Epidemiology of 631 Cases of COVID-19 Identified in Jiangsu Province Between January 1st and March 20th 2020: Factors Associated with Disease Severity and Analysis of Zero Mortality

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

AE 1 Hong Ji*
AC 1 Qigang Dai*
C 2 Hui Jin*
C 1 Ke Xu
F 1 Jing Ai
E 3 Xinyu Fang
C 2 Naiyang Shi
D 1 Haodi Huang
B 1 Ying Wu
B 3 Zhihang Peng
C 1 Jianli Hu
F 1 Liguo Zhu
A 1,4 Changjun Bao
AG 1,5 Ming Wu

1 Department of Acute Infectious Disease Control and Prevention, Jiangsu Provincial Center for Disease Control and Prevention, Nanjing, Jiangsu, P.R. China
2 Public Health School, Southeast University, Nanjing, Jiangsu, P.R. China
3 Public Health School, Nanjing Medical University, Nanjing, Jiangsu, P.R. China
4 National Health Commission Key Laboratory of Enteric Pathogenic Microbiology, Nanjing, Jiangsu, P.R. China
5 Public Health Research Institute of Jiangsu Province, Nanjing, Jiangsu, P.R. China

* Hong Ji, Qigang Dai and Hui Jin made equal contributions
Corresponding Authors: Changjun Bao, e-mail: bao2000_cn@163.com, Ming Wu, e-mail: jswuming@vip.sina.com
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Background: This retrospective study aimed to investigate the factors associated with disease severity and patient outcomes in 631 patients with COVID-19 who were reported to the Jiangsu Commission of Health between January 1 and March 20, 2020.

Material/Methods: We conducted an epidemiological investigation enrolling 631 patients with laboratory-confirmed COVID-19 from our clinic from January to March 2020. Patients' information was collected through a standard questionnaire. Then, we described the patients' epidemiological characteristics, analyzed risk factors associated with disease severity, and assessed causes of zero mortality. Additionally, some key technologies for epidemic prevention and control were identified.

Results: Of the 631 patients, 8.46% (n=53) were severe cases, and no deaths were recorded (n=0). The epidemic of COVID-19 has gone through 4 stages: a sporadic phase, an exponential growth phase, a peak plateau phase, and a declining phase. The proportion of severe cases was significantly different among the 4 stages and 13 municipal prefectures (P<0.001). Factors including age >65 years old, underlying medical conditions, highest fever >39.0°C, dyspnea, and lymphocytopenia (<1.0×10^9/L) were early warning signs of disease severity (P<0.05). In contrast, earlier clinic visits were associated with better patient outcomes (P=0.029). Further, the viral load was a potentially useful marker associated with COVID-19 infection severity.

Conclusions: The study findings from the beginning of the COVID-19 epidemic in Jiangsu Province, China showed that patients who were more than 65 years of age and with comorbidities and presented with a fever of more than 39.0°C developed more severe disease. However, mortality was prevented in this initial patient population by early supportive clinical management.

Keywords: COVID-19 • Epidemiologic Research Design • Risk Factors

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Background

The World Health Organization (WHO) declared COVID-19 a public health emergency requiring international concern on January 30, 2020 [1]. China has incorporated COVID-19 as a nationally notifiable disease since January 20, 2020 [2]. On March 20, 2020, a total of 80 859 laboratory-confirmed cases and 3100 deaths were documented in China [3]. Much effort was devoted to rapidly understanding the epidemiology, severity, and impact of COVID-19 [4]. The disease was first identified in Wuhan [5], and was shown to have a wide spectrum of severity [4]. Therefore, to better describe the epidemiological characteristics, investigate the factors associated with disease severity and patient outcomes, and to determine the causes of zero mortality, we performed an analysis of 631 patients with COVID-19 who were reported to the Jiangsu Commission of Health between January 1 and March 20, 2020.

Material and Methods

Ethics statement

The study was conducted in strict compliance with the ethical principles of the Declaration of Helsinki. The study protocol was reviewed and approved by the Ethics Committee of the Jiangsu Provincial Center for Disease Control and Prevention (JSCDC). It was concluded that the rights and interests of the subjects of this study had been fully protected, and the possible benefits of the issues outweigh the potential risks. Each study participant provided written informed consent.

Case definitions

Sputum and throat swab specimens were collected from all patients on admission. The presence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was confirmed on the basis of positive real-time reverse transcriptase-polymerase chain reaction (RT-PCR) assay for both open reading frame 1ab(ORF1ab) and nucleocapsid protein (N) in the same clinical specimen, or if only a single target (ORF lab or N target) was positive, but was still single positive through re-sampling and retesting, or if a single target (ORF lab or N target) was positive in 2 different clinical specimens, or if a single target (ORF lab or N target) was positive in the same clinical specimen collected on 2 or more days during the course of the illness. A cycle threshold value (Ct-value) less than 37 was defined as a positive test result, and a Ct-value of 40 or more was defined as a negative test. A medium load, defined as a Ct-value of 37 to less than 40, required confirmation by retesting. Laboratory confirmation of SARS-CoV-2 was performed at the JSCDC before February 2, 2020, and subsequently in 13 certified municipal laboratories in each city of

Jiangsu Province. The real-time RT-PCR assay was performed using a COVID-19 nucleic acid detection kit as per the protocol established by the WHO [6].

Cases were diagnosed according to the diagnostic criteria for the "Diagnosis and Treatment Protocol for COVID-19 (Trial Version 6)" released by National Health Commission of the People's Republic of China [7]. We defined the degree of severity of COVID-19 (severe vs non-severe) according to the above COVID-19 diagnosis and treatment guidelines and CDC criteria for disease severity [8]. Non-severe patients included mild illness and moderate illness, and severe patients included severe illness who had any of the following: 1) saturation of oxygen (SpO$_2$) <93% on room air at sea level; 2) a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO$_2$/FiO$_2$) <300 mmHg; 3) respiratory frequency >30 breaths/min; 4) lung infiltrates >50% in 24-48 h, and critical illness with respiratory failure, septic shock, and/or multiple organ dysfunction.

Data collection

Overall, 631 laboratory-confirmed COVID-19 cases were diagnosed and then reported to the Jiangsu Commission of Health between January 1 and March 20, 2020. Trained professionals from the local district CDCs were responsible for conducting epidemiological investigations of those cases, the epidemiological investigation reports drafted by them were sent to the Data Processing Center of JSCDC, and the formatted case questionnaire was uploaded to the China Information System for Disease Control and Prevention (CISDC). Key information was extracted from epidemiological investigation reports and cross-checked from the formatted case questionnaire in the CISDC to ensure consistency and reliability. If the core information was lost or there was a logistical error, the query form was sent to the local CDC, where the case was located. Local CDC staff were responsible for rechecking the information and for correcting and resubmitting the data to the CISDC and JSCDC.

Statistical analysis

Continuous variables are expressed as median and interquartile ranges (IQR) or simple ranges, as appropriate. Categorical variables are summarized as counts and percentages. No imputation was made for missing data. The 631 cases were divided into severe and non-severe groups, and the key time distribution was calculated. We performed stepwise logistic regression to identify predictors of severe outcomes, according to the exclusion criteria of P value ≥0.10 and chi-square (χ^2) test. The relationship between disease severity and viral load was also analyzed. The time-dependent reproductive number (R_t) was calculated using the method proposed by Thompson et al [9] and the daily number of reported COVID-19 cases and the serial
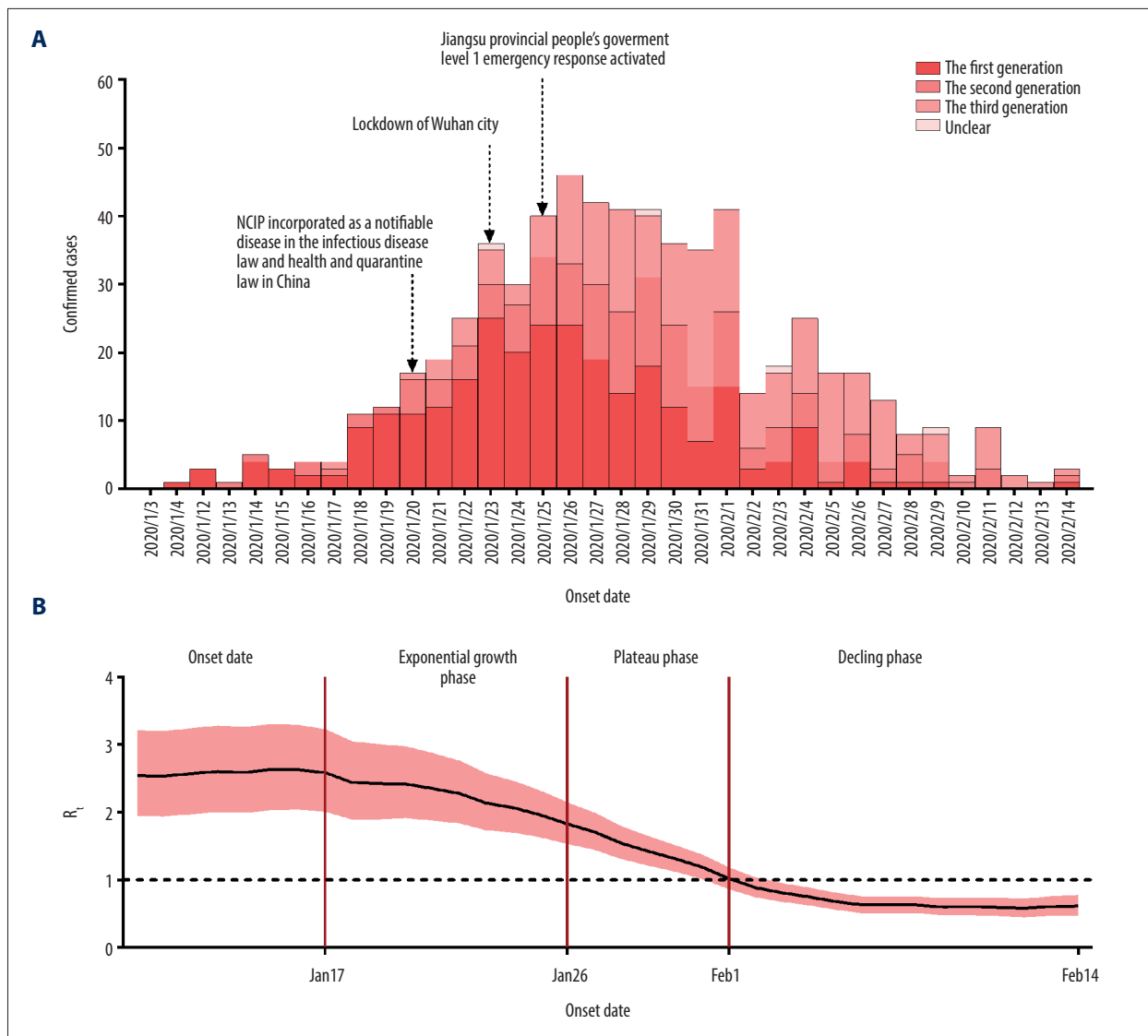
Figure 1. (A) Epidemic curve of confirmed coronavirus disease 2019 (COVID-19) cases reported in Jiangsu Province, Eastern China, by February 14, 2020 (data from February 15 were not available because since February 14, there has been no report on new confirmed cases). First-generation infection was defined as those who had a history of travel and residence in Wuhan City and surrounding areas or other communities with reported cases. Second-generation infection was defined as those who had contact with people from Wuhan City and surrounding areas or other communities with reported cases. Third-generation infection was defined as those who had contacted a locally confirmed or probable COVID-19 case. Unclear were defined as cases that did not belong to the above 3 categories and whose exposure sources cannot be traced. **(B)** R_t (time-dependent reproductive number, R_t) in different epidemic stages in Jiangsu Province, Eastern China, by February 14, 2020. The darkened horizontal line indicates $R_t=1$, below which sustained transmission is unlikely as long as the anti-transmission measures are sustained, indicating that the outbreak is under control. The 95% confidence intervals (CIs) are presented as shaded values.

interval derived from a previous study [10] were used to estimate R_t and its 95% confidence interval (95% CI) on each day via a 5-day moving average. All analyses were performed using R software (3.6.2, R Foundation for Statistical Computing). We also created a hierarchical color and point density map to illustrate the regional distribution using ArcGIS software version 10.0 (ESRI, Redlands, CA, USA).

Results

Epidemiological Characteristics of Confirmed COVID-19 Cases

A total of 631 laboratory-confirmed COVID-19 cases were identified. The mean age of the patients was 45.15±16.28 years. Male patients accounted for 54.52% (344/561). The

Table 1. Transmission characteristics and key time intervals in 4 stages of confirmed COVID-19 cases reported in Jiangsu Province, Eastern China, by March 20, 2020 (n=631).

Stage	Stage 1 (n=21)	Stage 2 (n=236)	Stage 3 (n=236)	Stage 4 (n=138)	Total (n=631)
Transmission classification % (n)					
The first generation infection[a]	71.43% (15)	64.41% (152)	36.02% (85)	18.12% (25)	43.90% (277)
The second generation infection[b]	23.81% (5)	20.34% (48)	28.39% (67)	24.64% (34)	24.41% (154)
The third generation infection[c]	4.76% (1)	14.83% (35)	35.17% (83)	55.80% (77)	31.07% (196)
Uncleard	0.00% (0)	0.42% (1)	0.42% (1)	1.45% (2)	0.63% (4)
Key time intervas (median (IQR))					
Onset-to- diagnosis	11.00 (10.00-12.50)	8.00 (5.00-10.75)	6.00 (4.00-10.00)	5.00 (3.00-7.00)	7.00 (4.00-10.00)
Onset-to-first medical visit	5.00 (3.00-7.00)	2.00 (0.00-4.00)	1.00 (0.00-3.75)	1.00 (0.00-3.00)	1.00 (0.00-4.00)
Onset-to-hospitalization	8.00 (6.50-9.00)	5.00 (1.25-7.00)	3.00 (0.00-5.00)	1.00 (0.00-3.25)	3.00 (1.00-6.00)

[a] 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; [b] The second generation infection was defined as those who had contacted people from Wuhan city and surrounding areas or other communities with reported cases; [c] The third generation infection was defined as those who had contacted a locally confirmed or probable COVID-19 case; [d] Unclear defined as cases that did't belong to the above three categories and whose exposure sources cannot be traced.

case-severity rate was 8.46% (53/631). Patients' responses to the questionnaire revealed that 68.30% (431/631) of patients met at least one of the following conditions: 1) history of travel and residence in Wuhan City and its surrounding areas or other communities with reported cases (first-generation infections); and 2) contact with people from Wuhan City and its surrounding areas or other communities with reported cases (the second-generation infections). The onset of the first case was on January 4, 2020, in a patient with recent travel history to Wuhan before the symptoms appeared.

The epidemic of COVID-19 has undergone 4 stages (**Figure 1**). The first stage was patients with illness onset between January 4 and January 17, when 3.32% (21/632) of cases occurred sporadically, of which 71.43% were first-generation infections and 23.81% were of second-generation type. Only 4.76% of patients had contact with a locally confirmed or probable COVID-19 cases (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. Precisely 37.40% (236/631) of patients were reported during the stage, when the proportion of first-generation infection (64.41%) had dropped slightly. Between January 27 and February 1, the epidemic peaked and entered the third stage of the platform period, during which a continuous human-to-human transmission occurred. However, 37.40% (236/631) of patients were identified, and the proportion of

first- and third-generation infections were relatively similar (36.02% vs 35.17%). The fourth stage was after February 2, during which 21.88% (138/631) of patients were identified, and the proportion of third-generation infections (55.80%) increased sharply. The cases gradually declined over time in the last stage, which was 35 consecutive days since February 14, without any new confirmed cases reported (**Figure 1A, Table 1**). The R_t declined from stage 1 to stage 4 and was less than 1.0 after February 1 (**Figure 1B**). Furthermore, there was a statistically significant difference in the occurrence of severe diseases in the 4 stages of the epidemic, and the proportion of severe infections showed a decreasing trend (P=0.034) (**Table 2**). We found that COVID-19 circulated in all of the cities of Jiangsu Province. Most cases came from Nanjing (93), the capital of Jiangsu Province, Suzhou (87), which was adjacent to Shanghai, Zhejiang Province, and Xuzhou (79), which is a national comprehensive transportation hub. The proportions of severe cases from 13 municipal prefectures in Jiangsu Province were significantly different (P=0.014) (**Figure 2**).

Clinical Characteristics of Confirmed COVID-19 Cases

A total of 631 cases were included in this study, of which 195 (30.90%) had at least one underlying medical condition such as hypertension and/or diabetes. The proportion of cases with each medical condition was as follows: hypotension (15.53%), diabetes (6.02%), cerebrovascular disease (5.39%), chronic
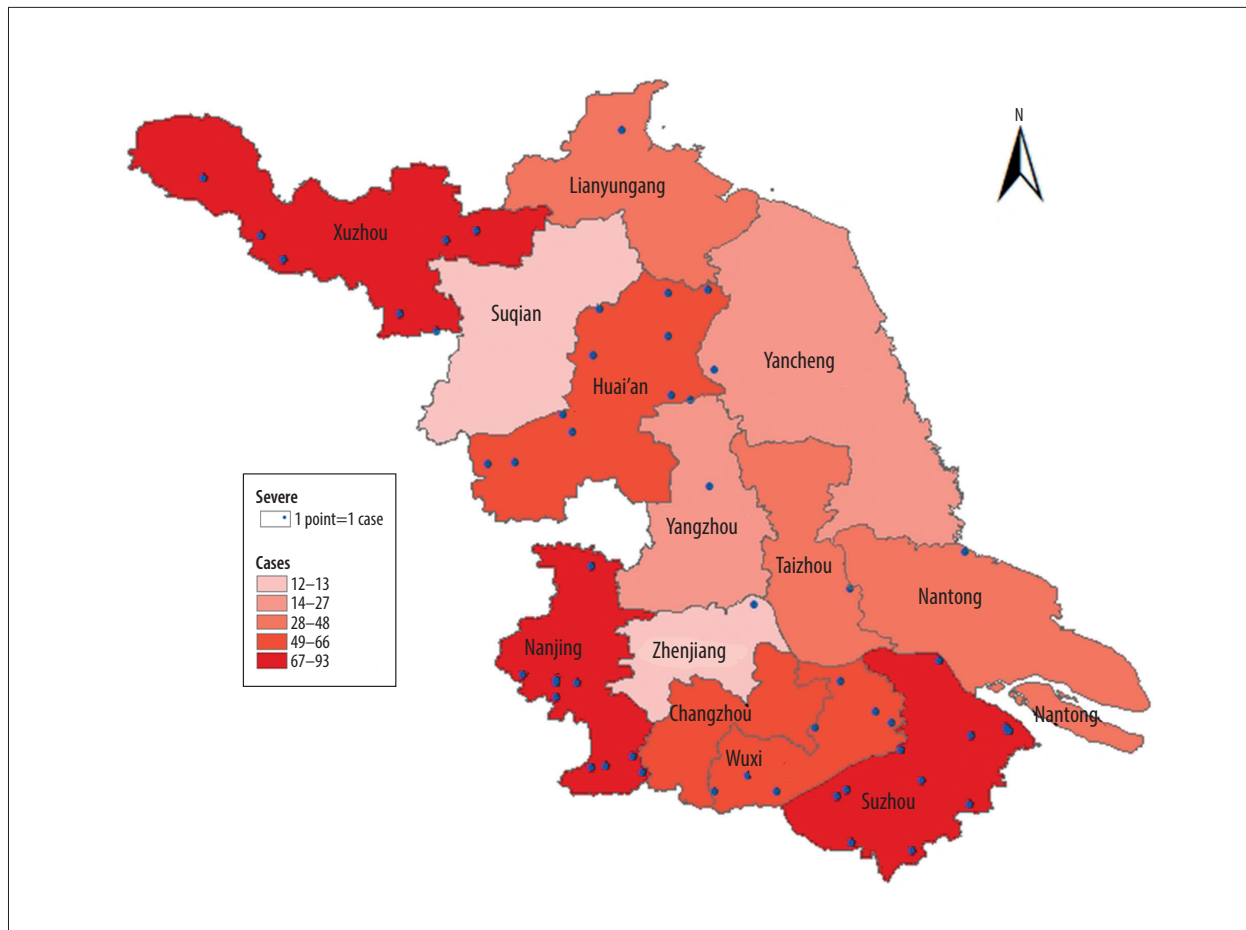
Figure 2. Geographical distribution of confirmed COVID-19 cases and severe cases reported in Jiangsu Province, Eastern China, by March 20, 2020 (n=631).

obstructive pulmonary disease (COPD) or renal/liver disease (3.33%), and pregnancy (0.48%). Fever was the most common symptom among the confirmed cases (77.02%), while dry cough ranked second (33.60%), followed by expectoration, fatigue, myalgia/arthralgia, and headache (>10.00%). Symptoms such as diarrhea, dyspnea, and vomiting were less common. Lymphocytopenia was present in 28.88% and leukopenia in 24.03% of cases (**Table 2**).

By March 20, all patients were cured and were discharged. The median time from onset of illness to the first hospital visit was 1.00 day (IQR: 0·00-4.00), to diagnosis was 7.00 days (IQR: 4.00-10.00), and to hospitalization was 3.00 days (IQR: 1.00-6.00). 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 in non-severe cases of COVID-19 (**Figure 3**), and the time intervals relative to the different epidemic phases gradually reduced from stage 1 to stage 4 (**Table 1**).

Risk Factors Associated with Confirmed Severe COVID-19

The severity of disease was positively correlated with age. The mean age of patients with severe COVID-19 was 56.94±14.71 years, which was significantly higher than that of non-severe cases, with a mean age of 44.07±16.00 years ($P<0.001$). Moreover, the elderly (>65 years) had a higher risk of progressing to severe disease (33.96% vs 9.69%, $P<0.001$). The underlying medical conditions, including hypertension, diabetes, and cerebrovascular disease, were more common among severe cases than among non-severe cases (62.26% vs 28.03%, $P<0.001$). Risk factors for severe outcomes included illness during the first and second stages of the epidemic and urban residence ($P<0.05$). Seeking health care within 1 day after the onset of illness and hospitalization within 3 days were protective factors that avoided or reduced severe disease ($P<0.05$). High fever (≥39.0°C), chills, shortness of breath, dyspnea, and chest tightness were all significantly more frequent in the severe cases group ($P<0.05$). Notably, the presence of lymphocytopenia ($<1.0×10^9$) was significantly higher in the severe group. ($P<0.001$) (**Table 2**).

Table 2. Epidemiological and clinical characteristics of severe (n=53) and non-severe (n=578) cases with reported confirmed cases of coronavirus disease 2019 (COVID-19) by March 20, 2020, Jiangsu Province, Eastern China.

Variable	All patients (n=631)		Severe (n=53)		Non-severe (n=578)		P-value	Unadjusted OR (95% CI)	
Sex									
Male	344	(54.5)	35	(66.04)	309	(53.46)	P=0.078	1.69	(0.94-3.06)
Female	287	(45.5)	18	(33.96)	269	(46.54)			
Age[a]									
Median (IQR)	46	(33-56)	56	(48-68)	44	(32-55)	P=0.000		NA
Distribution									
≤18 yrs	21	(3.33)	0	(0.00)	21	(3.64)			Reference
19-40 yrs	237	(37.56)	7	(13.21)	230	(39.79)	P=0.000	0.64	(0.08-5.45)
41-64 yrs	299	(47.39)	28	(52.83)	271	(46.88)		2.17	(0.28-16.75)
≥65 yrs	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)	P=0.000	**4.24**	**(2.36-7.60)**
Hypertension	98	(15.53)	19	(35.85)	79	(13.67)	P=0.000	**3.53**	**(1.92-6.49)**
Diabetes	38	(6.02)	10	(18.87)	28	(4.84)	P=0.000	**4.57**	**(2.08-10.02)**
Cerebrovascular disease	34	(5.39)	10	(18.87)	24	(4.15)	P=0.000	**5.36**	**(2.41-11.895)**
Chronic obstructive pulmonary disease	21	(3.33)	4	(7.55)	17	(2.94)	P=0.091	2.69	(0.87-8.32)
Liver and renal disease	21	(3.33)	4	(7.55)	17	(2.94)	P=0.074	2.69	(0.87-8.32)
Pregnancy	3	(0.48)	1	(1.89)	2	(0.35)	P=0.119	5.54	(0.49-62.11)
Transmission classification									
The first generation infections	277	(43.90)	21	(39.62)	256	(44.29)			Reference
The second generation infections	154	(24.41)	18	(33.96)	136	(23.53)	P=0.365	1.67	(0.92-3.05)
The third generation infections	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)	**P=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)	P=0.015	2.07	(1.14-3.78)
Rural	303	(48.02)	17	(32.08)	286	(49.48)			
Time from illness onset to first medical care (days)									
≤1 days	325	(55.56)	21	(40.39)	304	(57.04)	P=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)	P=0.045	**0.56**	**(0.32-0.99)**

Table 2 contributed. Epidemiological and clinical characteristics of severe (n=53) and non-severe (n=578) cases with reported confirmed cases of coronavirus disease 2019 (COVID-19) by March 20, 2020, Jiangsu Province, Eastern China.

Variable	All patients (n=631)	Severe (n=53)	Non-severe (n=578)	P-value	Unadjusted OR (95% CI)	
Time from illness onset to diagnosis						
≤7 days	364 (57.69)	25 (47.17)	339 (58.65)	P=0.105	0.63	(0.36-1.11)
Fever	486 (77.02)	48 (90.57)	438 (75.79)	P=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)		0.35	(0.05-2.58)
37.3-38.0°C	239 (50.53)	13 (30.95)	226 (52.44)	P=0.000	**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)
>39.0°C	39 (8.25)	10 (23.81)	29 (6.73)		**4.40**	**(2.01-9.63)**
Cough	212 (33.60)	17 (32.08)	195 (33.74)	P=0.806	0.93	(0.51-1.69)
Expectoration	135 (21.39)	15 (28.30)	120 (20.76)	P=0.200	1.51	(0.80-2.83)
Fatigue	132 (20.92)	15 (28.30)	117 (20.24)	P=0.167	1.56	(0.83-2.92)
Chill	81 (12.84)	13 (24.53)	68 (11.76)	P=0.008	**2.44**	**(1.24-4.79)**
Myalgia/arthralgia	79 (12.52)	9 (16.98)	70 (12.11)	P=0.305	1.48	(0.70-3.17)
Headache	74 (11.72)	8 (15.09)	66 (11.42)	P=0.426	1.38	(0.62-3.05)
Sore throat	58 (9.19)	5 (9.43)	53 (9.17)	P=1.000	1.03	(0.39-2.70)
Runny nose	49 (7.77)	1 (1.89)	48 (8.30)	P=0.161	0.21	(0.03-1.57)
Chest tightness	42 (6.06)	10 (18.87)	32 (5.54)	P=0.001	**3.97**	**(1.83-8.61)**
Diarrhea	36 (5.71)	4 (7.55)	32 (5.54)	P=0.768	1.39	(0.47-4.10)
Nasal congestion	32 (5.07)	1 (1.89)	31 (5.36)	P=0.604	0.34	(0.05-2.54)
Dyspnea	25 (2.06)	11 (20.75)	14 (2.42)	P=0.000	**10.55**	**(4.51-24.68)**
Vomit	13 (2.06)	2 (3.77)	11 (1.90)	P=0.680	2.02	(0.44-9.37)
White-cell count (×10⁹/L)[a]						
Median(IQR)	5.02 (4.00-6.18)	5.1 (4.00-6.28)	5.01 (4.00-6.11)	P=0.406	NA	
Distribution of white-cell count						
<4.0	136 (24.03)	11 (23.91)	125 (24.04)		1.00	(0.49-2.01)
4-10	419 (74.03)	33 (71.74)	386 (74.23)	P=0.383	0.88	(0.45-1.72)
>10	11 (1.94)	2 (4.35)	9 (1.73)		2.58	(0.54-12.32)
Lymphocytes counts (×10⁹/L)[a]						
Median(IQR)	1.23 (0.92-1.67)	1.00 (0.75-1.37)	1.27 (0.94-1.71)	P=0.491	**NA**	
Distribution of lymphocytes count						
<1.0	173 (28.88)	29 (56.86)	144 (26.28)	P=0.000	**3.70**	**(2.66-6.64)**
≥1.0	426 (71.12)	22 (43.14)	404 (73.72)			

Data are% (n/N), NA – not available, Among the 631 COVID-19 cases,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. Pearson Chi-square test was used, [a] is for independent samples t test.

Table 3. Multivariate analysis of factors associated with severe cases with reported confirmed cases of COVID-19 by March 20, 2020, Jiangsu Province, Eastern China.

Variable	β	S.E	Wald χ^2	P	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)

Using multivariate backward logistic regression for 14 predictors identified by univariate analysis, we identified that age >65 years, underlying medical conditions, high fever (≥39.0°C), dyspnea, and lymphocytopenia (<1.0×10^9/L) significantly increased the risk of severe disease, and were important early warning signs for COVID-19 disease severity ($P<0.05$). In contrast, earlier visits to the clinic were critical in reducing the progression to severe disease ($P<0.05$) (**Table 3**).

Reducing COVID-19 Mortality in Jiangsu Province

In the course of COVID-19 treatment, Jiangsu Province learned from the historical experience of the severe acute respiratory syndrome (SARS) and human infection with avian influenza, combined with the non-par intervention measures of COVID-19, the integration of traditional Chinese medicine (TCM) and Western medicine, scientific research and other measures, best efforts were made to reduce the case-fatality rate, achieving "zero deaths" among the confirmed cases.

First, on January 25, Jiangsu Province activated the first-level public health emergency response for the COVID-19 epidemic, and established joint prevention and control mechanisms to ensure rapid initiation and effective implementation of a region-specific, multi-level targeted approach to epidemic prevention and control.

Second, China has promoted best practices in prevention and control across the country, especially to the frontline medical staff, and timely updated diagnosis and treatment guidance of COVID-19. Since January 15, 2020, the Jiangsu Provincial Health Commission has organized training of medical workers throughout the province and helping them update the treatment principles for COVID-19 patients with varying disease severity.

Third, measures were taken to strengthen the "5 early strategies": early detection, early reporting, early diagnosis, early isolation, and early treatment. The measures implemented mainly include: 1) strengthened society-wide efforts to contain the epidemic, and firmly grasp the key measures such as temperature monitoring; 2)all medical institutions were required to strictly strengthen the monitoring and management of unexplained pneumonia; 3) strengthened the pre examination and triage and fever clinic monitoring in the hospital, which had played an important role in distinguishing and isolating COVID-19 patients from non-COVID-19 patients; 4)strengthened the management of personnel, whose with mild and asymptomatic infection were centrally isolated in designated locations, and treated as cases requiring treatment and medical management, which ensured the early treatment once symptoms appeared; 5)standardized and improved the information report and release mechanism, All confirmed and suspected cases must be reported directly online through the CISDC within 2 hours.

Fourth, we adhered to the principle of concentrations: treating the infected in dedicated facilities by medical specialists from all over the country and with all necessary resources. The measures involved mainly included the following. 1) Concentration of patients, in which all suspected and confirmed cases were admitted to designated hospitals with effective isolation and protection conditions for treatment and greatly expanded the occupancy load, isolation, and treatment capacity within a short time. Jiangsu set up the first group of 29 designated hospitals during the COVID-19 epidemic, including 13 infectious disease hospitals and 16 grade-III general hospitals, which could treat 1500 cases. The treatment capacity reserves of the second and third groups were 5000 and 7500 cases, respectively. 2) Setting up a clinical experts-guided, multi-disciplinary, province-wide hierarchical management group, in which remote and/or on-site consultations were carried out every day, greatly improving the quality and quantity of case treatment. Early diagnosis and early treatment of patients was facilitated by setting up an early warning system and screening procedures for all patients, as well as by the development and application of artificial intelligence (AI)-aided decision support systems in some places. The strategy of a dedicated team and a personalized treatment plan for each patient was implemented for severe and critical cases, and shifted forward critical care and
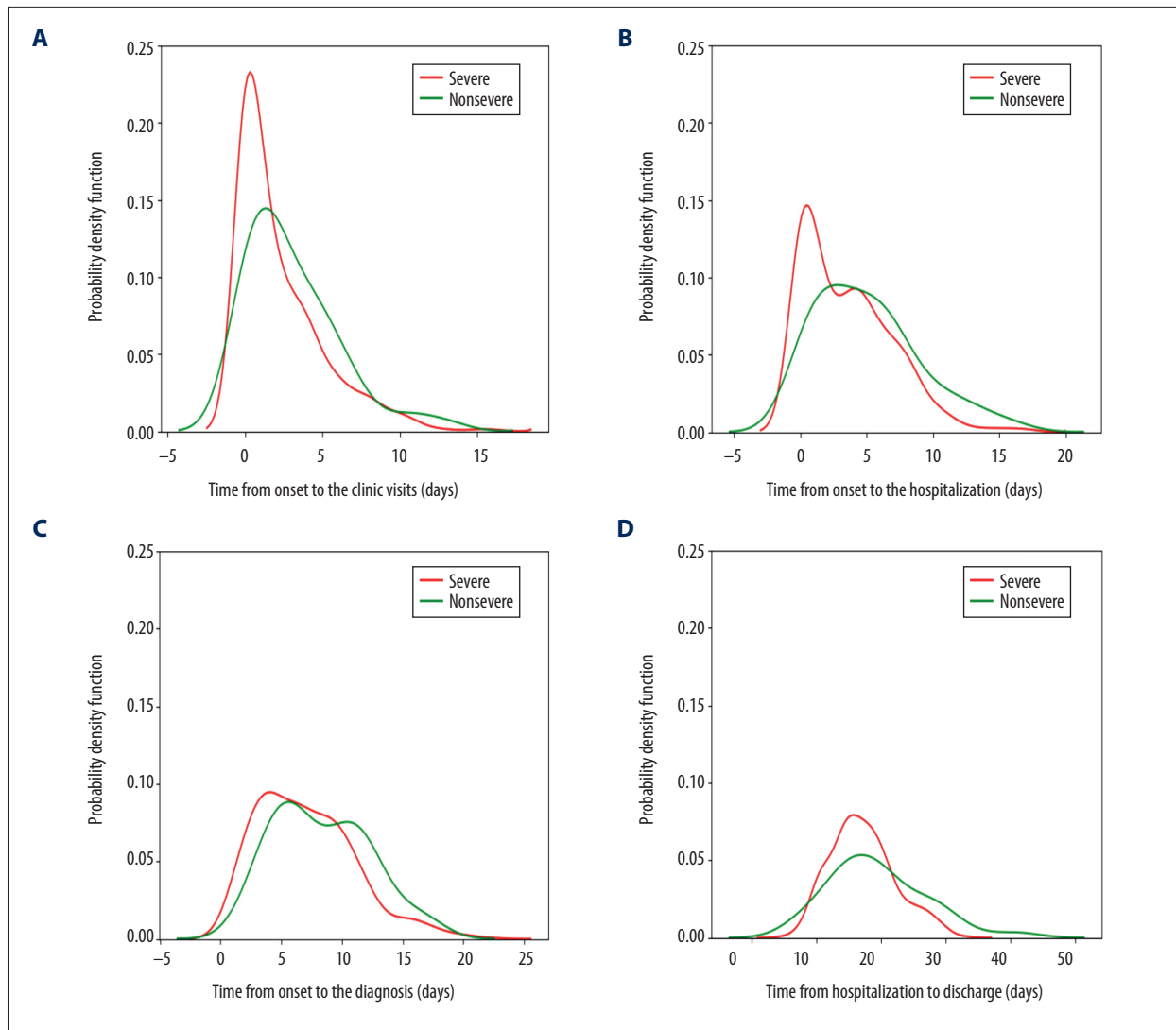
Figure 3. Estimates of an onset-to-first medical visit, onset-to-hospitalization, onset-to-diagnosis, and hospitalization-to-discharge distributions of severe and non-severe cases with reported confirmed cases of COVID-19 by March 20, 2020, Jiangsu Province. (**A**) Onset-to-first medical visit. (**B**) Onset-to-hospitalization. (**C**) Onset-to diagnosis. (**D**) hospitalization-to-discharge.

implement early screening for mild and moderate illness patients, which played an important role in curbing progression of the disease. 3) Concentration of resources to mobilize the medical resources of the whole province, which supports the treatment of patients in various cities. 4) All the patients were concentrated in the designated medical institutions with the most vigorous comprehensive treatment strength.

Fifth, collaboration was strengthened in key priority areas of scientific research. Lung transplantation (LT), as the sole therapy for end-stage pulmonary nasal high flow (NHF) related to acute respiratory distress syndrome or respiratory failure management, has been considered as the ultimate rescue therapy for these patients. Jiangsu Province successfully carried out the world's first lung transplant for COVID-19, and 2 of the 3

recipients survived after LT and started participating in a rehabilitation program.

Finally, in addition to the above strategies and measures, the early inclusion of TCM to the Chinese treatment protocol, that is, the integration of TCM and Western medicine, also contributed to the rapid containment of COVID-19 in China (**Figure 4**).

Association Between Viral Load and Disease Severity

We obtained viral load information for 311 cases, including 31 severe and 280 non-severe cases. The time from onset to sample collection was 4.00 days (IQR: 1.00-8.00 days) for severe cases and 3.00 days (IQR: 1.0-6.0days) for non-severe cases. We analyzed the relationship between viral load and disease
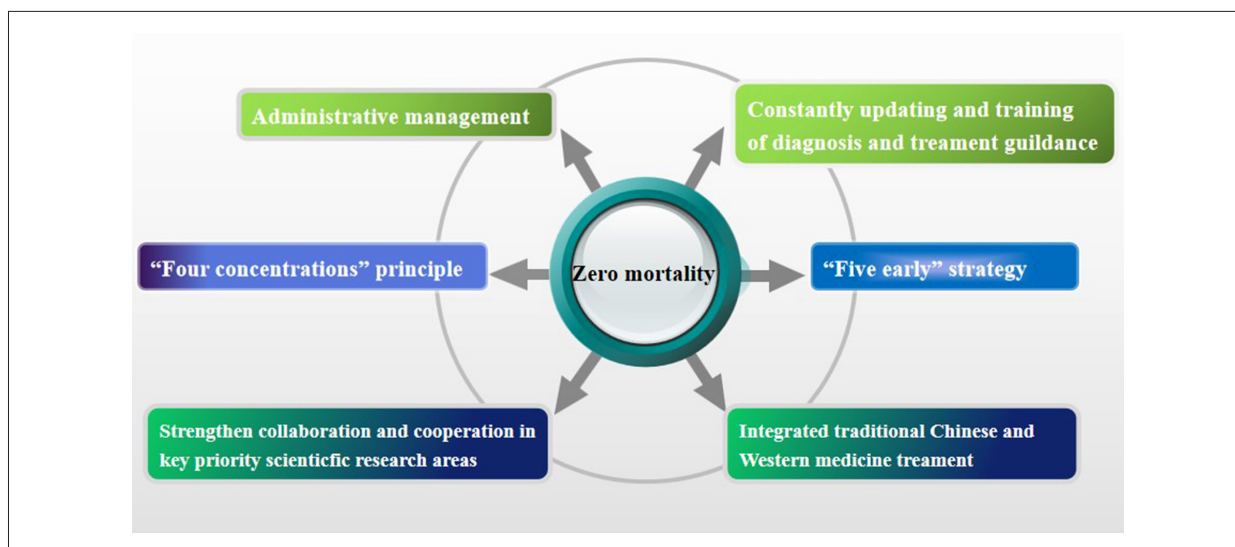
Figure 4. Core strategies and measures to reduce mortality for COVID-19 in Jiangsu Province.

severity and found a correlation ($P<0.05$). The median cycle threshold (Ct) values of the 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 were lower in severe cases (27.60 vs 30.30) (**Supplementary Figure 1**).

Discussion

We have described the detailed epidemiology and clinical features on the admission of 631 laboratory-confirmed COVID-19 cases identified during the study period, essential for a better understanding of the evolving epidemiology of the disease and the clinical spectrum. Moreover, we identified several important risk factors for severe outcomes, such as older age, co-existing disorder, fever above 39.0°C, dyspnea, and lympho-cytopenia. However, earlier visits to the clinic could reduce the risk of progression to severe stage of the infection, which should be beneficial to public health professionals and front-line clinicians responsible for the recognition and reporting of COVID-19. Additionally, severe cases with high viral loads might play a more significant role in spreading such a contagious disease. Notably, we also analyzed the causes of reduced mortality for COVID-19 in Jiangsu Province. Our findings provide substantial and valuable results for COVID-19, especially the identification and control of severe cases and death [11].

The epidemic intensity of COVID-19 in our region was significantly lower than that reported in Wuhan [10] due to our precise epidemic control strategies. We divided the modes of infection into 3 generations, and defined 4 epidemic curve phases, which more clearly described the main propagation mode in each stage. The result indicated that the development of the

epidemic followed an exponential growth in the second stage, during which a massive human migration took place through individuals who were traveling back to Jiangsu Province during the Chinese Lunar New Year holiday. In the third stage, the epidemic curve showed a continuous human-to-human transmission mode, largely due to the first generation of infected people spreading the virus. This differs from the report by Ke-wei Wang et al, which classified the source of infection in the cases defined by whether the patient lived or traveled to Hubei Province, as well as their close contacts [12]. During the above period, China's decision to implement a lockdown in Wuhan City and implement nationwide control measures efficiently prevented the exponential growth of case numbers [13-15]. Jiangsu Province officially launched the first-level response to a major public health emergency, as well as a series of measures to prevent the coronavirus from entering and spreading with the city/region, which was clearly described by Ke-wei Wang et al [12]. Additionally, Jiangsu Province applied information technologies such as mobile internet and big data to investigate patients' exposure and track close contacts. All cases and close contacts were centrally isolated in designated locations, which is a powerful way to prevent and mitigate COVID-19 transmission [16,17]. Especially in the early management of close contacts, Jiangsu Province defined close contacts screening time as "contact with cases 2 days before the onset", which has played a key role in the early detection of more than 80 cases of latent infection and nearly 20 days earlier than the guidelines for the COVID-19 close contacts management nationwide. As a result of these effective implementation measures, the time from onset-to-first medical visit and onset-to-hospitalization gradually fell at the different epidemic stages and decreased to 1 day at stage 4. Furthermore, the number of cases in the fourth stage declined when local transmission continued to decline and did not enter the local

outbreak phase. There were no new locally confirmed cases between February 14 and March 20, and no locally confirmed cases were reported for 213 consecutive days by September 14, 2020 [18]. Our study also found geographical differences, which showed that transportation and travel contributed to relatively frequent interactions with Wuhan residents, and indeed 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 infections requiring oxygen, and 5% were acute infections requiring ventilation [3]. Our study found that the case-severity rate was 8.46%; the data we have acquired so far indicate that the crude case-fatality rate was between 3% and 4%, while it reached as high as 6.8% in Italy and 4.6% in Wuhan [19]. Of course, these proportions of severe and critical infections were higher than those observed for influenza virus infection [20] but lower than those for SARS and Middle-East respiratory syndrome coronavirus (MERS-CoV) [21,22]. However, no deaths were recorded in Jiangsu Province; Jiangsu's vigorous, multifaceted response is likely to have provided a necessary foundation for this. In addition to early screening of critically ill patients and critical care-guided early intervention during the clinical work in Jiangsu Province [23], other comprehensive measures such as early detection, reporting, diagnosis, isolation, and treatment, treating the infected in dedicated facilities by medical specialists from all over the country and with all necessary resources, were the successful historical experience accumulated in the prevention and control of infectious diseases such as SARS and H7N9 influenza viruses, which were beneficial for keeping the epidemic under control and prevention of death, along with preventing an excess demand for ICU beds [17]. In 3 end-stage patients with respiratory failure due to COVID-19-related pulmonary fibrosis, we performed scientific exploration and found LT is the best way to reduce the mortality rate and to save the lives of patients with COVID-19 [24]. In addition to the above, integrated traditional Chinese and Western medicine has a long history against epidemic diseases and plays a significant role in combating COVID-19 [25].

The majority of infected patients were male, and the patients' age range was wide, which was consistent with a recent report [26]. Most of the patients had mild to moderate symptoms, and only 2.1% had dyspnea, which was consistent with a previous report [27]. In recent studies, fever and dry cough were the dominant symptoms, while gastrointestinal symptoms were uncommon [4,27]. On admission, COVID-19 patients are less likely to have fever than are patients with SARS-CoV or MERS-CoV [28], which was also revealed by our study, showing that fever was identified in 77.02% of the patients on presentation. As a result, temperature screening alone, regardless of exit or entry, was not an effective way to screen

suspected patients. More sensitive screening methods, such as 'drive-thru' coronavirus testing for populations at risk, should be urgently combined with the temperature monitoring[29].

People at most risks for severe influenza infection are children, pregnant women, older adults, those with underlying chronic medical conditions, and immunosuppressed individuals [30-32]. For COVID-19, our study found that severe patients were older and had a higher number of coexisting conditions than non-severe patients, which suggested that older age and underlying conditions increase the risk of severe infection, consistent with recent reports [4,33,34]. Zhou et al also reached a similar conclusion when they examined risk factors for mortality of adult inpatients with COVID-19 in a retrospective study [35]. However, in the multivariate analysis model, we did not conclude that the specific basic history of hypertension, diabetes, and cardiovascular and cerebrovascular diseases were risk factors for severe disease, which was different from Gold et al.'s results [36]. Symptoms of fever ($\geq$39.0°C), dyspnea, and lymphocytopenia were more common in severe patients on admission than in non-severe patients with COVID-19, in agreement with another study in the same province and in a systematic review and meta-analysis [34,37]; although we used different variables, we reached the same conclusion. Therefore, identifying these symptoms on admission might help physicians to monitor patients with poor prognoses. It is also worth mentioning that there were 3 pregnant women, one of whom was very seriously ill. We did not obtain any valuable results for either single or multiple risk factors for pregnant patients. One study showed that the clinical characteristics of COVID-19 pneumonia in pregnant women were similar to those reported for nonpregnant adult patients who developed COVID-19 pneumonia; however, the conclusions were limited by the small sample size [38]. Whether pregnant women are more likely to become severely ill requires further observation. Our severity data also found one independent protective factor, an earlier visit to first medical care, suggesting that the elderly or people with underlying medical conditions should immediately contact their healthcare practitioner for suspicious symptoms consistent with COVID-19 [26,39]. Additionally, the viral load was a potentially useful marker associated with the disease severity of COVID-19 in our study. It was essential to pay special attention to patients with the above-mentioned severe predisposition factors at the time of admission, who might be highly infectious and could even become super-spreaders.

Our study has some notable limitations. First, we did not collect sufficient information from all patients on laboratory results at the early stage, which limited the identification and comparison of differences. Second, we focused on patients who had obvious clinical symptoms and went to the hospital for treatment; thus, we might have missed patients without symptoms

who might be super-spreaders or who had mild symptoms, as well as those who did not seek hospital treatment.
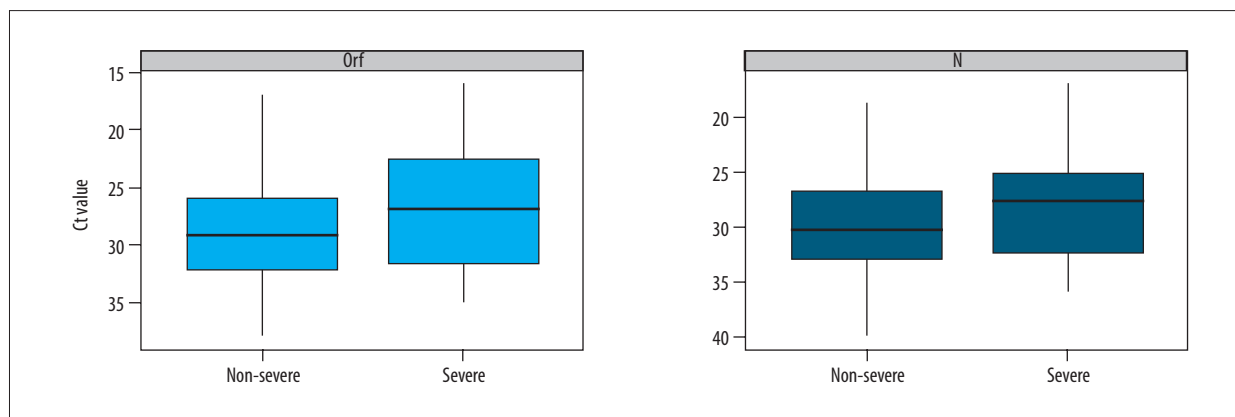
Conclusions

The findings from this retrospective observational clinical study of 631 patients with COVID-19 who were reported to the Jiangsu Commission of Health between January 1 and March 20, 2020 identified factors associated with disease severity and patient outcomes. Patients older than of concentrations age 65 years and with comorbidities and who presented with a fever above 39.0°C developed more severe disease. However, mortality was prevented in this initial patient population by early supportive clinical management. These findings have been supported by subsequent studies during the COVID-19 pandemic and have resulted in the development of clinical diagnostic and management guidelines. While there are still many important unknown parameters, expanded and enhanced surveillance would help in the early detection and diagnosis of suspected cases, thereby reducing the progression of COVID-19 infection to severe cases and preventing deaths.

Data Availability Statement

The epidemiology and clinical data of COVID-19 used and analyzed in this study were abstracted from the China Information System for Disease Control and Prevention (CISDC), the information system of infectious diseases of mandatory notification in mainland China. The data application website is: *http://wjw.jiangsu.gov.cn/*. The clinical information on symptoms and laboratory testing of COVID-19 consists of sensitive information on an individual level. Due to the protection of privacy, these 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.

Conflict of Interest

None.

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** – interquartile ranges; **Ct** – cycle threshold; **SARS** – severe acute respiratory syndrome; **MERS-CoV** – Middle-East respiratory syndrome coronavirus; **ORF** – open reading frame; **N** – nucleocapsid protein; **TCM** –taditional Chinese medicine; **LT** – lung transplantation; **NHF** – nasal high flow.

Supplementary Data

Supplementary Figure 1. Viral load detected in severe (n=31) and non-severe (n=284) cases with reported confirmed cases of COVID-19, Jiangsu Province, Eastern China.

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