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Original Article

Predictors of Coronavirus Disease 2019 Severity: A Retrospective Study of 64 Cases

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SUMMARY: This study aimed to analyze the clinical characteristics and potential predictors of disease severity in patients with coronavirus disease 2019 (COVID-19). We retrospectively analyzed the clinical data from 64 (37 male and 27 female) patients with COVID-19. Their mean age was 47.8 years; 43 (67.2%) cases were non-severe, 21 (32.8%) were severe, and 2 patients (3.1%) died. Age and serum ferritin levels were significantly associated with COVID-19 severity. There were no significant differences in the duration of severe illness or the number of days on high-level respiratory support between the low-dose and high-dose methylprednisolone groups. The mean number of days in hospital in the high-dose group was higher than that in the low-dose group. Repeated monitoring of ferritin, interleukin-6, C-reactive protein, lactic acid dehydrogenase, and erythrocyte sedimentation rate during COVID-19 treatment may assist in the prediction of disease severity and evaluation of treatment effects.

INTRODUCTION

In December 2019, cases of pneumonia of unknown etiology were reported in Wuhan City, Hubei Province, China. Epidemiological investigation indicated that these patients or their contacts might have been exposed at the Huanan wholesale seafood market in Wuhan (1–3). Sequencing of the viral genome from the lower respiratory tracts of patients implicated a novel coronavirus (4). The World Health Organization (WHO) subsequently named this virus as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease caused by the virus as coronavirus disease 2019 (COVID-19) (5). COVID-19 spread rapidly throughout China and other countries (3,6–11). By March 25, 2020, there had been 375,498 confirmed cases and 16,362 deaths in 195 countries. According to published reports, SARS-CoV-2 is mainly transmitted through respiratory droplets, aerosols, or direct contact, and people are generally susceptible to the virus. It mainly invades the respiratory system, and patients with mild disease seldom have serious damage to organ function and tend to make a full recovery. However, patients with severe disease can develop respiratory failure, multiple organ failure, and septic shock, leading to death.

To date, the pathogenesis of COVID-19 has not been clearly elucidated. Despite the concerted efforts of scientists, no specific antiviral drug or treatment for COVID-19 has been developed. Cumulative reports have described the clinical characteristics of COVID-19 (3,11–17), and the data indicate that its severity varies in different individuals. Given the unprecedented nature of the current epidemic, more studies are urgently needed to achieve a better understanding of the factors that predict COVID-19 severity. In the current study, we retrospectively reviewed 64 cases of COVID-19 patients treated at the Fifth Medical Center of Chinese PLA General Hospital between January 13, 2020 and March 10, 2020. The aims were to describe clinical characteristics, identify possible predictors of disease severity and mortality, and provide further insight into the treatment of COVID-19.

MATERIALS AND METHODS

Patients: All COVID-19 patients diagnosed at the Fifth Medical Center of Chinese PLA General Hospital between January 13, 2020 and March 10, 2020 were included in the study. Diagnostic criteria, degree of disease severity, and standards of clinical cure were determined in accordance with the guidelines for the Diagnosis and Treatment for Novel Coronavirus Pneumonia (version 7) (18) released by the National Health Commission of the People's Republic of China. SARS CoV-2 infection was confirmed in all patients

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included in the study via genetic sequencing or real-time reverse transcriptase polymerase chain reaction (RT-PCR). All patients were assessed for disease severity at the time of hospital admission. The specific criteria for assessing disease severity were as follows: (i) non-severe type—mild clinical symptoms, with or without fever, imaging with or without pneumonia; and (ii) severe type—dyspnea after any activity, or a respiratory rate ≥ 30 breaths/min, or oxygen saturation ≤ 93% without supplementary oxygen inhalation, or a PaO_2/FiO_2 < 300 mmHg. We defined patients as clinically recovered if their body temperatures returned to normal for > 3 days and they tested negative on two consecutive SARS-CoV-2 nucleic acid tests conducted > 1 day apart. Based on the mean methylprednisolone dose, the patients were divided into two groups: (i) high-dose group (> 1.5 mg/kg/day) and (ii) low-dose group (< 1.5 mg/kg/day).

This study was approved by the Institutional Review Board of the Fifth Medical Center of Chinese PLA General Hospital. The study subjects provided informed consent in accordance with the Declaration of Helsinki.

Data collection: All patient data were obtained via the hospital's medical information system. We retrieved their history of living in Wuhan or Hubei Province as well as medical history of any chronic diseases of the heart, lung, brain, kidney, or other organs. We recorded clinical symptoms, such as fever, cough, fatigue, chest distress, dyspnea, headache, nausea, vomiting, and diarrhea. Other data analyzed included the results of routine blood tests; erythrocyte sedimentation rate (ESR); blood biochemistry; serum levels of ferritin, procalcitonin, C-reactive protein (CRP), and interleukin-6 (IL-6); glucocorticoid dose and duration of administration; respiratory support mode; and prognosis.

SARS-CoV-2 nucleic acid detection: SARS-CoV-2 nucleic acid detection was conducted in accordance with the guidelines for laboratory testing of novel coronavirus infections released by the National Health Commission of the People's Republic of China; they have been approved by the WHO (19). Briefly, sputum, secretions from the nasopharynx, or secretions from the lower respiratory tract were collected, and real-time RT–PCR was used to detect the virus. Target 1 (ORF1ab) was amplified using the forward primer (F) ccctgtggtttacacttaa, the reverse primer (R) acgatttgcatcactga, and the probe (P) 5'−fam-ccgtctgcgtatgtggaaggtttagtg-bhq1−3'. Target 2 (N) was amplified using (F) gggggaacttcctgctagat, (R) cagacatttgctcacgtg, and (P) 5'−fam-ttgctgctgcttgagatt-tamra−3'. Laboratory confirmation of SARS-COV-2 was required to satisfy one of the following: (i) positive result for both targets (ORF1ab and N) in the same sample: if a single target was positive, another sample was collected to repeat the test, and the test was deemed positive, if the second sample was single-target positive; and (ii) positive result for a single target in two types of samples during simultaneous testing or in two different tests on the same type of sample.

Statistical analysis: Statistical analyses were performed using SPSS 25.0 software (Chicago, IL, USA). Quantitative data are expressed as mean ± standard deviation or median and quartile. Qualitative data are expressed as numbers or rates. The *t*-test, rank sum test, or analysis of variance was used to compare quantitative data between groups, and the chi-square test was used to compare qualitative data between groups. Logistic regression was used for multivariate analysis. Receiver operating characteristic (ROC) curve analysis was used to evaluate the ability of the predictors of disease severity, and only those with an area under curve > 0.7 were chosen for the ROC analysis. A $p < 0.05$ was deemed to indicate statistical significance.

RESULTS

Comparison of clinical characteristics, laboratory examination, and treatments between severe and non-severe types of COVID-19 patients: Of the 64 patients with COVID-19, 43 (67.2%) were of the non-severe type, 21 (32.8%) were of the severe type, and two patients (3.1%) died. Table 1 compares the clinical characteristics, laboratory examination, and treatments between the severe and non-severe types of COVID-19 patients. There were 37 (57.8%) male and 27 (42.2%) female patients. The mean age of all patients was 47.8 ± 18.5 years; the mean age of severe patients was significantly higher than that of non-severe patients (61.4 ± 16.4 years vs. 41.2 ± 15.7 years, $p = 0.001$). Half of the patients (32/64, 50%) had been in the Wuhan or Hubei provinces, and 27 (42.2%) were members of a cluster of infections. Regarding coexisting conditions, hypertension was significantly more prevalent in severe patients (42.9% vs. 11.6%, $p = 0.009$). The most common symptom was fever (87.5%); however, there was no significant difference in the duration of fever between non-severe (5.2 ± 3.4 days) and severe (6.9 ± 4.9 days) patients ($p = 0.18$). Other symptoms included cough (53.1%), fatigue (34.4%), chest distress (17.2%), dyspnea (9.4%), headache (20.3%), muscle soreness (15.6%), nausea (3.1%), and diarrhea (6.3%).

There were no significant differences in white cell counts or platelet counts between severe and non-severe patients. In severe patients, the mean number of granulocytes was significantly higher ($4.0 \pm 2.3 \times 10^9$/L vs. $2.6 \pm 0.9 \times 10^9$/L, $p = 0.001$), the median number of lymphocytes was lower (0.83×10^9/L vs. 1.53×10^9/L, $p = 0.001$), and the mean hemoglobin level was lower (128.2 ± 16.3 g/L vs. 138.1 ± 13.8 g/L, $p = 0.02$). Similarly, their serum albumin was lower (34.4 ± 5.2 g/L vs. 40.7 ± 4.0 g/L, $p = 0.001$), serum lactic acid dehydrogenase (LDH) was higher (356.9 ± 204.6 U/L vs. 209.2 ± 52.2 U/L, $p = 0.005$), and blood glucose was higher (7.4 ± 2.4 mmol/L vs. 5.3 ± 2.5 mmol/L, $p = 0.003$). Regarding coagulative function, there was no difference in the prothrombin time between the severe (12.7 ± 1.7 s) and non-severe (12.2 ± 1 s) patients ($p = 0.15$). Severe patients displayed significantly higher serum levels of IL-6 (median 18.7 pg/mL vs. 10.6 pg/mL; $p = 0.002$), CRP (median 19.5 mg/L vs. 6.7 mg/L; $p = 0.001$), and ferritin (766.1 ± 564.4 ng/mL vs. 304.3 ± 251.9 ng/mL, $p = 0.005$), as well as significantly higher ESR (42.6 ± 24.5 mm/h vs. 21.4 ± 18.3 mm/h, $p = 0.002$).

Forty-seven patients were treated with oral ritonavir/lopinavir combined with atomized inhalation of interferon alpha, one was treated with oral ritonavir/

Table 1. Comparison of clinical characteristics and laboratory tests between severe type and non -sever type patients with COVID-19

Charactersitc	Normal Range	All patients n = 64	Nonsevere n = 43	Severe n=21	*P* Value
Sex(M/F), n	NA	37/27	25/18	12/9	1.0
Age, yeas	NA	47.8 ± 18.5	41.2 ± 15.7	61.4 ± 16.4	0.001
BMI, Kg/m^2	NA	24.6 ± 3.37	24.2 ± 3.5	25.7 ± 2.8	0.07
Recently visited Wuhan, n (%)	NA	32 (50%)	24 (55.8%)	8 (38.1%)	0.18
Clustering infection, n (%)	NA	27 (42.2%)	18 (41.9%)	9 (42.9%)	0.94
Smoking history, n (%)	NA	7 (10.9%)	3 (7.0%)	4 (19.0%)	0.2
Alcohol intake history, n (%)	NA	14 (21.9%)	7 (16.3%)	7 (33.3%)	0.19
Comorbidity, n/%	NA				
Hypertension	NA	14 (21.9%)	5 (11.6%)	9 (42.9%)	0.009
Diabetes	NA	6 (9.4%)	3 (7.0%)	3 (14.3%)	0.38
Chronic kidney disease	NA	1 (1.6%)	0	1 (4.8%)	0.33
Cerebral infarction	NA	1 (1.6%)	0	1 (4.8%)	0.33
Asthma	NA	1 (1.6%)	1 (2.3%)	0	1.0
HIV	NA	1 (1.6%)	0	1 (4.8%)	0.33
Tumor	NA	1 (1.6%)	0	1 (4.8%)	0.33
Duration of fever, days	NA	5.8 ± 4.0	5.2 ± 3.4	6.9 ± 4.9	0.18
Blood routine					
White Blood Cell, $\times 10^9/L$	4-10	4.9 ± 1.7	4.7 ± 1.3	5.3 ± 2.3	0.2
Granulocyte, $\times 10^9/L$	2-7	3.1 ± 1.7	2.6 ± 0.9	4 ± 2.3	0.001
Lymphocyte, $\times 10^9/L$	0.8-4.0	1.42 (0.85, 1.68)	1.53 (1.25, 2.02)	0.83 (0.45, 1.47)	0.001
Platelet, $\times 10^9/L$	100-300	185.2 ± 61.8	180.5 ± 62.7	194.1 ± 61.9	0.41
Hemoglobin, g/L	110-160	134.9 ± 15.6	138.1 ± 13.8	128.2 ± 16.3	0.02
Biochemical test results					
Albumin, g/L	35-50	39.2±5.1	40.7±4.0	34.4 ± 5.2	0.001
Alanine aminotransferase, U/L	5-40	24 (14, 38)	22 (14, 36)	31 (14, 45)	0.47
Aspartate aminotransferase, U/L	5-40	25 (22, 38)	24 (21, 30)	29 (22, 60)	0.14
Total bilirubin, umol/L	3.4-17.1	11.2 (8.2 14.9)	10 (7.7, 15)	11.3 (8.5, 13.9)	0.98
Blood urea nitrogen, mmol/L	2.0-7.1	3.8 (3.3, 5.1)	3.7 (3.2, 4.3)	4.56 (3.4, 5.78)	0.01
Creatinine, umol/L	44-106	77.8 ± 14.7	77.2 ± 14.1	78.8 ± 16.2	0.68
Amylase, U/L	25-125	58.8 ± 22.3	60.9 ± 24.8	55.1 ± 14.9	0.34
Troponin, ng/mL	0-0.15	0.005 (0.004, 0.008)	0.004 (0.003, 0.005)	0.007 (0.004, 0.016)	0.003
Glucose, mmol/L	3.9-6.1	6.3 ± 2.3	5.3 ± 2.5	7.4 ± 2.4	0.003
Triglyceride, mmol/L	< 2.3	1.15 (0.85, 1.5)	1.09 (0.76, 1.5)	1.16 (1.0, 1.5)	0.19
Lactic dehydrogenase, U/L	109-245	246.6 ± 100.1	209.2 ± 52.2	356.9 ± 204.6	0.005
Natrium, mmol/L	136-145	137.7 ± 2.9	138.8 ± 2.6	136.8 ± 3.3	0.056
Potassium, mmol/L	3.5-5.5	4.3 (3.9, 4.5)	4.3 (4.0, 4.5)	4.1 (3.8, 4.5)	0.42
Chlorine, mmol/L	96-106	102.2 ± 5.3	102.0 ± 6.1	102.7 ± 3.5	0.612
Prothrombin time, seconds	11-15	12.4 ± 1.2	12.2 ± 1.1	12.7 ± 1.7	0.15
Procalcitonin, ug/L	< 0.5	0.051 (0.037,0.079)	0.043 (0.033,0.058)	0.085 (0.049,0.22)	0.001
Interleukin-6, pg/mL	0-7	12.5 (5.6,25.7)	10.6 (5.8, 21.4)	18.7(14.7, 43.7)	0.002
C-reactive protein, mg/L	0.068-8.2	8.5 (3.0, 21.3)	6.7 (1. 8, 10.7)	19.5(9.4, 41.1)	0.001
Erythrocyte sedimentation rate, mm/h	0-20	28.8 ± 24.3	21.4 ± 18.3	42.6 ± 24.5	0.002
Serum ferritin, ng/mL	13-150	461.3 ± 436	304.3 ± 251.9	766.1 ± 564.4	0.005
Antiviral therapy, n (%)	NA	57 (89.1%)	38 (88.4%)	19 (90.5%)	1.0
Litonavir/lopinavir + Interferon-a	NA	47 (73.4%)	34 (79.1%)	13 (61.9%)	
Litonavir/lopinavir + Arbidol	NA	1 (1.6%)	0	1 (4.8%)	
Arbidol + Interferon-a	NA	3 (4.7%)	1 (2.3%)	2 (9.5%)	
Interferon-a	NA	6 (9.3%)	3 (7.0%)	3 (14.3%)	
without antiviral drug	NA	7 (10.9%)	5 (11.6%)	2 (9.5%)	
Respiratory support therapy, n(%)	NA				
High flow humidification treatment	NA	19 (29.7%)	0	19 (90.5%)	

Charactersitc	Normal Range	All patients n = 64	Nonsevere n = 43	Severe n=21	*P* Value
Noninvasive mechanical ventilation	NA	9 (14.1%)	0	9 (42.9%)	
Invasive mechanical ventilation	NA	2 (3.1%)	0	2 (9.5%)	
Glucocorticoid Therapy, n(%)	NA	28 (43.8%)	7 (16.3%)	21 (100%)	0.00
> 1.5 mg/kg.d	NA	11 (17.2%)	1	10	
≤ 1.5 mg/kg.d	NA	17 (26.6%)	6	11	
Death, n(%)	NA	2 (3.1%)	0	2 (9.5%)	0.1
From illness to hospital, days	NA	7.1 ± 4.7	6.1 ± 4.3	9.0 ± 4.5	0.02
Hospital stay, days	NA	18 (10, 26)	15 (9, 19)	26 (17, 29)	0.00

NA, not applicable; the data of normal distribution is represented by mean and standard deviation, the data of non-normal distribution is represented by median and quartile. *P* value is the comparison between non-severe and sever patients; the tumor of 1 patient is prostate cancer.

Table 2. Logistic regression analyses for factors predicting the severity of COVID-19

Covariate	OR (95% CI)	*P*
Age, years	1.196 (1.005-1.422)	0.04
Serum ferritin, ng/mL	1.006 (1.001-1.012)	0.02
ALB	0.666 (0.362-1.228)	0.19
HGB	0.967 (0.819-1.141)	0.69
Lymphocytes	0.988 (0.961-1.016)	0.39
Glu	0.964 (0.409-2.268)	0.93
LDH, U/L	1.008 (0.978-1.039)	0.61
IL-6, pg/mL	0.979 (0.917-1.045)	0.52
CRP, mg/L	1.057 (0.955-1.169)	0.28
ESR, mm/h	0.979 (0.884-1.084)	0.68

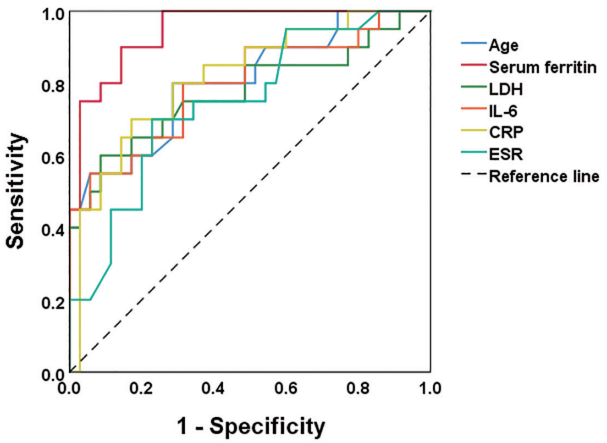

Fig. 1. (Color online) Indicators that can be used to judge coronavirus disease 2019 (COVID-19) severity. Receiver operating characteristic curve analysis suggested that age, interleukin 6, lactic acid dehydrogenase, C-reactive protein, erythrocyte sedimentation rate, and serum ferritin could be used to assist the prediction of COVID-19 severity.

lopinavir combined with arbidol, three were treated with oral arbidol combined with atomized inhalation of interferon alpha, six were treated with atomized inhalation of interferon alpha, and seven were not administered any antiviral drugs because of drug interactions or intolerance to side effects. There was no significant difference in antiviral therapy between severe and non-severe patients (p = 1.0). Nineteen patients (29.7%) underwent respiratory support therapy, and 28 were treated with methylprednisolone. The proportion and dose of methylprednisolone used for severe patients were significantly higher than those used for non-severe patients. The mean number of days from illness to hospitalization was 7.1 ± 4.7 d, and the median duration of hospital stay was 18 (10–26) d. The time from illness to hospitalization and the duration of hospital stay were significantly longer in severe patients (9.0 ± 4.5 d vs. 6.1 ± 4.3 d, p = 0.02; 26 (17–29) d vs. 15 (9–19) d, p = 0.00, respectively).

Analysis of predictors for the severity of COVID-19: We used the data with significant differences (Table 1) for logistic regression analysis. The results showed that age and serum ferritin level significantly associated with COVID-19 severity (Table 2). ROC curve analysis suggested that various parameters could be used to predict disease severity in patients with COVID-19 with area under the curve values of 0.80 for age, 0.79 for IL-6, 0.78 for LDH, 0.82 for CRP, 0.75 for ESR, and 0.95 for ferritin (Fig. 1). The specificity of predicting the severity of COVID-19 based on age > 48 years was 71.4%, and the sensitivity was 80.0%. For LDH > 258 U/L, the specificity was 99.1% and the sensitivity was 60.0%. For IL-6 > 3.8 pg/mL, the specificity was 69.6% and the sensitivity was 80.0%. For CRP > 11.6 mg/L, the specificity was 82.9% and the sensitivity was 70.0%. For ESR > 32 mm/h, the specificity was 77.1% and the sensitivity was 70%. For serum ferritin > 493 ng/mL, the specificity was 85.7% and the sensitivity was 90%. Over the course of

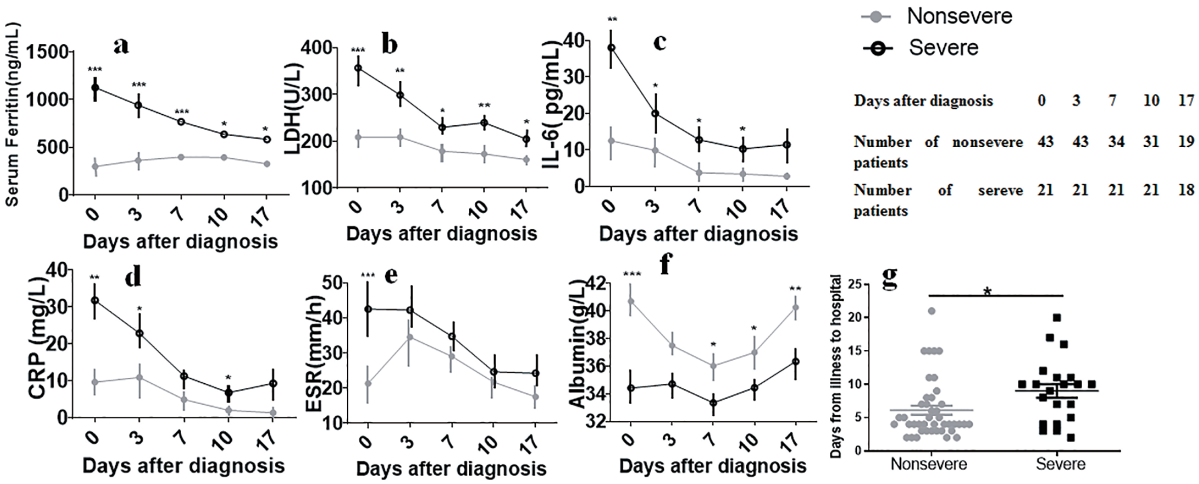

Fig. 2. (Color online) Comparison of indicators in patients with severe coronavirus disease 2019 (COVID-19) and patients with non-severe COVID-19. Serum ferritin (ng/mL) (a), lactic acid dehydrogenase (U/L) (b), interleukin 6 (pg/mL) (c), C-reactive protein (mg/L) (d), and erythrocyte sedimentation rate (mm/h) (e) were all higher in severe patients than in non-severe patients, and they all gradually decreased as disease improved. Albumin (g/L) kept higher in non-severe patients compared with severe patients (f). The time from symptom onset to hospitalization was significantly longer in severe patients than in non-severe patients (g).

Table 3. Prognosis comparison of sever patients with different doses of methylprednisolone

	Average dose of prednisolone (mg/kg.d)		*P*
	≤ 1.5	> 1.5	
Numbers, n	11	10	
Days of methylprednisolone usage, days	6.8 ± 2.1	11.6 ± 6.3	0.04
Dose of methylprednisolone, mg/kg.d	0.9 ± 0.3	3.3 ± 0.6	0.000
Duration of severe illness, days	12.7 ± 5.6	13.3 ± 7.4	0.82
Days of high levels respiratory support, days	13.3 ± 6.1	11.6 ± 7.3	0.59
Hospital stay, days	23.3 ± 7.3	32.3 ± 7.8	0.01
Death, n	0	2	0.21

Severe illness refer to patients with shortness of breath or dyspnea after activity, or a respiratory rate ≥ 30 breaths/min, or oxygen saturation ≤ 93% without supplementary oxygen inhalation, or an oxygenation index of < 300 mmHg. Days of high levels respiratory support mean the days that patients treated with high flow humidification treatment, noninvasive mechanical ventilation and invasive mechanical ventilation.

treatment and with improvement in patient condition, the levels of serum ferritin, LDH, CRP, and IL-6 and ESR decreased gradually in the severe group, whereas that of albumin gradually increased (Fig. 2).

Effects of glucocorticoid therapy on the prognosis of severe COVID-19: Studies investigating the virus responsible for severe acute respiratory syndrome (SARS; formally named SARS-CoV) in 2003 (20–22) and the virus responsible for Middle East respiratory syndrome (MERS; formally named MERS-CoV) (23) implied that glucocorticoid administration may reduce lung inflammation and improve prognoses. However, high dose corticosteroid therapy may have some disadvantages (24). In the current study, all patients with severe disease were treated with methylprednisolone. The mean days of methylprednisolone use were 6.8 ± 2.1 d in the low-dose group and 11.6 ± 6.3 d in the high-dose group. The mean methylprednisolone doses were 0.9 ± 0.3 mg/kg/day in the low-dose group and 3.3 ± 0.6 mg/kg/day in high-dose group. There were no significant differences in the death rate, days of high-level respiratory support, or duration of severe illness between the low-dose and high-dose groups (Table 3). Patients in the high-dose group had a significantly longer stay in the hospital than those in the low-dose group (32.3 ± 7.8 d vs. 23.3 ± 7.3 d, $p = 0.01$).

DISCUSSION

SARS-CoV-2 reportedly has high affinity for angiotensin-converting enzyme 2 receptors in the human airway, rendering humans highly susceptible to infection. COVID-19 has rapidly become a worldwide epidemic with enormous effects. Recent WHO estimates suggest that the death rates associated with COVID 19 vary from 2% to 12% in different countries. Despite unprecedented efforts by governments and scientists, to date, no reliable treatment for COVID-19 has been developed. The main treatments are respiratory support, organ function maintenance, and experimental antiviral

therapy. Diligent and accurate recording and timely reporting of the clinical aspects of as many COVID-19 patients as possible during early stage of the pandemic, particularly those of severe patients, will provide valuable insights into the development of effective treatment strategies.

In the current study, fever and cough were the most common symptoms in our COVID-19 patients. Additionally, there was no significant association between fever duration and the severity of COVID-19. SARS-COV-2 evidently invaded the lungs, potentially leading to pneumonia and hypoxemia of varying severity. However, whether the virus caused damage to other organs was uncertain. Blood indices of the heart, kidney, and pancreas were all within normal ranges in most patients on admission; there were no significant differences between the severe and non-severe patients in these parameters. These results are consistent with some previous reports (3,25). In contrast, other reports detected functional abnormalities of the liver, kidney, brain, and other systems to different degrees (26–29), which may be related to organ injury due to prolonged hypoxemia.

In the present study, serum ferritin, CRP, IL-6, LDH, and ESR were significantly higher in severe patients than in non-severe patients, and these parameters gradually decreased as their conditions improved. These results are consistent with those reported by Cao et al. (30). In logistic regression analysis, age and serum ferritin were significantly associated with COVID-19 severity. The ROC curve analysis implied that these parameters could predict the severity of COVID-19. Serum ferritin levels > 493 ng/mL predicted severe COVID-19 with a specificity of 85.7% and sensitivity of 90%. These data suggest that CRP, IL-6, ESR, LDH, and serum ferritin should be closely monitored to facilitate timely evaluation of severity and recovery in patients with COVID-19, especially in patients aged > 48 years.

Zhe et al. (31) reported that some COVID-19 patients exhibited systemic inflammatory responses, particularly pulmonary inflammatory responses. In the present study, IL-6 levels were significantly higher in patients with severe disease. Similarly, multiple previous studies (32–34) have reported that other inflammatory factors increased in patients with severe COVID-19. These reports imply that inflammatory response levels are closely related to the progression of COVID-19 severity. Inflammatory responses can aid in viral clearance, but excessive inflammatory responses can cause severe lung injury and even lung failure, possibly increasing the severity of COVID-19. Timely control of excessive inflammatory responses in COVID-19 patients may contribute to inhibiting the progression to severe disease.

Previous studies investigating MERS and SARS suggest that glucocorticoids may contribute to patient recovery (20–23,35). Russell et al. (24) reported that glucocorticoids could delay disease progression, but that excessive use of glucocorticoids may prolong viral clearance. Such varying conclusions may be attributed to different doses and timing of glucocorticoid administration in different studies. In the current study, there were no significant differences in the durations of severe illness or days on high-level respiratory support in the high-dose and low-dose methylprednisolone treatment groups. In contrast, the duration of hospital stay was longer in the high-dose group. Further research is required to investigate whether high-dose methylprednisolone administration causes immunosuppression, resulting in delayed virus clearance. Currently, the treatment of severe COVID-19 with glucocorticoids remains controversial. Large-scale randomized controlled clinical studies are needed to further clarify the clinical effects of glucocorticoids in treating COVID-19, the duration of its administration, and the individualized dose for each patient.

To date, evidence suggests that the overall mortality rate of infection with SARS CoV-2—at least in those who develop clinical disease—is higher than that of infection with SARS-CoV and lower than that of infection with MERS-CoV. With appropriate care, the vast majority of COVID-19 patients recover. COVID-19 can become severe relatively rapidly in older patients; additionally, such rapid progression is associated with a poor prognosis. Accordingly, older patients should be monitored closely in clinical practice. The small number of cases is a limitation of the present study.

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Conflict of interest None to declare.

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