

A retrospective analysis from a single center for 60 COVID-19 patients with asymptomatic, mild to moderate, and severe conditions in Wuxi, China

Jiehui Huang, BM, Chao Qian, MM, Tao Bian, MM, Meiping Chu, MM, Weiwei Yin, MM, Yonghua Pang, MM, Jinmei Bai, MM, Yanjie Huang, BM^{*}

Abstract

The aim of this study was to retrospectively analyze the clinical data of COVID-19 patients with different severity during February 2020 in Wuxi, China.

The present retrospective study included a total of 60 cases who were diagnosed as COVID-19 patients and hospitalized in the Wuxi Fifth People's Hospital during February 2020 to March 2020. Among all patients 14 cases were asymptomatic, 25 cases were with mild stage, 13 cases were with moderate stage, and 8 cases were with severe stage. Basic clinical data as well as clinical characteristics, including temperature, respiratory rate, heart rate, blood gas analysis data, whole blood test data, and the prognosis condition, were collected and analyzed. Statistical analysis was conducted in different severity stage patients.

Among the patients, the median temperature gradually increased from the asymptomatic to the severe patients and the median age increased from the mild to the severe patients with statistical difference. The hospitalization duration was the highest in severe patients. Higher heart rate, as well as lower oxygen partial pressure and oxygenation index were observed in severe patients than the other groups. Besides, higher CRP and globulin levels after admission were found in severe patients, and were gradually increased from the asymptomatic patients to the severe patients. On the contrary, the lymphocyte ratio and count was significant lower in severe patients. We also observed higher D-Dimer levels in the severe patients and the difference was statistical. Among all patients, 2 cases (3.33%) died and other patients were all cured after treatment.

Statistical difference was mainly found mainly in age, hospitalization duration, temperature, CRP levels, O₂ partial pressure and oxygenation index, globulin, lymphocyte ratio, and D-Dimer in patients with different severity. The higher CRP levels, lower O₂ partial pressure and oxygenation index, higher globulin, lower lymphocyte ratio, and higher D-Dimer might be associated with the patients' severity.

Abbreviations: ARDS = acute respiratory distress syndrome, CDC = Chinese Center for Disease Prevention and Control, COVID-19 = 2019 novel coronavirus disease, FiO₂ = oxygen concentration, PaO₂ = arterial oxygen partial pressure, WHO = World Health Organization.

Keywords: COVID-19, CRP, different severity, immune indices, retrospective study

1. Introduction

Up to February 2021, the latest data by the World Health Organization (WHO) showed over 1 billion (112,209,815 cases) of people has been diagnosed with the 2019 novel coronavirus

disease (COVID-19), including 2,490,776 deaths, and the daily increase diagnosed patients are up to 100 thousands^[1] (https:// www.who.int, Accessed February 26, 2021). Although COVID-19 is also caused by coronavirus, such as SARS-CoV, the

Editor: Jinfeng Li.

Received: 4 December 2020 / Received in final form: 24 March 2021 / Accepted: 8 July 2021

The authors were supported financially by [No. N2020X009] Study on the cluster treatment of severe and critically ill patients with covid-19 to improve the success rate of rescue. The present study was approved by the ethic committee of The Fifth Peoples Hospital of Wuxi.

All authors agreed the submission and the policy of the journal and copyright.

All data in this study can be obtained by proper request from the authors.

The authors declare there is no conflict of interest in this study.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Department of Respiratory Medicine, The Fifth Peoples Hospital of Wuxi, Wuxi, Jiangsu, China.

^{*} Correspondence: Yanjie Huang, No. 1215, Guangrui Road, Department of Respiratory Medicine, The Fifth Peoples Hospital of Wuxi, Wuxi, 214000 Jiangsu, China (e-mail: yanjieh1975@126-web.net).

Copyright © 2021 the Author(s). Published by Wolters Kluwer Health, Inc.

This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial License 4.0 (CCBY-NC), where it is permissible to download, share, remix, transform, and buildup the work provided it is properly cited. The work cannot be used commercially without permission from the journal.

How to cite this article: Huang J, Qian C, Bian T, Chu M, Yin W, Pang Y, Bai J, Huang Y. A retrospective analysis from a single center for 60 COVID-19 patients with asymptomatic, mild to moderate, and severe conditions in Wuxi, China. Medicine 2021;100:30(e26748).

http://dx.doi.org/10.1097/MD.000000000026748

difference is obvious and is noticed by more and more people. Compared with SARS-CoV, COVID-19 affected hundreds of times the population and influences all regions worldwide.^[2,3] The symptoms of COVID-19 are slighter and incubation period is longer.^[4] Besides, more and more evidence indicated the asymptomatic patients are an important infection source, who are hardly to find and diagnose.^[5]

Currently, there is still no specific drug for COVID-19 and the treatment strategy mainly contains broad spectrum antiviral and antibacterial drugs, oxygen inhalation, and supportive treatment.^[6–9] Fortunately, vaccines for COVID-19 are developed and several vaccines have been gradually applied.^[10,11] However, the rampant COVID-19 is still far from the end. Now, many studies showed clinical characteristics for COVID-19 patients. Generally, cough, fever, fatigue are the early symptoms, and dyspnea and decreased blood oxygen saturation indicated severe symptoms, which might lead to acute respiratory failure or respiratory distress syndrome.^[12–14] Besides, in many cases, the alteration in inflammation system and coagulation function has also been noticed.^[15,16]

Despite the researches, now, characteristics for COVID-19 patients are still lacking and more clinical findings showed be shared, especially for characteristics in patients with different severity. In the present study, we conducted a retrospective analysis for 60 COVID-19 patients with different severity of asymptomatic, mild to moderate, and severe COVID-19 during February 2020 to March 2020 in Wuxi, China.

2. Methods and materials

2.1. Patients and diagnosis

This retrospective study included a total of 60 cases of COVID-19 patients who were hospitalized in the Wuxi Fifth People's Hospital during February 2020 to March 2020. The diagnosis of the patients was according to the quick advice guide for diagnosis and treatment for COVID-19 of Chinese National Health Commission (http:// www.nhc.gov.cn/xcs/zhengcwj/202001/f492c9153ea9437bb587 ce2ffcbee1fa/files/39e7578d85964dbe81117736dd789d8f.pdf, accessed at 2020-05-26), as well as well as the World Health Organization interim guidance.^[17] Among all patients, only 2 cases showed negative for nucleic acid test and the other 58 cases were all positive. The 2 nucleic acid test negative patients showed typical ground glass lesion on computed tomography (CT) and other typical symptoms were also observed, including dry cough, fever, and dyspnea. The samples for nucleic acid test were obtained from pharyngeal swab and were confirmed by the by the Chinese Center for Disease Prevention and Control (CDC). The patients were divided into asymptomatic, mild to moderate, and severe according to their symptoms. For the severity division, according to the quick advice guide for diagnosis and treatment for COVID-19 of Chinese National Health Commission, mild patients were defined as mild symptoms with no imaging evidence for pneumonia; moderate patients were defined as patients with typical symptoms such as fever and cough and with imaging evidence for pneumonia; severe patients were defined as respiratory rate >30/min, blood oxygen saturation <93% when rest, or arterial oxygen partial pressure (PaO₂)/oxygen concentration (FiO₂) ≤300 mm Hg, or advanced disease was observed >50% by imaging evidence within 24 to 48 hours. The asymptomatic patients were patients who showed no imaging evidence and with no or only 1 slight symptom, who were mainly found by epidemiological track. Patients' characteristics were

observed during the hospitalization duration and were analyzed. The present study was approved by the Ethic committee of the Fifth Peoples Hospital of Wuxi.

2.2. Clinical measurement and data collection

Demographic data were collected from all patients, including age, sex, medical history, and pretreatment complications. CT scan and X-ray were performed for all patients. Temperature was detected and symptoms were recorded. Laboratory tests, including whole blood test, blood gas assay, electrolyte analysis, and coagulation analysis, were conducted and vital signs were monitored. All patients were hospitalized during February 2020 to March 2020. The outcomes of the patients were recorded during the hospitalization duration.

2.3. Statistical analysis

The measurement data were expressed by median (range). The normal distribution of all continuous data was tested by Kolmogorov–Smirnov test and all data were not normally distributed. Comparisons were conducted using Kruskal–Wallis test among different groups and Mann–Whitney test was used between 2 groups. It was considered to be statistically significant when *P* value was less than .05. All calculations were made using SPSS 18.0 (SPSS Inc., Chicago, USA).

3. Results

3.1. Basic clinical characteristics of all patients

Among all 60 COVID-19 patients, 14 cases (23.33%) were asymptomatic, 25 cases (41.67) were mild, 13 cases (21.67%) were moderate, and 8 cases (13.33%) were severe. The basic characteristics were collected. From the mild to severe patients, the median age of the patients was gradually increased, and the median age of the severe patients was markedly higher than the mild patients (P < .05, Table 1). Besides, significant difference was also found in temperature of different patients. The temperature of moderate and severe patients was remarkably higher than the asymptomatic and the mild patients (P < .05). Similarly, hospitalization duration of the severe patients was the longest and was significantly higher than the asymptomatic and the mild patients (P < .05). The pre-treatment complications and symptoms were also differently presented in patients with different severity. Generally, ratio of patients with pre-treatment complications and typical symptoms was the highest in the severe patients and the lowest in the asymptomatic patients. At last, nucleic acid test showed only 2 patients were not positive, but ground glass lesion on CT was found in these 2 cases and typical symptoms were also observed. The ground glass lesion on CT was found in a total of 45 cases (75%) (Fig. 1). The most regular symptoms of the patients were fever in 36.00 (60.00%) cases, cough in 26.00 (43.33%) cases, fatigue in 19.00 (31.67%) cases, expectoration in 18.00 (30.00%) cases, headache in 7.00 (11.67%) cases, diarrhea in 8.00 (13.33%) cases, and dyspnea in 7.00 (11.67) cases.

3.2. Treatment, complications, and outcomes

For all patients, the basic treatment protocol was antiviral therapy combined with support treatment. Antiviral therapy was

Table 1

Basic clinical characteristics of all patients.

Variables	Asymptomatic, n=14	Mild, n=25	Moderate, $n = 13$	Severe, n=8	All	P
Age, yr	44.5 (6~57) [¶]	35 (5∼79) [¶]	50 (10~75)	58 (36~75) ^{†,‡}	45 (5~79)	.035
Sex, male: female	6 (42.86):8 (57.14)	13 (52.00):12 (48.00)	8 (61.54):5 (38.46)	4 (50):4 (50)	31 (51.67):29 (48.33)	.068
Temperature, °C	36.80 (36.60~38.20) ^{‡,§,¶}	37.70 (36.50~38.70) ^{†,§,¶}	38.70 (36.20~39.30) ^{†,‡}	38.20 (37.20~39.90) ^{†,‡}	37.6 (36.2~39.9)	<.001
Respiratory rate, /min	18.00 (15.00~21.00)	18.00 (17.00~24.00)	20.00 (16.00~30.00)	18.00 (18.00~26.00)	18 (15~30)	.422
Hospitalization duration, d	15 (10∼22) ^{§,¶}	19 (11~25) [¶]	20 (11~29) [†]	22.5 (14~35) ^{†,‡}	18.5 (10~35)	.015
Complication, n (%)						<.001
Hypertension	7 (50.00)	3 (12.00)	4 (30.77)	3 (37.50)	17 (28.33)	
Diabetes	0 (0)	4 (16.00)	2 (15.38)	4 (50.00)	10 (16.67)	
Coronary heart disease	0 (0)	0 (0)	2 (15.38)	0 (0)	2 (3.33)	
Cerebrovascular disease	0 (0)	0 (0)	1 (7.69)	0 (0)	1 (1.67)	
Cancer	0 (0)	1 (4.00)	1 (7.69)	0 (0)	2 (3.33)	
Chronic renal disease	0 (0)	0 (0)	0 (0)	1 (12.50)	1 (1.67)	
Liver diseases	1 (7.14)	0 (0)	1 (7.69)	0 (0)	2 (3.33)	
Current smoker	0 (0)	0 (0)	3 (23.08)	0 (0)	3 (5.00)	
Other	1 (7.14)	5 (20.00)	3 (23.08)	0 (0)	9 (15.00)	
Symptoms, n (%)						<.001
Fever	3 (21.43)	16 (64.00)	10 (76.92)	7 (87.50)	36.00 (60.00)	
Cough	1 (7.14)	12 (48.00)	7 (53.85)	6 (75.00)	26.00 (43.33)	
Fatigue	0 (0)	13 (52.00)	3 (23.08)	3 (37.50)	19.00 (31.67)	
Expectoration	0 (0)	7 (28.00)	6 (46.15)	5 (62.50)	18.00 (30.00)	
Headache	0 (0)	2 (8.00)	2 (15.38)	3 (37.50)	7.00 (11.67)	
Diarrhea	0 (0)	4 (16.00)	3 (23.08)	1 (12.50)	8.00 (13.33)	
Dyspnea	0 (0)	1 (4.00)	2 (15.38)	4 (50.00)	7.00 (11.67)	
Other	1 (7.14)	3 (12.00)	0 (0)	0 (0)	4.00 (6.67)	
Nucleic acid test positive, n (%)	14 (100.00)	24 (96.00)	12 (92.31)	8 (100.00)	58.00 (96.67)	
Ground glass lesion on CT, n (%)	8 (57.14)	18 (72.00)	11 (84.62)	8 (100.00)	45.00 (75.00)	

* P value was calculated among 3 groups of mild, moderate, and severe patients using Kruskal–Wallis test among different groups and Mann–Whitney test was used between 2 groups. † Asymptomatic.

[‡] mild.

§ moderate.

[¶] severe.

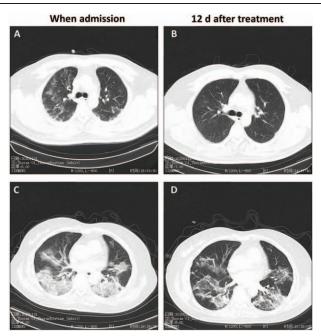


Figure 1. CT scan for a 36-year-old male moderate patient when admitted (A) and 12 days after treatment (B). And CT scan for a 61-year-old female severe patient when admitted (C) and 12 days after treatment (D). In (A) and (C), clear and obvious ground glass lesions could be seen when admission. After treatment, the ground glass lesions of both patients obviously decreased.

used in all patients, and antibacterial treatment was used in 22 (36.67%) cases (Table 2). Gamma globulin was only for 2 cases with severe symptoms after admission to enhance the immunity. Thymosin and probiotics were also used in 12.00 (20.00%) and 19.00 (31.67%) cases, respectively. Intranasal oxygen inhalation was applied in 24.00 (40.00%) cases and high flow oxygen absorption was applied in only 2 (3.33%) severe patients. Besides, low molecular weight heparin was used in 3 (5.00%) cases to reduce the incidence of venous embolism. Glucocorticoid was used in only 1(1.67%) case with severe symptoms. A total of 2 cases (3.33%) died during hospitalization. One was a 62-yearold female patient with diabetes before treatment, the other one was a 23-year-old female patient with no pre-treatment complications. The cause of death was respiratory failure for both. During the treatment, respiratory failure was found in 5 (8.33%) cases in all patients, and 4 cases were in the severe group; no case was found in asymptomatic and mild patients. The other most common complications were liver dysfunction in 10 cases (16.67%), might partly be due to the application of multiple medications.

3.3. Difference of heart rate, oxygen partial pressure, and oxygenation index in COVID-19 patients with different severity

The decrease of blood oxygen saturation is one of the typical symptoms in COVID-19 patients and might lead to acute respiratory distress syndrome (ARDS). Thus, blood gas analysis

Treatment, complications, and outcomes of all patients

Variables	Asymptomatic, n=14	Mild, n=25	Moderate, $n = 13$	Severe, n=8	All	P
Treatment method, n (%)						<.00
Antiviral therapy	14 (100.00)	25 (100.00)	13 (100.00)	8 (100.00)	60.00 (100.00)	
Antibacterial treatment	0 (0)	11 (44.00)	5 (38.46)	6 (75.00)	22.00 (36.67)	
Gamma globulin	0 (0)	0 (0)	1 (7.69)	1 (12.50)	2.00 (3.33)	
Thymosin	1 (7.14)	3 (12.00)	4 (30.77)	4 (50.00)	12.00 (20.00)	
Probiotics	4 (28.57)	8 (32.00)	5 (38.46)	2 (25.00)	19.00 (31.67)	
Intranasal oxygen inhalation	1 (7.14)	10 (40.00)	5 (38.46)	8 (100.00)	24.00 (40.00)	
High flow oxygen absorption	0 (0)	0 (0)	0 (0)	2 (25.00)	2.00 (3.33)	
Low molecular weight heparin	0 (0)	0 (0)	1 (7.69)	2 (25.00)	3.00 (5.00)	
Glucocorticoid	0 (0)	0 (0)	0 (0)	1 (12.50)	1.00 (1.67)	
Complications, n (%)						<.00
Respiratory failure	0 (0)	0 (0)	1 (7.69)	4 (50.00)	5.00 (8.33)	
Acute respiratory distress syndrome	0 (0)	0 (0)	1 (7.69)	1 (12.50)	2.00 (3.33)	
Renal dysfunction	0 (0)	1 (4.00)	0 (0)	1 (12.50)	2.00 (3.33)	
Liver dysfunction	4 (28.57)	1 (4.00)	2 (15.38)	3 (37.50)	10.00 (16.67)	
Myocardial dysfunction	0 (0)	0 (0)	1 (7.69)	0 (0)	1.00 (1.67)	
Double infection	0 (0)	1 (4.00)	1 (7.69)	1 (12.50)	3.00 (5.00)	
Outcomes, n (%)						<.00
Deceased	0 (0)	1 (4.00)	1 (7.69)	0 (0)	2.00 (3.33)	
Cured	14 (100.00)	24 (96.00)	12 (92.31)	8 (100.0)	58.00 (96.67)	

* P value was calculated among three groups of mild, moderate, and severe patients using Kruskal-Wallis test among different groups and Mann-Whitney test was used between 2 groups.

and related data are important in diagnosis. As we observed, the heart rate was gradually increased along with the severity and the heart rate in severe patients was the highest, and significantly higher than the asymptomatic and mild patients (P < .05, Table 3). No significant difference was found in blood gas pH, CO₂ partial pressure, and oxygen flow. However, remarkably lower O₂ partial pressure and oxygenation index were observed in severe patients than all other groups (P < .05).

3.4. Whole blood test and CRP in COVID-19 patients with different severity

The whole blood test result is summarized in Table 4. Significantly higher fasting blood level was found in severe patients (P < .05), which was due to the ratio of diabetes. Besides, remarkably higher lymphocyte ratio was observed in asymptomatic patients compared with the other groups (P < .05). The lymphocyte count was also the lowest in the severe patients and the highest in the asymptomatic patients with significant difference (P < .05). Lower hemoglobin and higher neutrophil count were observed in severe patients; however, the difference was not significant. Significant difference was also found in the highest CRP level during hospitalization, which was the highest in the severe patients and the lowest in the asymptomatic patients (P < .05). The PCT level was also higher in severe patients; however, only 1 case showed an abnormal level of 161 ng/mL and most patients showed PCT level <0.2 ng/mL. Obvious difference was also found in globulin levels in severe patients compared with the mild and moderate patients, (P < .05), however not different from the asymptomatic patients. Red blood cell distribution width was significantly higher in severe patients than the asymptomatic patients and platelet volume was higher in moderate patients than the asymptomatic and mild patients (P < .05); however, no significant difference was found in other groups. Besides, platelet distribution width was significantly higher in mild and moderate groups than the asymptomatic patients (P < .05); neutrophil count was obviously higher in severe patients than the mild patients (P < .05), and hemoglobin level was the lowest in the severe patients (P < .05). Creatinine was observed to be significantly higher in moderate patients than

6		HC 4

Blood gas analysis in COVID-19 patients with different sever	ity.
--	------

Blood gas analysis in COVID-19 patients with different severity.						
Variables	Asymptomatic, n=14	Mild, n=25	Moderate, n=13	Severe, n=8	All	P *
Heart rate	82.50 (62.00~102.00) ^{§,¶}	84.00 (65.00~110.00) [¶]	94.00 (52.00~120.00) [†]	107.00 (66.00~130.00) ^{†,‡}	87.5 (52~130)	.027
Blood gas pH	7.40 (7.34~7.45)	7.40 (7.35~7.47)	7.42 (7.33~7.49)	7.44 (7.33~7.50)	7.41 (7.33~7.50)	.275
CO ₂ partial pressure, mm Hg	45.00 (40.00~50.00)	42.00 (38.00~55.00)	43.00 (32.00~55.00)	42.50 (37.00~51.00)	43 (32~55)	.713
O ₂ partial pressure, mm Hg	107.50 (78.00~228.00) [¶]	113.00 (73.0~228.00) [¶]	100.00 (73.00~169.00) [¶]	73.00 (61.00~130.00) ^{†,‡,§}	103 (61~223)	.015
Oxygen flow (%)	21.00 (21.00~21.00)	21.00 (21.00~29.00)	21.00 (21.00~21.00)	21.00 (21.00~29.00)	21 (21~29)	.129
Oxygenation index	500.00 (390.00~1085.00) [¶]	538.00 (338.00~1085.00) [¶]	476.00 (348.00~623.00) [¶]	347.50 (1.00~619.00) ^{†,‡,§}	480 (1~1085)	.025

* P value was calculated among 3 groups of mild, moderate, and severe patients using Kruskal–Wallis test among different groups and Mann–Whitney test was used between 2 groups. * Asymptomatic.

* mild.

§ moderate.

[¶] severe.

	•]	

Whole blood test in COVID-19 patients with different severity.

Variables	Asymptomatic, n=14	Mild, $n = 25$	Moderate, n=13	Severe, n=8	All	P
Lactic acid, mg/dL	1.50 (0.90~2.90)	1.80 (0.80~3.40)	1.60 (0.50~3.50)	1.80 (1.00~3.90)	1.70 (0.50~3.90)	0.378
Fasting blood glucose, mmol/L	5.30 (4.20~8.30) [¶]	6.50 (3.20~18.50) [¶]	6.30 (4.80~17.70) [¶]	11.95 (6.30~18.30) ^{†,‡,§}	6.5 (3.50~18.50)	0.003
White cell, 10 ⁹ /L	5.16 (3.37~7.47)	5.42 (2.57~8.48)	5.41 (3.47~7.91)	4.87 (2.73~12.63)	4.44 (2.57~12.63)	0.942
Neutrophil ratio (%)	50.05 (30.00~70.30)	56.00 (0.44~90.00)	57.60 (0.56~79.80)	61.45 (0.77~98.40)	56.00 (0.44~98.40)	0.805
Lymphocyte ratio (%)	37.85 (20.20~59.30) ^{‡,§,¶}	28.70 (0.45~52.60) ^{†,§}	22.20 (0.25~37.70) ^{†,‡}	21.15 (0.05~36.02)*	28.05 (0.05~59.03)	0.002
Monocyte ratio (%)	9.20 (5.70~11.90)	10.90 (0.04~18.70)	7.30 (0.08~19.40)	8.40 (0.03~10.10)	8.85 (0.03~19.04)	0.295
Neutrophil count, 10 ⁹ /L	2.53 (1.14~4.60)	2.90 (1.66~6.50) [¶]	3.06 (2.00~5.94)	3.52 (1.42~12.44) ^b	3.01 (1.41~12.44)	0.414
Lymphocyte count, 10 ⁹ /L	2.31 (0.68~2.78) ^{§,¶}	1.40 (0.45~3.59)	1.33 (0.61~1.88) ^{†,¶}	0.96 (0.33~5.00) ^{†,§}	1.40 (0.33~5.00)	0.019
Monocyte count, 10 ⁹ /L	0.52 (0.30~5.50) ¹	0.51 (0.04~1.01)	0.47 (0.30~1.05) ¹	0.28 (0.12~0.61) ^{†,§}	0.48 (0.04~5.50)	0.080
Red blood cell count, 10 ⁹ /L	4.43 (3.93~6.54) [¶]	4.59 (3.58~5.93)	4.66 (3.80~5.51) [¶]	4.18 (2.97~5.11) ^{†,§}	4.53 (2.97~6.54)	0.146
Hemoglobin, g/L	138.00 (122.00~171.00)	142.00 (12.90~166.00)	143.00 (86.00~159.00) [¶]	120.50 (14.00~156.00) [§]	140.00 (12.90~171.00)	0.105
Hematocrit (%)	39.50 (0.37~48.00)	39.00 (0.38~154.00)	29.00 (0.43~44.00)	34.00 (0.22~123.00)	38.50 (0.22~154.00)	0.327
Platelet count	192.50 (144.00~281.00)	191.00 (45.00~344.00)	180.00 (129.00~216.00)	175.00 (38.00~303.00)	186.50 (38.00~344.00)	0.728
Red blood cell distribution width (%)	11.75 (10.90~14.80) [¶]	12.30 (11.00~244.00)	12.40 (11.60~36.50)	13.70 (11.80~179.00)*	12.30 (10.90~244.00)	0.041
Platelet volume, fL	10.85 (9.40~13.40) [§]	11.00 (9.10~23.40) [§]	12.10 (10.90~15.50) ^{†,‡}	11.25 (8.80~17.40)	11.20 (8.80~23.40)	0.047
Platelet distribution width, fL	12.45 (9.40~18.60) ^{‡,§}	14.10 (9.60~22.70) [†]	14.20 (12.10~20.40) [†]	14.30 (9.70~16.50)	14.00 (9.40~22.70)	0.066
Thromboplastin (%)	8.12 (0.16~34.00)	19.50 (0.15~36.00) [§]	0.24 (0.15~26.00)*	14.70 (0.18~27.00)	16.00 (0.15~36.00)	0.155
The highest CRP level after admission, mg/L	3.40 (0.50~24.60) ^{§,¶}	8.50 (0.50~140.70) [¶]	23.00 (0.50~131.90) ^{†,¶}	93.58 (17.06~192.43) ^{†,‡,§}	11.60 (0.05~192.43)	0.001
The highest PCT level after admission, ng/mL	0.20 (0.20~0.20)	0.20 (0.20~5.40)	0.20 (0.20~0.58)	0.20 (0.20~161.00)	0.20 (0.20~161)	0.059
Alanine aminotransferase, U/L	29.50 (11.00~138.00)	19.00 (8.00~98.00)	21.00 (13.00~74.00)	23.50 (10.00~142.00)	21.00 (8.00~142.00)	0.455
Glutamic oxaloacetylase, U/L	24.50 (15.00~90.00)	23.00 (18.00~40.00)	25.00 (15.00~52.00)	26.50 (20.00~51.00)	24.50 (15.00~90.00)	0.602
Total bilirubin, µmol/L	8.50 (2.00~40.00)	5.00 (1.00~17.00)	7.00 (1.00~25.00)	8.00 (3.00~17.00)	7.00 (1.00~40.00)	0.207
Albumin, g/L	42.50 (37.00~47.00)	43.00 (33.00~52.00)	41.00 (35.00~47.00)	39.000 (32.00~76.00)	42.00 (32.00~76.00)	0.197
Globulin, g/L	27.00 (22.00~63.00)	26.00 (21.00~40.00) [¶]	26.00 (22.00~35.00) [¶]	30.00 (25.00~44.00)*.8	27.00 (21.00~63.00)	0.078
Urea, mmol/L	4.50 (2.80~9.40)	3.80 (2.10~9.87)	4.10 (3.30~7.00)	5.15 (3.10~22.90)	4.05 (2.10~22.90)	0.501
Creatinine, µmol/L	58.00 (32.00~90.00)	52.00 (19.00~87.00) [§]	66.00 (38.00~68.00)*	62.50 (37.00~267.00)	56.00 (19.00~267.00)	0.132

* P value was calculated among three groups of mild, moderate, and severe patients using Kruskal–Wallis test among different groups and Mann–Whitney test was used between 2 groups. † Asymptomatic.

§ moderate.

[¶] severe.

the mild patients (P < .05). At last, electrolyte analysis and coagulation analysis were also performed. Significantly higher D-D level was found in moderate and severe patients (P < .05, Table 5). There was also no significant difference in K⁺, Na⁺, and Cl⁻.

4. Discussion

From December 2019, COVID-19 has infected millions of people worldwide with an astonishing speed. Up to now, there is still no specific medicine, vaccine, or treatment method for COVID-19, and the characteristics of this virus are still far from clearly known.^[18] Thus, more clinical evidence for COVID-19 patients is still needed and urgent. In the present study, we conducted a retrospective study to analyze the clinical characteristics of

COVID-19 patients with different severity and found severe patients might have higher CRP levels during hospitalization, longer hospitalization duration, higher temperature, lower O₂ partial pressure and oxygenation index, higher globulin, lower lymphocyte ratio, and count and higher D-Dimer.

The relationship between age and prognosis of COVID-19 patients has been widely noticed. In 1 study from the CDC COVID-19 response team, about 81% deaths occurred among adults aged ≥ 60 years.^[19] In another study including 5319 patients, it a relatively low incidence risk was observed for young people but a very high mortality risk for seniors, especially for patients older than 80 years.^[20] However, the infection sensitivity seems to cover all ages. It was found that COVID-19 could rapidly infect young people from 16 to 23 years of age by a asymptomatic transmission way in a prospective contact-tracing

Table 5				
Floctrolyto	analysis a	and coa	aulation	analveie

Electrolyte analysis ar	lectrolyte analysis and coagulation analysis.						
Variables	Asymptomatic, $n = 14$	Mild, $n=25$	Moderate, $n = 13$	Severe, n=8	All	P	
International normalized ratio	1.00 (1.00~1.10)	1.01 (1.00~1.16)	1.01 (1.00~1.10)	1.00 (1.00~1.07)	1.00 (1.00~1.16)	.525	
PT, s	13.20 (12.30~14.30)	13.20 (11.40~14.90)	13.20 (11.90~14.20)	13.15 (12.00~14.00)	13.20 (11.40~14.90)	.517	
APTT, s	37.30 (12.30~44.40)	38.70 (33.90~49.00)	38.60 (30.70~44.40)	36.95 (28.60~47.00)	38.30 (13.20~49.00)	.376	
TT, s	16.00 (14.90~18.80)	16.20 (13.30~18.50)	16.20 (12.60~17.30)	16.45 (13.40~17.80)	16.20 (12.60~18.80)	.957	
D-Dimer, µg/mL	0.25 (0.22∼1.17) [§]	0.22 (0.22~2.02) ^{§,¶}	0.43 (0.22~5.05) ^{†,‡}	0.59 (0.22~1.60)‡	0.27 (0.22~5.05)	.009	
K ⁺ , μmol/L	4.15 (3.10~4.70)	4.10 (2.90~5.30) [¶]	4.20 (2.60~4.80) [¶]	3.55 (2.80~4.30) ^{‡,§}	4.10 (2.60~5.30)	.100	
Na ⁺ , μmol/L	142.00 (140.00~144.00)	142.00 (138.00~145.00)	142.00 (140.00~145.00)	140.50 (137.00~145.00)	142.00 (137.00~145.00)	.424	
Cl⁻, µmol/L	105.00 (103.00~108.00)	104.00 (101.00~108.00)	103.00 (99.00~109.00)	105.00 (95.00~109.00)	105. (95.00~109.00)	.115	

* P value was calculated among three groups of mild, moderate, and severe patients using Kruskal-Wallis test among different groups and Mann-Whitney test was used between 2 groups. † Asymptomatic.

[‡] mild.

§ moderate.

[¶] severe.

Asymp

[‡] mild.

study in Wuhan city.^[21] In this research, we observed COVID-19 patients from 5 to 79 years with a very wide range. However, the only 2 cases of deaths (3.33% mortality rate) occurred in a 62-year-old patient and a 23-year-old case. For the 62-year-old patient, we observed high CPR level as 138.03 mg/L, and the patient had severe diabetes before admission. Unfortunately, we did not obtain a clear and detailed reason for the 23-year-old patient, who showed sudden severe respiratory failure during treatment. We speculated that some factors, such as inflammatory factor storm that we did not notice occurred while admission. And the lack of treatment experience might be also a factor.

Decreased blood oxygen saturation is one of the typical symptoms of COVID-19, which might lead to dyspnea and even respiratory failure. In most severe patients, the oxygen saturation was less than 94% and thus oxygen supply is one of the key treatment methods.^[22] In the study by Lyons and Callaghan,^[23] the high-flow nasal oxygen was recommended to the physicians, as the authors demonstrated low-flow nasal oxygen or facemask oxygen was not enough to provide adequate respiratory support in many cases. In a recent retrospective research, authors observed decreased oxygen saturation in 14 cases in 85 COVID-19.^[24] In our research, we also observed significantly lower O₂ partial pressure and oxygenation index in severe patients, and in asymptomatic patients, the levels were the highest. The increased heart rate in severe patients might be also related to decreased O₂ partial pressure.

The change of immune system and inflammation response are also important factors in COVID-19 patients. In the research by Runa et al,^[25] the authors observed remarkably higher levels of IL-6 and CRP, as well as myoglobin and cardiac troponin in deceased patients than the survival. Both IL-6 and CRP could reflect the inflammation response, and cardiac troponin might be associated with the pretreatment cardiovascular complications. In another research by Luo et al,^[26] the authors also found higher CRP and IL-6 levels in COVID-19 patients and the application of tocilizumab might improve the situation. More importantly, CRP levels might reflect lung lesions and disease severity in early stage of COVID-19. In our research, we also found remarkably higher CRP levels in severe patients than the other patients. And we also found higher globulin, which might be also related to activated inflammation response. Besides, the lower lymphocyte ratio, count, and lower monocyte count and hemoglobin might have resulted from damaged immunity.

Finally, coagulation alteration is noticed in some researches for COVID-19 patients. COVID-19 patients might have a higher risk for venous embolism, especially for patients with severe respiratory or systemic manifestations. Thrombocytopenia, elevated D-dimer, prolonged prothrombin time, and disseminated intravascular coagulation were found in COVID-19 patients.^[27] And the alteration of coagulation might be also associated with cytokine storm caused by COVID-19.^[28] In an analysis of 22 COVID-19 cases, the authors observed severe hypercoagulability in patients with acute respiratory failure.^[29] The D-Dimer level reflects venous thrombosis formation, and we also observed remarkably higher D-Dimer level in severe patients, indicating severe patients had a higher risk for the incidence of venous embolism and anticoagulant therapy could be used. We also observed higher red blood cell distribution width in severe patients and higher platelet volume in moderate patients with unclear reason, which need more studies to confirm.

This study also has some obvious limitations, including small sample size and single center. We did not measure the IL-6 or other interleukin levels during the hospitalization. This might also influence the analysis of inflammation condition.

5. Conclusion

This retrospective analysis for 60 COVID-19 patients with different severity demonstrated that higher CRP levels, lower O_2 partial pressure and oxygenation index, higher globulin, lower lymphocyte ratio, and higher D-Dimer might be associated with aggravating severity of the patients. This study might provide more clinical evidence for characteristics of COVID-19 patients. The clinical physicians should keep regulating the treatment strategies according to the updating clinical findings.

Author contributions

JHH conducted most of the experiments and wrote the manuscript; CQ, TB, MPC, WWY, YHP, and JMB conducted the experiments and analyzed the data, YJH designed the study and revised the manuscript.

- All authors have read and approved the manuscript.
- Conceptualization: Yanjie Huang.
- Data curation: Jiehui Huang, Chao Qian, Tao Bian, Meiping Chu, Weiwei Yin, Yonghua Pang, Jinmei Bai.
- Formal analysis: Chao Qian, Tao Bian, Meiping Chu, Weiwei Yin, Yonghua Pang, Jinmei Bai.
- Funding acquisition: Yanjie Huang.
- Investigation: Chao Qian.
- Methodology: Chao Qian, Tao Bian, Meiping Chu, Weiwei Yin, Yonghua Pang, Jinmei Bai.
- Project administration: Yanjie Huang.

Resources: Chao Qian, Tao Bian, Meiping Chu, Weiwei Yin, Yonghua Pang, Jinmei Bai.

- Software: Jinmei Bai.
- Validation: Tao Bian, Meiping Chu, Weiwei Yin, Yonghua Pang.
- Visualization: Weiwei Yin, Yonghua Pang, Jinmei Bai.
- Writing original draft: Jiehui Huang.
- Writing review & editing: Yanjie Huang.

References

- WHO. Coronavirus disease 2019 (COVID-19): situation report, 72. 2020. https://apps.who.int/iris/bitstream/handle/10665/331686/nCoVsi trep02Apr2020-eng.pdf?sequence=1
- [2] Rothan HAB, Siddappa N. The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. J Autoimmun 2020;109: 102433.
- [3] Liu YGA, Wilder-Smith A, Rocklöv J. The reproductive number of COVID-19 is higher compared to SARS coronavirus. J Travel Med 2020;27:taaa021.
- [4] Lauer SA, Grantz KH, Bi Q, et al. The incubation period of coronavirus disease 2019 (COVID-19) from publicly reported confirmed cases: estimation and application. Ann Intern Med 2020;172:577–82.
- [5] Kannan S, Shaik Syed Ali P, Fau-Sheeza A, et al. COVID-19 (Novel Coronavirus 2019): recent trends. Eur Rev Med Pharmacol Sci 2020;24:2006–11.
- [6] Song Y, Zhang M, Yin L, et al. COVID-19 treatment: close to a cure? A rapid review of pharmacotherapies for the novel coronavirus (SARS-CoV-2). Int J Antimicrob Agents 2020;56:106080. doi:10.1016/j. ijantimicag.2020.106080.
- [7] Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med 2020;288:192–206.
- [8] Rabby MII. Current drugs with potential for treatment of COVID-19: a literature review. J Pharm Pharm Sci 2020;23:58–64.
- [9] Alexpandi R, De Mesquita JF, Pandian SK, Ravi AV. Quinolines-based SARS-CoV-2 3CLpro and RdRp inhibitors and Spike-RBD-ACE2

inhibitor for drug-repurposing against COVID-19: an in silico analysis. Front Microbiol 2020;11:1796.

- [10] Yamey G, Schäferhoff M, Hatchett R, et al. Ensuring global access to COVID-19 vaccines. Lancet 2020;395:1405–6.
- [11] Hotez PJ, Corry DB, Strych U, Bottazzi ME. COVID-19 vaccines: neutralizing antibodies and the alum advantage. Nat Rev Immunol 2020;20:399–400.
- [12] Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records [published correction appears in Lancet. Lancet 2020;395:809–15.
- [13] Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med 2020;8:420–2.
- [14] Lake MA. What we know so far: COVID-19 current clinical knowledge and research. Clin Med 2020;20:124–7.
- [15] Hanley BLS, Youd E, Swift B, Osborn M. Autopsy in suspected COVID-19 cases. J Clin Pathol 2020;73:239–42.
- [16] Jiang FDL, Zhang L, Cai Y, et al. Review of the clinical characteristics of coronavirus disease 2019 (COVID-19). J Gen Intern Med 2020;35:1545–9.
- [17] World Health Organization. (2020). Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance. In Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: Interim guidance (pp. 21-21). https://pesquisa. bvsalud.org/portal/resource/pt/biblio-1053426
- [18] Meng L, Hua F, Bian Z. Coronavirus disease 2019 (COVID-19): emerging and future challenges for dental and oral medicine. J Dent Res 2020;99:481–7.
- [19] COVID CT, ResponseSevere outcomes among patients with coronavirus disease 2019 (COVID-19)—United States, February 12–March 16. MMWR Morb Mortal Wkly Rep 2020;69:343–6.

- [20] Li H, Wang S, Zhong F, et al. Age-dependent risks of incidence and mortality of COVID-19 in Hubei Province and other parts of China. Front Med 2020;7:190.
- [21] Huang L, Zhang X, Zhang X, et al. Rapid asymptomatic transmission of COVID-19 during the incubation period demonstrating strong infectivity in a cluster of youngsters aged 16-23 years outside Wuhan and characteristics of young patients with COVID-19: a prospective contacttracing study. J Infect 2020;80:e1–3.
- [22] Wang Y, Zhang D, Du G, et al. Remdesivir in adults with severe COVID-19: a randomised, double-blind, placebo-controlled, multicentre trial. Lancet 2020;395:1569–78.
- [23] Lyons C, Callaghan M. The use of high-flow nasal oxygen in COVID-19. Anaesthesia 2020;75:843–7.
- [24] Yang W, Cao Q, Qin LE, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. J Infect 2020;80:388–93.
- [25] Ruan QYK, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med 2020;1–3.
- [26] Luo PLY, Qiu L, Liu X, et al. Tocilizumab treatment in COVID-19: a single center experience. J Med Virol 2020;92:814–8.
- [27] Giannis D, Ziogas IA, Gianni P. Coagulation disorders in coronavirus infected patients: COVID-19, SARS-CoV-1, MERS-CoV and lessons from the past. J Clin Virol 2020;127:104362.
- [28] Jose RJ, Manuel A. COVID-19 cytokine storm: the interplay between inflammation and coagulation. Lancet Respir Med 2020;8: e46-7.
- [29] Spiezia L, Boscolo A, Poletto F, et al. COVID-19-related severe hypercoagulability in patients admitted to intensive care unit for acute respiratory failure. Thromb Haemost 2020;120:998– 1000.