Clinical characteristics and risk factors of patients with severe COVID-19 in Jiangsu province, China

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Abstract

Background

To describe the characteristics of patients with Coronavirus Disease-2019 (COVID-19) and factors associated with severe or critically ill presentation.

Methods

Multicentre retrospective cohort study of all individuals with confirmed Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2) infections diagnosed at 24 COVID-19-designated hospitals in Jiangsu province between the 10th January and 15th March 2020. Demographic, clinical, laboratory, and radiological data were collected at hospital admission and data on disease severity were collected at from admission. Patients were categorised as asymptomatic/mild/moderate, and severe/critically ill according to the worst level of COVID-19 recorded during hospitalisation.

Results

A total of 625 patients, 64 (10.2%) were severe/critically ill and 561 (89.8%) were asymptomatic/mild/moderate. All patients were discharged and no patients died. Multivariable regression showed that odds of being a severe/critically ill case were associated with age (year) (OR, 95%CI 1.06, 1.03–1.09), lymphocyte count (10^9/L) (OR 0.25, 0.08–0.74), and pulmonary opacity in CT (per 5%) on admission (OR 1.31, 95%CI 1.15–1.51).

Conclusions

Severe or critically ill patients with COVID-19 is about one-tenths of patients in Jiangsu. Age, lymphocyte count, and pulmonary opacity in CT on admission were associated with risk of severe or critically ill COVID-19.

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Background

Coronavirus Disease 2019 (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV2), was first reported from Wuhan, Hubei province, China, in December 2019 and spread quickly from a focal outbreak with 41 countries to over 570,000 cases with more than 26,000 deaths affecting more than 110 countries by March 2020.[1] The World Health Organization (WHO) declared a pandemic affecting all continents the 11th March 2020.[2]

China has reported the highest number of cases, with over 81,000 confirmed cases by the 13th March.[1] Although the epicentre of the epidemic was located in Wuhan, other provinces became affected in the following weeks. In a case series of the first 44,672 confirmed cases, 1023 patients had died, with a crude

case fatality rate (CFR) of 2.3%, and mortality was higher among critically ill patients, who had a CFR of 49%.[3] In Hubei, the proportion of severe COVID-19 cases was higher than in other provinces (17.7% and 7.0%, respectively) and cases outside the epicentre may have other differences due to active case finding, better screening tests and increase disease awareness.

COVID-19 initial symptoms are not specific, presenting with fever, and cough, which can then resolve spontaneously or progress to shortness of breath, dyspnoea, and pneumonia, leading to severe acute respiratory syndrome (SARS), renal failure, coagulation dysfunction, multiple organ failure and death. Understanding the factors associated with COVID-19 disease severity could support the early identification of patients with high risk for disease progression and inform prevention and control activities and reduce mortality. Furthermore, understanding differences in the epidemiology and characteristics of patients outside Hubei is important for disease forecasting and to inform prevention and control strategies.

Jiangsu, a province over 600 kms from Hubei without common geographical borders and 80 million population, reported over 600 patients, but the epidemiological and clinical characteristics of these patients has not been described. We report here an analysis of all cases in Jiangsu province to describe the epidemiological and clinical characteristics of cases and to identify risk factors for severe/critically ill COVID-19 presentation.

Methods

Study Design and Population

This is a multicentre retrospective cohort study. All patients were included if they (1) were clinically diagnosed and then confirmed to have COVID-19 in Jiangsu province up to the 15th March 2020. (2) fulfilled the diagnostic criteria for the “Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)” released by National Health Commission & National Administration of Traditional Chinese Medicine of China;[4] and (3) were admitted to COVID-19-designated hospitals. Patients without medical records were excluded.

The Ethics Committee of Zhongda Hospital, Affiliated to Southeast University, approved the study protocols (2020ZDSYLL013–P01 and 2020ZDSYLL019–P01). Patient informed consent was waived due to the retrospective study and the public health emergency.

Data Measures

The primary outcome was severe or critically ill within the follow up period. Patients were categorised by disease severity into (1) asymptomatic or mild, (2) moderate, and (3) severe or critically ill, according to “Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)”.[4] Asymptomatic infections were defined as the absence of clinical symptoms with a positive nucleic acid test. Mild COVID-

19 disease was defined as the presence of mild clinical symptoms without respiratory distress and the absence of imaging manifestations of pneumonia. Moderate disease was defined as the presence of fever, with respiratory symptoms and an image of pneumonia in computer tomography (CT) scans. Severe disease was defined as the presence of at least one of a) respiratory distress, a respiratory rate ≥ 30 beats / min; oxygen saturation in resting state ≤ 93% or an arterial blood oxygen partial pressure / oxygen concentration ≤ 300 mmHg (1 mmHg = 0.133 kPa). Critically ill was defined as having respiratory failure requiring mechanical ventilation, shock or combined organ failure requiring intensive care unit (ICU) monitoring and treatment. Clustering onset defined as familial clustering and single onset was not. Incubation times were estimated as the time from contacting the patient with COVID-19 to the time of confirmation of the infection in the contact. All patients followed up to the 15th March 2020.

Data was collected using case record forms and electronic medical record systems and included epidemiological, laboratory and imaging information, treatment and clinical outcome. Information of patients transferred to other hospitals was retrieved from the destination hospital. The day of admission to a COVID-19-designated hospital was considered the first day of hospitalisation. The severity of illness and the score of lung injury was assessed by two physicians and vital signs, symptoms. Severity was assessed at days 1, 2, 3, 4, 5, 6, 7 and 14 after admission and patients were followed for up to discharge. ICU admissions were recorded. Imaging grading was performed by two independent radiologists with more than 5 years' experience in pulmonary imaging. Chest CT axial sections were divided into quadrants (left and right anterior and posterior) by drawing horizontal and vertical lines through the centre of the chest. Quadrant scores were estimated as the sum of quadrants with pulmonary opacities extending from the proximal to the distal end of the chest and ranged from 0 and 4. For pulmonary opacity, bilateral lungs were scored manually and assigned an estimated percentage of pulmonary opacity relative to the whole lung, rounded to the nearest 5%.

Statistical Analysis

Continuous variables were described using means (standard deviations, SD) or medians (with inter-quartile range, IQR) by disease severity and were compared using ANOVA or Kruskal-Wallis tests as appropriate. Categorical variables were summarised using frequencies and percentages and compared using Fisher exact tests.

Logistic regression models were used to identify the risk factors for having a severe or critically ill status. Analysis was performed in 2 steps. Firstly, a univariate logistic regression model was fitted. As there are many potential predictors, we chose the variables for univariate regression analysis if a variable is significant at 5%. Respiratory rate and SpO_2 were not included in the regression analyses since they were part of criterion for classifying the disease severity. All variables selected for univariate regression analysis were also included in the second stage of the multivariate logistic regression. Missing covariates at admission were imputed with multiple imputation using a Markov Chain Monte Carlo simulation method with 10 iterations. In the logistic regression analysis, odds ratios for having a disease progression for each variable were calculated along with 95% confidence intervals (CIs). A sensitivity analysis was

performed on the completed cases. The 2-tailed $P < 0.05$ was considered as statistically significant for all analyses. The analyses were performed using SAS 9.4 (SAS Institute).

Results

A total of 721 patients with confirmed SARS-CoV2 infections were admitted to the twenty-four COVID-19 designated hospitals between the 10th January and the 15th March 2020 (Fig. 1). Of these, 625 (99.0%) had retrievable medical records and were included in the analysis.

Table 1 describes the characteristics of patients at the time of admission by disease severity and Table S1 provides a more detailed description of the five severity categories. 561 (89.8%) patients were asymptomatic/mild/moderate and 64 (10.2%) patients were severe or critically ill. Patients with severe/critically ill COVID-19 were more likely to be older and to be single onset (i.e. not to a cluster of cases in family/community). Patients with moderate or severe/critically ill presentation were more likely to have a medical history of hypertension, coronary heart disease, and diabetes. Patients with moderate/severe COVID-19 on admission had higher temperature, faster respiratory rates, lower peripheral capillary oxygen saturation (SpO_2), and higher CT image quadrant scores and pulmonary opacity percentage (Table 1 and Table S1).

Table 1
Demographic and clinical characteristics of patients with COVID-19 at admission

		Severe/Critically ill			
Category	Characteristics	Yes (N = 64)	No (N = 561)	All (N = 625)	P-value
Demographic,, n/N(%), N,mean(SD)					
	Male	41/64(64.1%)	288/561(51.3%)	329/625(52.6%)	0.0534
	Age (year)	64,59.53(13.43)	561,42.72(16.73)	625,44.44(17.19)	< .0001
	≤ 18 years	0/64(0.0%)	37/561(6.6%)	37/625(5.9%)	< .0001
	19–44 years	6/64(9.4%)	255/561(45.5%)	261/625(41.8%)	
	45–64 years	32/64(50.0%)	216/561(38.5%)	248/625(39.7%)	
	65 + years	26/64(40.6%)	53/561(9.4%)	79/625(12.6%)	
Exposure type, n/N(%)					
	Imported cases	25/64(39.1%)	194/561(34.6%)	219/625(35.0%)	0.4765
	Local cases	39/64(60.9%)	367/561(65.4%)	406/625(65.0%)	
Types of disease onset, n/N(%)					
	Single onset	40/64(62.5%)	270/561(48.1%)	310/625(49.6%)	0.0294
	Clustering onset	24/64(37.5%)	291/561(51.9%)	315/625(50.4%)	
Initial symptoms, n/N(%)					
	Fever	52/64(81.3%)	360/561(64.2%)	412/625(65.9%)	0.0063
	Cough	44/64(68.8%)	300/561(53.5%)	344/625(55.0%)	0.0200
	Sputum	25/64(39.1%)	141/561(25.1%)	166/625(26.6%)	0.0168
Medical history, n/N(%)					
	Hypertension	19/64(29.7%)	72/561(12.8%)	91/625(14.6%)	0.0003
	Diabetes	10/64(15.6%)	30/561(5.3%)	40/625(6.4%)	0.0015
	Stroke	2/64(3.1%)	8/560(1.4%)	10/624(1.6%)	0.2736
Vital signs, N,mean(SD)					
	Temperature (°C)	64,37.30(0.94)	561,37.02(0.70)	625,37.05(0.73)	0.0040
	HR (bpm)	64,89.98(15.06)	561,86.84(13.25)	625,87.17(13.46)	0.0772

		Severe/Critically ill			
	Respiratory rate (breath per min)	64,20.98(4.87)	561,18.87(2.04)	625,19.08(2.56)	< .0001
	SpO_2 (%)	64,95.53(4.70)	561,97.92(1.15)	625,97.68(1.99)	< .0001
CT image, N,median(IQR)					
	Quadrant score (1–4)	58,4.0(4.0–4.0)	438,2.0(1.0–4.0)	496,2.0(1.0–4.0)	< .0001
	Pulmonary opacity (%)	58,50.0(35.0–70.0)	438,20.0(5.0–30.0)	496,20.0(5.0–40.0)	< .0001
Laboratory test, N,median(IQR)					
	WBC Count (10^9/L)	52,4.3(3.4–5.8)	461,5.0(4.0-6.3)	513,4.9(3.9–6.2)	0.0440
	Neutrophil (10^9/L)	52,2.9(2.0-4.4)	455,3.0(2.2-4.0)	507,3.0(2.2-4.0)	0.7435
	Lymphocyte (10^9/L)	52,0.7(0.5-1.0)	453,1.4(1.0-1.8)	505,1.3(0.9–1.7)	< .0001
	Platelet (10^9/L)	48,154.0(118.0-185.0	446,188.5(154.0-222.0)	494,183.5(151.0-219.0)	< .0001
	Albumin (g/L)	48,39.7(34.2–41.4)	432,42.0(38.0-45.7)	480,41.4(38.0-45.1)	< .0001
	Creatinine (umol/L)	49,64.0(51.0–83.0)	427,63.8(51.0–79.0)	476,63.9(51.0–79.0)	0.6950
	C-reactive protein (mg/L)	44,40.1(8.6–92.7)	430,10.0(2.6–19.3)	474,10.0(2.7–22.6)	< .0001
	Activated partial thromboplastin time (s)	54,32.6(28.5–36.5)	459,32.2(27.9–37.4)	513,32.2(28.0-37.2)	0.8158
	Fibrinogen (g/L)	53,4.3(3.2–5.9)	443,3.4(2.7–4.1)	496,3.5(2.7–4.2)	< .0001
	D-dimer (mg/L)	51,0.3(0.2-1.0)	424,0.2(0.1–0.4)	475,0.2(0.1–0.4)	0.0003

Cases with severe/critically ill presentation were more likely to have increased C-reactive protein, procalcitonin, fibrinogen, and D-dimer than asymptomatic/mild/moderate cases (Table 1). Similarly, severe/critically ill cases had lower white blood cells, lymphocyte, and platelet counts and albumin. As expected, severe cases were more likely to use supportive treatments and medical drugs, including antibiotics and antivirals (Table 2).

Table 2
Clinical management and outcome

		n(%) or median(IQR)			
		Severe/Critically ill			
Category	Clinical management and outcome	Yes (N = 64)	No (N = 561)	All (N = 625)	P-value
Supportive treatments	Inotropic and vasoconstrictive agents	5(7.8%)	0(0.0%)	5(0.8%)	< .0001
	Nasal cannula	53(82.8%)	168(29.9%)	221(35.4%)	< .0001
	Mask	12(18.8%)	2(0.4%)	14(2.2%)	< .0001
	High-flow nasal cannula oxygen therapy	24(37.5%)	1(0.2%)	25(4.0%)	< .0001
	Non-invasive ventilation	34(53.1%)	0(0.0%)	34(5.4%)	< .0001
	Intermittent mandatory ventilation	5(7.8%)	0(0.0%)	5(0.8%)	< .0001
	Prone position	17(26.6%)	1(0.2%)	18(2.9%)	< .0001
	Continuous renal replacement therapy	1(1.6%)	0(0.0%)	1(0.2%)	0.1024
	Extracorporeal membrane oxygenation	2(3.1%)	0(0.0%)	2(0.3%)	0.0103
	Lung transplantation	2(3.1%)	0(0.0%)	2(0.3%)	0.0103
Medical drugs	Traditional Chinese medicine	29(45.3%)	69(12.3%)	98(15.7%)	< .0001
	Immunoglobulin	50(78.1%)	106(18.9%)	156(25.0%)	< .0001
	Interferon	47(73.4%)	456(81.3%)	503(80.5%)	0.1363
	Antioxidants	35(54.7%)	117(20.9%)	152(24.3%)	< .0001
	Glucocorticoid	52(81.3%)	90(16.0%)	142(22.7%)	< .0001
	Thymosin	43(67.2%)	101(18.0%)	144(23.0%)	< .0001
	Neurotrophic drugs	21(32.8%)	81(14.4%)	102(16.3%)	0.0005
	Any antibiotics	59(92.2%)	277(49.4%)	336(53.8%)	< .0001
	Any antivirals	64(100%)	516(92.0%)	580(92.8%)	0.0098
Clinical outcome	Death	0(0.0%)	0(0.0%)	0(0.0%)	NC

	n(%) or median(IQR)			
Hospital stay	21.5(15.0–29.0)	15.0(12.0–21.0)	16.0(12.0–22.0)	< .0001

None of the patients died and 625 (100%) of patients were discharged by the end of study (15th March 2020). The results from the univariate and multivariate logistic regression analyses are presented in Table 3. Factors independently associated with severe or critically ill infection included age (year) (OR, 95%CI 1.06, 1.03–1.09), lymphocyte count (10^9/L) (OR 0.25, 0.08–0.74), and pulmonary opacity in CT (per 5%) on admission (OR 1.31, 95%CI 1.15–1.51). Sensitivity analysis showed that they remained statistically significant in a logistic model with only above three variables based on the completed cases without missing data.

Table 3
Factors associated with severe/critically ill in patients with COVID-19: Results from logistic regression analysis

	Univariate analysis*		Multivariate analysis**	
Variables	Odds ratio (95%CI)	P-value	Odds ratio (95%CI)	P-value
Age (year)	1.07(1.05,1.09)	< .0001	1.06(1.03,1.09)	< .0001
Single onset	1.80(1.05,3.06)	0.0311	0.92(0.43,1.96)	0.8275
Fever	2.42(1.26,4.64)	0.0078	1.50(0.64,3.54)	0.3542
Cough	1.91(1.10,3.33)	0.0216	1.24(0.54,2.87)	0.6110
Sputum	1.91(1.12,3.27)	0.0183	1.12(0.48,2.60)	0.7994
Hypertension	2.87(1.59,5.18)	0.0005	1.06(0.47,2.40)	0.8874
Diabetes	3.28(1.52,7.07)	0.0025	1.64(0.52,5.22)	0.4004
Temperature (°C)	1.59(1.15,2.19)	0.0046	0.95(0.61,1.47)	0.8133
Lymphocyte (10^9/L)	0.03(0.01,0.08)	< .0001	0.25(0.08,0.74)	0.0161
Platelet (10^9/L)	0.99(0.98,0.99)	0.0003	1.00(0.99,1.00)	0.5147
Albumin (g/L)	0.91(0.87,0.96)	0.0002	0.99(0.92,1.07)	0.8344
C-reactive protein (mg/L)	1.02(1.01,1.02)	< .0001	1.00(0.99,1.01)	0.9789
Fibrinogen (g/L)	1.87(1.50,2.32)	< .0001	1.04(0.72,1.49)	0.8327
D-dimer (mg/L)	1.28(1.06,1.55)	0.0088	1.17(0.83,1.66)	0.3625
Quadrant score (1–4)	2.28(1.71,3.05)	< .0001	0.90(0.56,1.47)	0.6811
Pulmonary opacity (per 5%)	1.38(1.28,1.49)	< .0001	1.31(1.15,1.51)	0.0001
* Univariate analysis is based on the complete cases without missing value.				
** Multivariate analysis is based on imputed values for missing data in Lymphocyte, Platelet, Albumin, C-reactive protein, Fibrinogen, D-dimer, Quadrant score and Pulmonary opacity using multiple imputation method.				

Discussion

In this large multicentre cohort, 64 (10.2%) of 625 patients were severe or critically ill. This proportion is lower than the 17.7% reported among the 44 672 cases from Wuhan but similar to the 7.0% reported for areas outside Hubei province,[3] which are lower than reported from several case series from Wuhan including 13 (32%) ICU admission among 41 cases with 6 (15%) deaths;[5] 11 (11%) deaths among 99 cases;[6] and 36 (26.1%) ICU admissions among 138 patients, with 6 deaths (4.3%).[7] Our lower proportion

is likely due to several factors, including more adequate medical resources, better disease recognition and testing capacity, earlier identification of asymptomatic and mild cases and a more informed supportive care in COVID-19-designated hospitals.

Despite this being a hospital-based study, some patients had no symptoms. This is likely due to testing of contacts after the identification of an index case and the policy of hospitalization of all infected individuals at the initial stages of the epidemic, independently of the presence of symptoms. Fever, cough, and sputum were very common among patients and more frequent in patients with severely or critically illness. Fever and cough are the most common symptoms in SARS and MERS cases.[8,9] Fever is a primary symptom for cytokine storms, with the production of high concentrations of cytokines stimulating abnormally excessive immune responses and inflammation. Vital signs showed severe or critically ill patients had higher body temperature and respiratory rate, and lower SpO_2 on admission. $SpO_2 < 90\%$ has been used as a marker for the use of glucocorticoids during the outbreak,[10] and the oxygenation saturation index is associated with ARDS severity and increased mortality.[11,12]

Sex seems does not have an impact on severe COVID-19. Although early reports from Wuhan indicated more men than women had severe COVID-19,[5,6,13] following studies reported similar proportions of men and women admitted to ICUs, suggesting sex differences disappeared with higher incidence. Earlier reports may have included more males due to a higher occupational infection risk for males in the markets and congregation places.[7]

Our study found that age was independently associated with severe or critically ill presentation. Age is a well well-established factor for severe/critically ill COVID-19 for individuals > 60, and especially over 80 years old.[14,15] Similarly, previous reports have indicated patients in ICUs are older than non-ICU patients,[7] and that CFRs are higher among older individuals.[5,6,13] Older patients also have faster disease progression than younger patients,[16] which is similar to the MERS and SARS presentations, in which, older age (> 60 or 45) is associated with disease severity (MERS),[17,18] and mortality.[19,20] Older age reflects a greater likelihood of underlying medical conditions such as hypertension, coronary heart disease, and diabetes, which predisposes to immunological vulnerabilities. Also, age-related immunosenescence may also contribute to the severe disease.[21]

The mean incubation period for severe or critically ill cases in Jiangsu (7 days) was longer than the 5 days (95% CI, 4.1-7.0) reported for the first 425 Wuhan patients with confirmed COVID-19.[22] The mean incubation period was slightly longer for less severe than for severe or critically ill patients. Although this was not statistically significant, larger series should explore this finding, as shorter incubation periods may reflect the higher infecting doses often observed at the start of epidemics, as reported for the Middle East Respiratory Syndrome (MERS).[23]

In our cohort, patients with local and known exposures to confirmed COVID-19 cases were less likely to have severe/critically ill infections than patients who had been or had visitors from Wuhan and those

who had no identifiable exposure. As patients with known local exposure were more likely second or third generation SARS-CoV2 transmissions and the virulence of the virus may have changed, as seen for other infections. These patients may have also been aware of the infection risk and taken protective measures which could have reduced the infection dose.

In Wuhan, many asymptomatic patients had abnormal lung CT findings on admission, which then progressed to diffuse ground-glass opacities and consolidation.[24] In Jiangsu, several asymptomatic cases also had radiological changes presented as low quadrant scores and pulmonary opacity scores on admission and severe/critically-ill cases had higher CT quadrant and pulmonary opacity scores than moderate cases. Our study also identified pulmonary opacity as an independent predictor of severe/critical illness. This is consistent with the previous study reporting that the CT visual quantitative evaluation of acute lung inflammatory lesions involving each lobe in severe or critical cases was significantly higher than less severe cases.[25]

We found severe or critically ill patients had more obvious damage of white blood cells and immune cells such as lymphocytes with lymphocytes identified as an independent predictor of more severe disease. COVID-19 may cause the reduced T lymphocytes, especially CD4 + T and CD8 + T cells, leading to reduced IFN-γ production, which may be related to the severity of disease.[26] In addition, severe or critically ill patients showed more serious organ dysfunction like reduce albumin on admission which may be a sign of reduced liver production and increased gastrointestinal or renal loss, and increased fibrinogen on admission responding to systemic inflammation and tissue damage, and more fierce inflammatory response presented as much higher level of inflammatory markers, such as C-reactive protein.

This study has several strengths. Firstly, this is one of the largest studies describing the clinical characteristics of patients with COVID-19 and risk factors for severe/critically ill infection outside the Wuhan epicentre. Secondly, the cohort includes almost all COVID-19 cases in the province, which may have reduced selection bias. Thirdly, Jiangsu province, which is far from Hubei, provides an opportunity to assess the epidemiological, laboratory and clinical features of cases imported from other provinces and local cases. Fourthly, asymptomatic and mild cases were included, which provides a more comprehensive description of the characteristics of COVID-19 cases with a broad spectrum of disease severity.

There are also limitations that need mentioning. Firstly, laboratory and radiological data had a large amount of missing data preventing their integration in the analysis. Secondly, the predictive factors identified may be subject to uncontrolled confounders by unknown/unmeasured factors such as occupation and pregnancy. Medical staff and pregnant women may have different severity profiles. Thirdly, this is a retrospective observational study and data is susceptible to measurement and information bias.

In conclusion, this study demonstrates that patients with COVID-19 in Jiangsu had a low rate of severe or critically ill presentation, with no deaths recorded. The COVID-19 severity is associated with

epidemiological and clinical characteristics, laboratory tests, and radiological findings. Age, lymphocyte count, and pulmonary opacity in CT on admission were independently associated with risk of severe or critically ill COVID-19 presentation.

Declarations

Declaration Of Competing Interest

We declare no competing interests.

Contributors

YY, SJ and DW conceived and designed the study. SL, HL and YW contributed to the literature search. SL, YW, SJ, YY, and DW contributed to data collection, quality checks and data management. DW, SJ, SL, HL, LEC, YW and YY contributed to data analysis and results presentation. DW, SJ, SL, LEC, HL and YY were responsible for results interpretation. SL, HL, YW, DW, LEC, SJ, and YY contributed in the drafting and review of the manuscript.

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Ethics Approval And Consent To Participate

The Ethics Committee of Zhongda Hospital, Affiliated to Southeast University, approved the study protocols (2020ZDSYLL013–P01 and 2020ZDSYLL019–P01). Patient informed consent was waived due to the retrospective study and the public health emergency.

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Figures

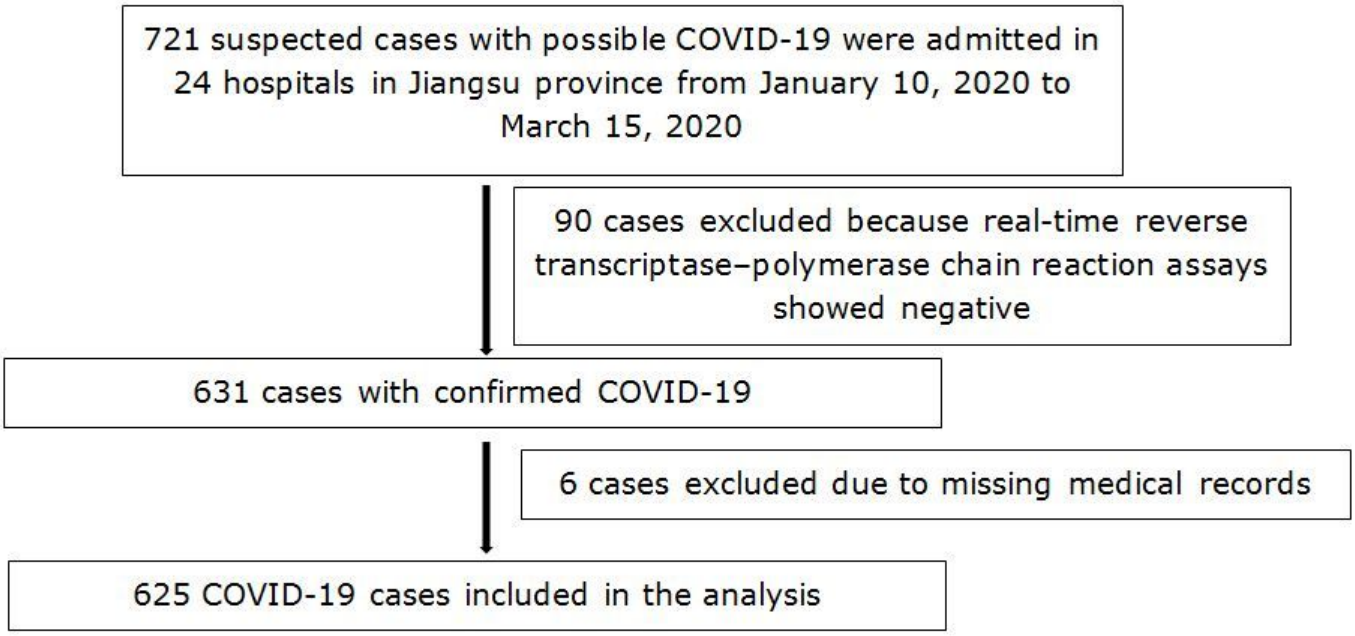

Figure 1

Study flow diagram