ethics approval and consent to participate**

The study protocol has been reviewed by the ethics committee of the JSCDC. It was concluded that the rights and interests of the subjects of this study have been fully protected, and the possible benefits of the subjects outweigh the possible risks.

**Consent for publication**

Not applicable

**Availability of data and materials**
The epidemiology and clinic data of COVID-19 used and analyzed in this study were abstracted from National Notifiable Disease Reporting System (NDRS), the information system of infectious diseases of mandatory notification in mainland China. Data application website: http://wjw.jiangsu.gov.cn/. The clinical information referred to symptoms and laboratory testing of COVID-19 analyzed consist of sensitive information on an individual level. Due to protection of privacy, the data are not publicly available. However, the datasets of this section are available from the first author Hong Ji (E-mail: jihong1982@sina.cn) for scientific purposes.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors' contributions**

H.J., Q.D., H.J., C.B and M.W conceived and designed the study, K.X., H.H., Y.W and X.F collected the questionnaire, H.J., N.S and J.A analyzed the data, H.J., Q.D., and Z. P contributed reagents/materials/analysis tool, H.J., Q., D., H.J and C.B wrote the paper. All authors read and approved the final manuscript.

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**Tables**
Table 1: Epidemiological and clinical characteristic of severe (n=53) and non-severe (n=578) cases with reported confirmed cases of COVID-19 by 09 March 2020, Jiangsu Province, Eastern China.

| Variable                  | All patients | Severe group | Non-severe group | P-value | Unadjusted OR (95%CI) |
|---------------------------|--------------|--------------|------------------|---------|-----------------------|
| Sex                       |              |              |                  |         |                       |
| Male                      | 344(54.5)    | 35(66.04)    | 309(53.46)       | 0.078   | 1.69(0.94-3.06)       |
| Female                    | 287(45.5)    | 18(33.96)    | 269(46.54)       |         |                       |
| Age                       |              |              |                  |         |                       |
| Median(IQR)               | 46.02(33-56) | 56(48-68)    | 44(32-55)        | 0.000   | NA                    |
| Distribution              |              |              |                  |         |                       |
| ≤18yrs                    | 21(3.33)     | 0(0.00)      | 21(3.64)         | 0.000   | Reference             |
| 19-40yrs                  | 237(37.56)   | 7(13.21)     | 230(39.79)       | 0.64(0.08-5.45) |                       |
| 41-64yrs                  | 299(47.39)   | 28(52.83)    | 271(46.88)       | 2.17(0.28-16.75) |                       |
| ≥65yrs                    | 74(11.73)    | 18(33.96)    | 46(9.69)         | 8.22(1.03-65.69) |                       |
| Coexisting disorder       |              |              |                  |         |                       |
| Any                       | 195(30.90)   | 33(62.26)    | 162(28.03)       | 0.000   | 4.24(2.36-7.60)       |
| Hypertension              | 98(15.53)    | 19(35.85)    | 79(13.67)        | 0.000   | 3.53(1.92-6.49)       |
| Diabetes                  | 38(6.02)     | 10(18.87)    | 28(4.84)         | 0.000   | 4.57(2.08-10.02)      |
| Cerebrovascular disease   | 34(5.39)     | 10(18.87)    | 24(4.15)         | 0.000   | 5.36(2.41-11.895)     |
| Chronic obstructive pulmonary disease | 21(3.33) | 4(7.55) | 17(2.94) | 0.091 | 2.69(0.87-8.32) |
| Liver and Renal disease   | 21(3.33)     | 4(7.55)      | 17(2.94)         | 0.074   | 2.69(0.87-8.32)       |
| Pregnancy                 | 3(0.48)      | 1(1.89)      | 2(0.35)          | 0.119   | 5.54(0.49-62.11)      |
| Transmission classification | First-generation infections | Reference | second-generation infections | Reference | Third-generation infections | Reference |
|-----------------------------|----------------------------|-----------|-----------------------------|-----------|-----------------------------|-----------|
|                             | 277(43.90)                 | 21(39.62) | 256(44.29)                  | 0.365     | 196(31.06)                  | 14(26.42) | 182(31.49)                  | 0.87(0.46-1.64) |

| Different stage             | Stage 1                    | 21(3.33)  | 4(7.55)                     | 17(2.94)  | 6.26(1.53-25.59)           |
|                             | Stage 2                    | 236(37.40)| 25(47.17)                   | 211(36.51)| 0.034                      | 3.15(1.18-8.43) |
|                             | Stage 3                    | 236(37.40)| 19(35.85)                   | 217(37.54)| 1.35(0.72-2.53)           |
|                             | Stage 4                    | 138(21.87)| 5(9.43)                     | 133(23.01)| Reference                  |

| Region                      | Urban                      | 328(51.98)| 36(67.93)                   | 292(50.52)| 0.015                      | 2.07(1.14-3.78) |
|                             | Rural                      | 303(48.02)| 17(32.08)                   | 286(49.48)| Reference                  |

| Time from illness onset to first medical care (days) | ≤1 days | 325(55.56) | 21(40.39) | 304(57.04) | 0.021 | 0.51(0.29-0.91) |

| Time from illness onset to hospitalization | ≤3 days | 331(52.79) | 21(39.62) | 310(54.01) | 0.045 | 0.56(0.32-0.99) |

| Time from illness onset to diagnosis | ≤7 days | 364(57.69) | 25(47.17) | 339(58.65) | 0.105 | 0.63(0.36-1.11) |
|                                    | Fever   | 486(77.02) | 48(90.57) | 438(75.79) | 0.016 | 3.07(1.20-7.86) |

| Distribution of the highest temperature | <37.3°C   | 30(6.34)   | 0(0.00)   | 30(6.96)   | 0.000 | 0.35(0.05-2.58) |
|                                      | 37.3-38.0°C | 239(50.53) | 13(30.95) | 226(52.44) | 0.51(0.05-2.58) |
|                                      | 38.01-39.0°C | 165(34.88) | 19(45.24) | 146(33.87) | 1.65(0.92-2.99) |
| Symptom                  | Median(IQR) | 33.60% | 20.30% | 11.72% |
|--------------------------|-------------|--------|--------|--------|
|                      | >39.0℃      | 39(8.25) | 10(23.81) | 29(6.73) |
|                      | 39(8.25)    | 0.008   |        |        |
|                      | 39(8.25)    | 0.93(0.51-1.69) |        |        |
|                      | 4.40(2.01-9.63) |        |        |        |
|                      | Cough       | 212(33.60) | 17(32.08) | 195(33.74) |
|                      | 212(33.60)  | 0.200   |        |        |
|                      | 212(33.60)  | 1.51(0.80-2.83) |        |        |
|                      | 212(33.60)  | 0.008   |        |        |
|                      | Expectoration| 135(21.39) | 15(28.30) | 120(20.76) |
|                      | 135(21.39)  | 0.008   |        |        |
|                      | 135(21.39)  | 1.56(0.83-2.92) |        |        |
|                      | 135(21.39)  | 0.008   |        |        |
|                      | Fatigue     | 132(20.92) | 15(28.30) | 117(20.24) |
|                      | 132(20.92)  | 0.167   |        |        |
|                      | 132(20.92)  | 1.56(0.83-2.92) |        |        |
|                      | 132(20.92)  | 0.167   |        |        |
|                      | Chill       | 81(12.84)  | 13(24.53) | 68(11.76) |
|                      | 81(12.84)   | 0.008   |        |        |
|                      | 81(12.84)   | 2.44(1.24-4.79) |        |        |
|                      | 81(12.84)  | 0.008   |        |        |
|                      | Myalgia/arthralgia | 79(12.52) | 9(16.98) | 70(12.11) |
|                      | 79(12.52)   | 0.305   |        |        |
|                      | 79(12.52)   | 1.48(0.70-3.17) |        |        |
|                      | 79(12.52)  | 0.305   |        |        |
|                      | Headache    | 74(11.72)  | 8(15.09)  | 66(11.42) |
|                      | 74(11.72)   | 0.426   |        |        |
|                      | 74(11.72)   | 1.38(0.62-3.05) |        |        |
|                      | 74(11.72)  | 0.426   |        |        |
|                      | Sore throat | 58(9.19)   | 5(9.43)   | 53(9.17) |
|                      | 58(9.19)    | 1.000   |        |        |
|                      | 58(9.19)    | 1.03(0.39-2.70) |        |        |
|                      | 58(9.19)  | 1.000   |        |        |
|                      | Runny nose  | 49(7.77)   | 1(1.89)   | 48(8.30) |
|                      | 49(7.77)    | 0.161   |        |        |
|                      | 49(7.77)    | 0.21(0.03-1.57) |        |        |
|                      | 49(7.77)  | 0.161   |        |        |
|                      | Chest tightness | 42(6.06)  | 10(18.87) | 32(5.54) |
|                      | 42(6.06)    | 0.001   |        |        |
|                      | 42(6.06)    | 3.97(1.83-8.61) |        |        |
|                      | 42(6.06)  | 0.001   |        |        |
|                      | Diarrhea    | 36(5.71)   | 4(7.55)   | 32(5.54) |
|                      | 36(5.71)    | 0.768   |        |        |
|                      | 36(5.71)    | 1.39(0.47-4.10) |        |        |
|                      | 36(5.71)  | 0.768   |        |        |
|                      | Nasal congestion | 32(5.07)  | 1(1.89)   | 31(5.36) |
|                      | 32(5.07)    | 0.604   |        |        |
|                      | 32(5.07)    | 0.34(0.05-2.54) |        |        |
|                      | 32(5.07)  | 0.604   |        |        |
|                      | Shortness of breath | 19(3.01)  | 8(15.09) | 11(1.90) |
|                      | 19(3.01)    | 0.000   |        |        |
|                      | 19(3.01)    | 9.17(3.51-23.93) |        |        |
|                      | 19(3.01)  | 0.000   |        |        |
|                      | Dyspnea     | 13(2.06)   | 9(16.98) | 4(0.69) |
|                      | 13(2.06)    | 0.000   |        |        |
|                      | 13(2.06)    | 29.35(8.69-99.13) |        |        |
|                      | 13(2.06)  | 0.000   |        |        |
|                      | Vomit       | 13(2.06)   | 2(3.77)   | 11(1.90) |
|                      | 13(2.06)    | 0.680   |        |        |
|                      | 13(2.06)    | 2.02(0.44-9.37) |        |        |
|                      | 13(2.06)  | 0.680   |        |        |

White-cell count (x10⁹/L)

| Median(IQR) | 33.60% | 20.30% | 11.72% |
|-------------|--------|--------|--------|
| White-cell count | 5.02(4.00-6.18) | 5.12(4.00-6.28) | 5.01(4.00-6.11) | 0.406 | NA |

Distribution of white-cell count

| <4.0          | 136(24.03) | 11(23.91) | 125(24.04) | 0.383 | 1.00(0.49-2.01) |
|---------------|------------|-----------|-----------|-------|-----------------|
| 4-10          | 419(74.03) | 33(71.74) | 386(74.23) | 0.88(0.45-1.72) |  |
| >10           | 11(1.94)   | 2(4.35)   | 9(1.73)   | 2.58(0.54-12.32) |  |

Lymphocytes counts (x10⁹/L)
Median(IQR)  1.23(0.92-1.67)  1.00(0.75-1.37)  1.27(0.94-1.71)  0.491  NA

Distribution of lymphocytes count

|       | <1.0  |  ≥1.0 |
|-------|-------|-------|
|       | 173(28.88) | 426(71.12) |
|       | 29(56.86)   | 22(43.14)   |
|       | 144(26.28)  | 404(73.72)  |

0.000  3.70(2.66-6.64)

* Data are %(n/N); NA: not available, + Among the 631 COVID-19 cases, a Wilcoxon rank-sum test., b Independent samples t test., c Fisher’s exact test., 578 non-severe cases including 129 patients(20.4%) diagnosed with mild without pneumonia, 449 patients(71.2%) with mild with pneumonia, 53 severe cases including 45 patients (7.1%) with severe pneumonia, and 8 patients(1.3%) with critically ill.

Table 2 Multivariate analysis of factors associated with severe cases with reported confirmed cases of COVID-19 by 09 March 2020, Jiangsu Province, Eastern China.

| Variable                       | β     | S.E  | Wald   | P     | Adjusted OR(95%CI) |
|--------------------------------|-------|------|--------|-------|--------------------|
| Age(≥65yrs)                    | 0.64  | 0.32 | 4.167  | 0.041 | 1.91(1.03-3.54)    |
| Coexisting disorder            | 0.93  | 0.44 | 4.443  | 0.035 | 2.53(1.07-5.99)    |
| Highest body temperature (≥39.0°C) | 1.29 | 0.27 | 22.872 | 0.000 | 3.64(2.15-6.19)    |
| Dyspnea                        | 3.12  | 0.74 | 17.875 | 0.000 | 22.66(5.33-96.30)  |
| Lymphocytopenia (<1.0×10⁹)     | 1.10  | 0.39 | 7.785  | 0.005 | 2.99(1.39-6.46)    |
| Onset-to-first medical visit (≤ 1 days) | -0.86 | 0.40 | 4.772  | 0.029 | 0.42(0.19-0.91)    |
Figures
Figure 1

1-A. Epidemic curve of confirmed COVID-19 cases reported in Jiangsu Province, Eastern China, by 09 March 2020 (Data from February 15th were not available since February 14 without any new confirmed cases).
reported). The first-generation infection was defined as those who had the history of travel and residence of Wuhan city and surrounding areas or other communities with reported cases. The second-generation infection was defined as those who had contacted people from Wuhan city and surrounding areas or other communities with reported cases. The third-generation infection was defined as those who had contacted a locally confirmed or probable COVID-19 case. Unclear defined as cases that didn't belong to the above three categories and whose exposure sources cannot be traced. Figure 1-B. Rt in different epidemic stage in Jiangsu Province, Eastern China, by 09 March 2020 The darkened horizontal line indicates Rt=1, below which sustained transmission is unlikely so long as antitransmission measures are sustained, indicating that the outbreak is under control. The 95% credible intervals (Crls) are presented as shading.
Figure 2

Geographical distribution of confirmed COVID-19 cases and severe cases reported in Jiangsu Province, Eastern China, by 09 March 2020 (n=631)
Figure 3

Estimates of onset-to-first medical visit, onset-to-hospitalization, onset-to-diagnosis, and hospitalization-to-discharge distributions of severe and non-severe cases with reported confirmed cases of COVID-19 by 09 March 2020, Jiangsu Province, Eastern China. (A) Onset-to-first medical visit. (B) Onset-to-hospitalization. (B) Onset-to-diagnosis. (D) Hospitalization-to-discharge

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