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RESEARCH ARTICLE

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Analysis of clinical features and outcomes of 161 patients with severe and critical COVID-19: A multicenter descriptive study

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Abstract

Background: This study aimed to investigate clinical characteristics, laboratory indexes, treatment regimens, and short-term outcomes of severe and critical coronavirus disease 2019 (COVID-19) patients.

Methods: One hundred and sixty one consecutive severe and critical COVID-19 patients admitted in intensive care unit (ICU) were retrospectively reviewed in this multicenter study. Demographic features, medical histories, clinical symptoms, lung computerized tomography (CT) findings, and laboratory indexes on admission were collected. Post-admission complications, treatment regimens, and clinical outcomes were also documented.

Results: The mean age was 59.38 ± 16.54 years, with 104 (64.60%) males and 57 (35.40%) females. Hypertension (44 [27.33%]) and diabetes were the most common medical histories. Fever (127 [78.88%]) and dry cough (111 [68.94%]) were the most common symptoms. Blood routine indexes, hepatic and renal function indexes, and inflammation indexes were commonly abnormal. Acute respiratory distress syndrome (ARDS) was the most common post-admission complication (69 [42.86%]), followed by electrolyte disorders (48 [29.81%]), multiple organ dysfunction (MODS) (37 [22.98%]), and hypoproteinemia (36 [22.36%]). The most commonly used antiviral drug was lopinavir/ritonavir tablet. 50 (31.06%) patients died, while 78 (48.45%) patients healed and discharged, and the last 33 (20.50%) patients remained in hospital. Besides, the mean hospital stay of deaths was 21.66 ± 11.18 days, while the mean hospital stay of discharged patients was 18.42 ± 12.77 days. Furthermore, ARDS ($P < .001$) and MODS ($P = .008$) correlated with increased mortality rate.

Conclusion: Severe and critical COVID-19 presents with high mortality rate, and occurrence of ARDS or MODS greatly increases its mortality risk.

KEYWORDS

clinical features, clinical outcomes, COVID-19, laboratory indexes, post-admission complications

Shi and Chen contributed equally to this study.

1 | INTRODUCTION

Since December 2019, some hospitals in Wuhan City, Hubei Province have successively found multiple cases of unexplained pneumonia with a history of exposure to the South China Seafood Market, which have now been confirmed as an acute respiratory infection caused by a new type of coronavirus infection. The coronavirus isolated from the lower respiratory tract of patients with unexplained pneumonia in Wuhan this time is a new type of coronavirus belonging to the genus β and named as a new type of coronavirus disease (COVID-19). As to March 13 81 003 confirmed cases of COVID-19 in China, and a total of 3181 deaths nationwide, with a crude fatality rate of 3.93%. From the existing data, the mortality rate of COVID-19 is lower than the pneumonia which caused by SARS-CoV (9.6%)[1] and MERS-CoV (34%).[2]

After more than 2 months of treatment experiences, we have accumulated some data in the detection of COVID-19 and the treatment of critical illness. At present, there have been a few clinical reports on the characteristics and outcomes of COVID-19 patients, but the evidences are quite insufficient especially for several and critical cases. Based on these, we collected the clinical data of severe and critical COVID-19 patients in five designated hospitals and analyzed their clinical characteristics, laboratory indicators, treatment regimens, and short-term clinical outcomes, in order to provide help for the clinical treatment and prognosis judgment of severe and critical COVID-19 patients.

2 | MATERIALS AND METHODS

2.1 | Patients

In this retrospective multicenter study, we retrospectively reviewed 161 severe and critical COVID-19 patients who were admitted to intensive care unit (ICU) in our hospitals (including Hainan General Hospital, Huanggang Central Hospital, Shiyan Renmin Hospital, Wuxue people's Hospital, and Qichun people's Hospital) from January 1 to March 1, 2020, consecutively. The diagnosis criteria and classification of severe/critical disease refer to 7th version of the guidelines on the Diagnosis and Treatment of COVID-19 issued by the National Health Commission of China (available at: http://www.nhc.gov.cn/). The study was approved by the Ethics Committee of Principal Investigator (PI) Hospital, and all patients or their families provided written informed consents or oral informed consents with tape recording.

2.2 | Definition of severe and critical disease

Severe and critical disease was defined according to 7th version of the guidelines on the Diagnosis and Treatment of COVID-19 issued by the National Health Commission of China as follows: (a) Severe disease, met anyone of the following criteria: shortness of breath, respiratory rate (RR) ≥30 times/min; finger pulse oxygen saturation ≤93% in resting state; arterial partial oxygen pressure (PaO_2)/oxygen absorption concentration (FiO_2) ≤300 mm Hg (1 mm Hg = 0.133 kpa); pulmonary imaging showed that the lesions progressed more than 50% within 24-48 hours. (b) Critical disease, met anyone of the following conditions: respiratory failure and need mechanical ventilation; shock; and other organ failure requiring ICU monitoring and treatment.

2.3 | Data collection

Clinical data of severe and critical COVID-19 patients were retrieved from the Medical Records System, which included (a) demographic features, medical histories, clinical symptoms and lung computerized tomography (CT) findings on admission; (b) laboratory indexes on admission; (c) post-admission complications; (d) treatment regimens; and (e) clinical outcomes (i. remained in hospital, ii. dies, and iii. healed and discharged). Of note, healed and discharged requirements were set as follows: (a) the body temperature returned to normal for more than 3 days; (b) the respiratory symptoms improved significantly; (c) the pulmonary imaging showed that the acute exudative lesions improved significantly; and (d) the nucleic acid test of respiratory samples such as sputum and nasopharynx swab was negative twice in a row (the sampling time interval was at least 24 hours).

2.4 | Statistical analysis

The continuous variable of normal distribution was represented as mean ± standard deviation (SD), while the continuous variable of non-normal distribution was represented by median (interquartile range [IQR]). The categorical variable was displayed as count (percentage). The chi-square test was used to compare the mortality rate between or among groups. SPSS 25.0 statistical software (IBM) was used for the statistical analysis. $P < .05$ was considers as significant.

3 | RESULTS

3.1 | Clinical characteristics of severe and critical COVID-19 patients

The mean age of patients was 59.38 ± 16.54 years, with 104 (64.60%) males and 57 (35.40%) females. In terms of medical history, 44 (27.33%), 25 (15.53%), 11 (6.83%), 10 (6.21%), 10 (6.21%), 8 (4.97%), and 7 (4.35%) had history of hypertension, diabetes, chronic obstructive pulmonary disease, chronic kidney disease, cerebral infarction, coronary heart disease, and malignancies, respectively. Regarding clinical symptoms on admission, the most common symptoms were fever (127 [78.88%]) and dry cough (111 [68.94%]), followed by chest

tightness and shortness of breath (36 [22.36%]). In aspect of lung CT findings, 141 (87.58%), 10 (6.21%), and 10 (6.21%) exhibited multiple lobe lesion, left lobe lesion, and right lobe lesion, respectively. The detailed information about demographic features, medical histories, clinical symptoms, and lung CT findings of severe and critical COVID-19 patients on admission was presented in Table 1.

TABLE 1 Clinical features of patients with severe and critical COVID-19

Parameters	Patients (N = 161)
Age	
Overall age (years), Mean ± SD	59.38 ± 16.54
≤44 years, n (%)	29 (18.01%)
45-59 years, n (%)	49 (30.43%)
60-74 years, n (%)	50 (31.06%)
≥75 years, n (%)	33 (20.50%)
Gender, n (%)	
Male	104 (64.60%)
Female	57 (35.40%)
Medical history, n (%)	
Hypertension	44 (27.33%)
Diabetes	25 (15.53%)
Chronic obstructive pulmonary disease	11 (6.83%)
Chronic kidney disease	10 (6.21%)
Cerebral infarction	10 (6.21%)
Coronary heart disease	8 (4.97%)
Malignancies	7 (4.35%)
Others	18 (11.18%)
Symptoms, n (%)	
Fever	127 (78.88%)
37.5-37.9°C	21 (13.04%)
38-38.9°C	65 (40.37%)
39-40.9°C	41 (25.47%)
Dry cough	111 (68.94%)
Chest tightness and shortness of breath	36 (22.36%)
Expectorant	19 (11.80%)
Fatigue and muscle aches	17 (10.56%)
Nausea, anorexia, diarrhea	6 (3.73%)
Dizziness, headache	5 (3.11%)
Others	34 (21.12%)
Asymptomatic	17 (10.56%)
Lung CT findings, n (%)	
Multiple lobe lesion	141 (87.58%)
Left lobe lesion	10 (6.21%)
Right lobe lesion	10 (6.21%)

Abbreviations: COVID-19, coronavirus disease 2019; SD, standard deviation.

3.2 | Laboratory findings of severe and critical COVID-19 patients

As to blood routine indexes, 77 (47.83%), 107 (66.46%), 128 (80.12%), 99 (61.49%), and 46 (28.57%) patients presented abnormal white blood cell count, neutrophil percentage, lymphocyte percentage, hemoglobin, and platelet count, respectively. With respect to hepatic and renal function, 141 (87.58%), 42 (26.09%), 82 (50.93%), 60 (37.27%), and 75 (46.58%) showed abnormal albumin, alanine aminotransferase, aspartate aminotransferase, urea, and creatinine, respectively. In terms of coagulation and inflammation, 17 (10.56%), 22 (13.66%), 100 (62.11%), 123 (76.40%), and 51 (31.68%) disclosed activated partial thromboplastin time (APTT), prothrombin time (PT), D-dimer, C-reactive protein, and procalcitonin, respectively. The detailed information about laboratory findings of severe and critical COVID-19 patients on admission was presented in Table 2.

3.3 | Post-admission complications of severe and critical COVID-19 patients

Acute respiratory distress syndrome (ARDS) was the most common complication (69 [42.86%]), followed by electrolyte disorders (48 [29.81%]), multiple organ dysfunction (MODS) (37 [22.98%]), hypoproteinemia (36 [22.36%]), and sepsis (17 [10.56%]). The detailed information about post-admission complications of severe and critical COVID-19 patients was presented in Table 3.

3.4 | Treatment regimens of severe and critical COVID-19 patients

With regard to antiviral drugs, 151 (93.79%), 130 (80.75%), 122 (75.78%), 110 (68.32%), 49 (30.43%), 34 (21.12%), and 26 (16.15%) received lopinavir and ritonavir tablets, Chinese medicine, arbidol, interferon alpha, oseltamivir, ribavirin, and chloroquine phosphate, respectively. As for other treatments, 138 (85.71%), 109 (67.70%), and 83 (51.55%) received antibiotics, immunoglobulin, and glucocorticoid, respectively. The detailed information about treatment regimens of severe and critical COVID-19 patients was presented in Table 4.

3.5 | Clinical outcomes of severe and critical COVID-19 patients

A total of 50 (31.06%) patients died, while 78 (48.45%) patients healed and discharged, and the last 33 (20.50%) patients remained in hospital (Table 5). Besides, the mean hospital stay of deaths was 21.66 ± 11.18 days, while the mean hospital stay of discharged patients was 18.42 ± 12.77 days.

TABLE 2 Laboratory indexes of severe and critical COVID-19 patients

Parameters	Patients (N = 161)
Blood routine	
White blood cell count (×10^9/L), Median (IQR)	7.45 (4.44-11.62)
Abnormal, n (%)	77 (47.83%)
Normal, n (%)	84 (52.17%)
Neutrophil percentage (%), Mean ± SD	78.99 ± 13.43%
Abnormal, n (%)	107 (66.46%)
Normal, n (%)	54 (33.54%)
Lymphocyte percentage (%), Mean ± SD	13.49 ± 9.74%
Abnormal, n (%)	128 (80.12%)
Normal, n (%)	32 (19.88%)
Hemoglobin (g/L), Mean ± SD	123.09 ± 22.28
Abnormal, n (%)	99 (61.49%)
Normal, n (%)	62 (38.51%)
Platelet count (×10^9/L), Mean ± SD	179.49 ± 81.56
Abnormal, n (%)	46 (28.57%)
Normal, n (%)	115 (71.43%)
Hepatic and renal function	
Albumin (g/L), Mean ± SD	34.19 ± 5.25
Abnormal, n (%)	141 (87.58%)
Normal, n (%)	20 (12.42%)
Alanine aminotransferase (u/L), Median (IQR)	26.2 (18.0-40.0)
Abnormal, n (%)	42 (26.09%)
Normal, n (%)	119 (73.91%)
Aspartate aminotransferase (u/L), Median (IQR)	35.6 (24.0-51.9)
Abnormal, n (%)	82 (50.93%)
Normal, n (%)	79 (49.07%)
Urea (mmol/L), Median (IQR)	6.85 (4.30-9.10)
Abnormal, n (%)	60 (37.27%)
Normal, n (%)	101 (62.73%)
Creatinine (μmol/L), Median (IQR)	77.85 (60.95-95.30)
Abnormal, n (%)	75 (46.58%)
Normal, n (%)	86 (53.42%)
Coagulation and inflammation	
APTT (s), Mean ± SD	32.94 ± 10.05
Abnormal, n (%)	17 (10.56%)
Normal, n (%)	144 (89.44%)
PT (s), Mean ± SD	13.72 ± 8.59
Abnormal, n (%)	22 (13.66%)
Normal, n (%)	139 (86.34%)
D-dimer (μg/mL), Median (IQR)	0.84 (0.32-2.55)
Abnormal, n (%)	100 (62.11%)
Normal, n (%)	61 (37.89%)
C-reactive protein (mg/L), Median (IQR)	36.50 (10.08-83.98)
Abnormal, n (%)	123 (76.40%)
Normal, n (%)	38 (23.60%)
Procalcitonin (ng/mL), Median (IQR)	0.19 (0.07-0.70)
Abnormal, n (%)	51 (31.68%)
Normal, n (%)	110 (68.32%)

Abbreviations: APTT, activated partial thromboplastin time; COVID-19, coronavirus disease 2019; IQR, interquartile range; PT, prothrombin time; SD, standard deviation.

TABLE 3 Post-admission complications of severe and critical COVID-19 patients

Parameters	Patients (N = 161)
ARDS, n (%)	69 (42.86%)
Electrolyte disorders, n (%)	48 (29.81%)
MODS, n (%)	37 (22.98%)
Hypoproteinemia, n (%)	36 (22.36%)
Sepsis, n (%)	17 (10.56%)
Heart failure only, n (%)	9 (5.59%)
Respiratory failure only, n (%)	6 (3.73%)
Malignant arrhythmia, n (%)	3 (1.86%)
Gastrointestinal bleeding, n (%)	3 (1.86%)
Myocardial infarction, n (%)	2 (1.24%)
Pneumothorax, n (%)	1 (0.62%)
Impaired kidney function only, n (%)	1 (0.62%)

Abbreviations: ARDS, acute respiratory distress syndrome; COVID-19, coronavirus disease 2019; MODS, multiple organ dysfunction.

3.6 | Subgroup analysis of mortality based on age and common complications

The mortality rate was 24.13%, 34.69%, 36.00%, and 24.24% in patients aged ≤44 years, patients aged 45-59 years, patients aged 60-74 years, and patients aged ≥75 years, respectively; further comparison analysis revealed that no difference was found among these four group patients ($P = .525$) (Figure 1). Notably, ARDS ($P < .001$) and MODS ($P = .008$) correlated with increased mortality rate, while electrolyte disorders ($P = .249$) and hypoproteinemia ($P = .248$) did not associated with mortality risk (Figure 2).

4 | DISCUSSION

In this study, we overviewed the clinical features, post-admission complications, treatments, and outcomes in 161 patients with severe

TABLE 4 Treatments of severe and critical COVID-19 patients

Parameters	Patients (N = 161)
Antiviral drugs, n (%)	
Lopinavir and Ritonavir Tablets	151 (93.79%)
Chinese medicine	130 (80.75%)
Arbidol	122 (75.78%)
Interferon alpha	110 (68.32%)
Oseltamivir	49 (30.43%)
Ribavirin	34 (21.12%)
Chloroquine Phosphate	26 (16.15%)
Other treatments, n (%)	
Antibiotic	138 (85.71%)
Immunoglobulin	109 (67.70%)
Glucocorticoid	83 (51.55%)
Invasive ventilator	70 (43.48%)
Non-invasive ventilator	51 (31.86%)
High flow oxygen	30 (18.63%)
Continuous renal replacement therapy	24 (14.91%)
Low flow oxygen	10 (6.21%)
Plasma exchange	7 (4.35%)
Extracorporeal membrane oxygenation	6 (3.73%)
Antifungal	3 (1.86%)

Abbreviation: COVID-19, coronavirus disease 2019.

TABLE 5 Clinical outcomes of patients with severe and critical COVID-19

Parameters	Patients (N = 161)
Remained in hospital, n (%)	33 (20.50%)
Died, n (%)	50 (31.06%)
Healed and discharged, n (%)	78 (48.45%)
Hospital stay of deaths (day), Mean ± SD	21.66 ± 11.18
Hospital stay of discharged patients (day), Mean ± SD	18.42 ± 12.77

Abbreviations: COVID-19, coronavirus disease 2019; SD, standard deviation.

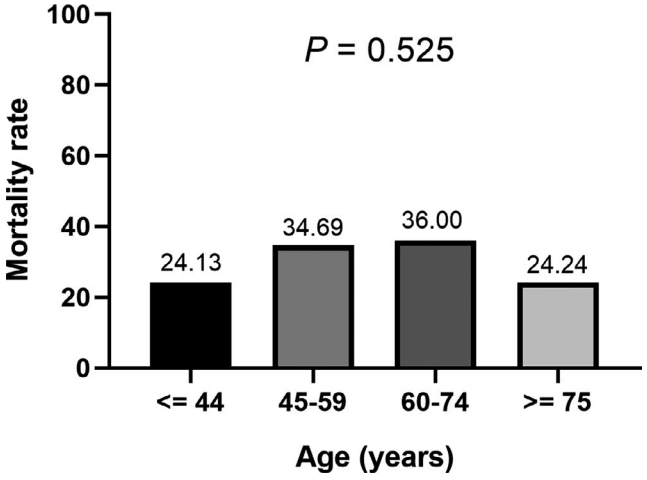

FIGURE 1 Mortality rate among different age-subgroups

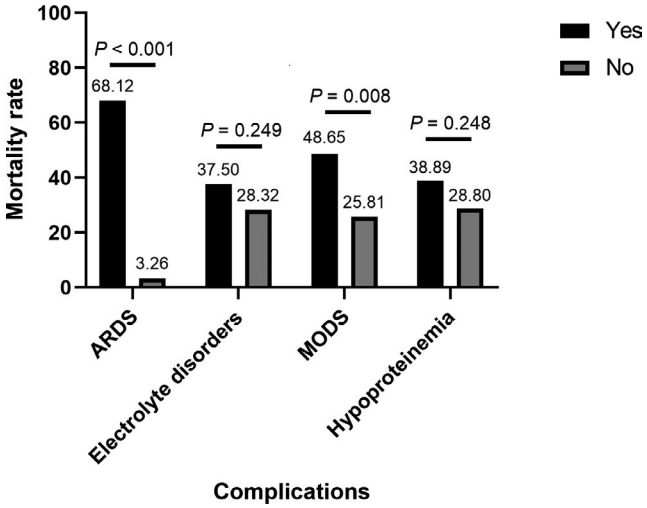

FIGURE 2 Correlation of common complications post-admission with mortality rate. ARDS, acute respiratory distress syndrome; MODS, multiple organ dysfunction

and critical COVID-19, which observed several key findings: (a) Fever and dry cough were the most common symptoms of severe and critical COVID-19 patients; (b) blood routine indexes, hepatic and renal function indexes, and inflammation indexes were commonly abnormal in severe and critical COVID-19 patients; (c) ARDS was the most common complication, followed by electrolyte disorders, MODS and hypoproteinemia in severe and critical COVID-19 patients; and (d) the mortality rate was as high as 31.06% in severe and critical COVID-19 patients.

According to 2012-2018 the MERS Global Death Factors Survey, MERS patients aged ≥60 years exhibited the highest incidence of severe and critical illness as well as the highest mortality rate.[3] Meanwhile, an earlier study focusing Chinese COVID-19 patients observes their median age is around 41 years.[4] Our study disclosed that the mean age of severe and critical COVID-19 patients was 59.38 years, indicating the severe and critical disease is more popular in aged population, which might result from that the elders had poor immunity and increased basic diseases. In terms of gender, we found that the proportion of men was about twice as that of women in severe and critical COVID-19 patients, which might be due to the men were more commonly outside and in public place instead of women in severe and critical COVID-19 patients, and the complications such as lung diseases were also more common in men. So as to medical history, we observed that hypertension and diabetes were most common in severe and critical COVID-19 patients, which was in line with the conditions of MERS.[5]

With regard to the clinical symptoms of severe and critical COVID-19 patients on admission, we observed that fever and dry

cough were the most common symptoms, which were in accordance with findings in previous studies of COVID-19,[6] and were similar to patients with MERS-CoV and SARS coronavirus infection.[7,8] In terms of laboratory indexes, we discovered that blood routine indexes, hepatic and renal function indexes, and inflammation indexes were commonly abnormal in severe and critical COVID-19 patients, these might be account of that (a) COVID-19 mainly acted on lymphocytes, especially T lymphocytes, which was similar to SARS-CoV[9] and MERS-CoV,[10] therefore affected the blood routine indexes; (b) COVID-19 viral particles spread through the respiratory mucosa, induced a cytokine storm in the body, generated a series of immune responses, and caused changes in peripheral leukocytes and immune cells (such as lymphocytes),[11] therefore elevated the inflammation level, which was also similar to conditions in MERS-CoV[12] and SARS-CoV[13]; and (c) severe and critical COVID-19 were accompanied with MODS including hepatic and renal dysfunction.

So as to post-admission complications in severe and critical COVID-19 patients, we observed that ARDS was the most common complication, followed by electrolyte disorders, MODS, and hypoproteinemia. Meanwhile, ARDS and MODS were closely correlated with worse prognosis in severe and critical COVID-19 patients, and therefore, it was essential to timely monitor and prevent ARDS and MODS potency. However, electrolyte disorders and hypoproteinemia were not associated with prognosis, but the latter was previously reported to be independent risk factor for severe MERS-CoV infection[14] and serum albumin could reflect nutritional status therefore related to severe and critical COVID-19. In aspect of treatment regimen, all the treatment procedures were set according to the guidelines and accumulating clinical experience, based on antiviral drugs and other supported treatments. And among the antiviral drugs, the most commonly used was lopinavir and ritonavir tablets.

The clinical outcome of COVID-19 patients is an essential issue to be explored. According to a previous meta-analysis, the mortality rate of COVID-19 patients ranges from 2.0% to 4.4%.[15] Meanwhile, the severe COVID-19 patients present with a higher mortality rate of 8.1%, but at the time of this study disclosed, 89.0% patients were still in hospitalization, and therefore, the mortality rate might be greatly underestimated.[16] As to outcome of critical-ill COVID-19 patients, seldom report is disclosed. In this study, we found that the mortality rate was as high as 31.06% in severe and critical COVID-19 patients, which was higher than previous studies. These might be to be: (a) the longer follow-up duration of our study and (b) critical-ill patients were also included in our study. Furthermore, the previous study reveals that the mortality rate of severe MERS is around 43.75%,[5] which is higher compared to severe and critical COVID-19 patients in our study. As to healed and discharged rate, 48.45% severe and critical COVID-19 patients realized it, which was acceptable. Notably, we observed that a small proportion of patients who were discharged in accordance with the current discharge standard were tested positive for the new type of coronavirus nucleic acid again within 14 days of isolation and returned to hospital for treatment. Therefore, we suggested at least three consecutive negative tests were a necessity for discharge.

Some limitations existed in this study: Firstly, since this was a retrospective study, potential bias and residual confounding might exist; secondly, all the patients were retrieved from ICU database, and therefore, these patients might not represent all general severe and critical COVID-19 patients; thirdly, there were still a proportion of patients in hospitalization, and therefore, the mortality rate and discharged rate might be influenced.

In summary, severe and critical COVID-19 presents with high mortality rate, and occurrence of ARDS or MODS greatly increases its mortality risk. Therefore, it is essential for early intervention to prevent mild/moderate COVID-19 from progressing to severe and critical COVID-19, and early prevention of ARDS and MODS is also important, as so to improve the prognosis of COVID-19.

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