

Clinical characteristics and outcomes of 2019-nCoV-infected patients admitted at different time periods

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Abstract. – **OBJECTIVE:** The outbreak of the 2019 Novel Coronavirus Disease (COVID-19) is seriously threatening the health of people all over China and the world. This study aims to investigate the clinical characteristics and outcomes of COVID-19 patients admitted at different time periods.

PATIENTS AND METHODS: A total of 132 discharged cases and 10 deaths of laboratory or clinically confirmed cases were retrospectively collected from The First People's Hospital of Jingzhou, Hubei. All cases were divided into two groups according to different admission times (group 1 from 2020-1-23 to 2020-2-3 and group 2 from 2020-2-4 to 2020-2-15). Individual data, clinical data, laboratory indices and prognosis were collected for the two groups, and statistical analysis was performed using the t-test or chi-square test to assess differences between the groups.

RESULTS: Among the 142 cases, there were 67 in the first group and 75 in the second group. According to the individual data and clinical manifestations of the two groups, the hospital stay in the first group was significantly longer than that of the second group (26 [9-39] compared with 20 [6-30], $p=0.000$). There were more clinical symptoms upon admission in group 1 than in group 2; although 66.2% of all patients had fever, the proportion of patients with fever on admission in the first group was significantly higher than that in the second group (79.1% compared with 54.7%, $p=0.002$). The proportion of patients with chills in the first group was higher than that in the second group (16.4% compared with 5.3%, $p=0.032$), and the proportion of patients with dyspnea was also higher than that in the second group (17.9% compared with 4%, $p=0.007$). Four of the 67 patients in the first group had symptoms of ocular discomfort, but none in the second group had this symptom (6.0% compared with 0, $p=0.032$). Based on laboratory examination, the inflamma-

tory index of patients in the first group was higher than that in the second group, and the proportion of patients with a C-reactive protein (CRP) increase was also significantly higher (60% compared with 38.7%, $p=0.020$). The main difference in routine blood tests involved white blood cell and lymphocyte counts and the lymphocyte percentage. The proportion of patients with reduced white blood cell counts in the first group was higher than that in the second group (23.9% compared with 10.7% $p=0.036$). Moreover, more patients in the first group had a reduced lymphocyte count and percentage (71.6% compared with 30.7% $p=0.000$; 49.3% compared with 29.7% $p=0.015$, respectively), and the former was significantly lower than that in the second group (0.94 [0.24-2.42] compared with 1.365 [0.22-3.62], $p=0.000$). Regarding prognosis, the proportion of severe cases and mortality in the first group were slightly higher than in the second group ($p>0.05$).

CONCLUSIONS: The clinical manifestations, blood changes and outcomes differed in patients admitted at different time periods. In the second group of patients, clinical symptoms were less common than in the first group, routine blood changes and inflammatory indices were milder, and the clinical prognosis was better.

Key Words:

Clinical characteristics, 2019-nCoV, Infected

Abbreviations

2019-nCoV: 2019 novel coronavirus; 2019-SARS-CoV-2: severe acute respiratory syndrome coronavirus 2; COVID-19: 2019 novel coronavirus disease; CRP: C-reactive protein; RT-PCR: Reverse Transcription-Polymerase Chain Reaction; RR: respiratory rate; PaO₂: partial pressure of oxygen; FiO₂: fraction of inspired oxygen; ICU: intensive care unit; COPD: chronic obstructive pulmo-

nary disease; T: temperature; ALT: alanine aminotransferase; AST: aspartate aminotransferase; LDH: lactate dehydrogenase; CK: creatine kinase; CK-MB: creatine kinase-MB; HCoV: Human Coronavirus; SARS-CoV: Severe Acute Respiratory Syndrome Coronavirus; MERS-CoV: Middle East Respiratory Syndrome Coronavirus; ACE2: angiotensin-converting enzyme 2.

Introduction

The 2019 Novel Coronavirus disease (COVID-19) has spread across China and the world. As of March 9, 2020, there were 80,754 confirmed cases of COVID-19 in China and more than 30,000 cases overseas¹. At present, some achievements have been made in the prevention and control of COVID-19 in China, and the number of new cases and new deaths has been greatly reduced². Nonetheless, the continuous emergence of imported cases will bring new challenges³. The passage and adaptation of viruses to different hosts has been associated with various changes. For example, population genetic analyses of SARS-CoV-2 genomes indicates 149 recent point mutations in the 2019 Novel Coronavirus (2019-nCoV) and the evolution of two major types (designated L and S)⁴. However, whether such mutation affects the pathogenicity and transmissibility of the virus is unknown. Since the emergence of 3rd- and even 4th-generation transmission and signs of asymptomatic carrier transmission of COVID-19^{5,6}, prevention and control has entered a new phase. Based on comparative analysis of clinical characteristics, laboratory examinations and outcomes of hospitalized patients in different periods, this study aims to uncover the different characteristics of the virus over time and to provide some new ideas for the diagnosis, treatment, prevention and control measures for COVID-19.

Patients and Methods

Data Sources

The patients included in the study had been diagnosed with COVID-19-associated pneumonia between January 23, 2020, and February 15, 2020, by real-time Reverse Transcription-Polymerase Chain Reaction (RT-PCR) or clinical confirmation and were hospitalized at The First People's Hospital of Jingzhou, Hubei. This study was a retrospective study, and all patients were discharged or expired. All patients met the diagnostic criteria in "Diagnosis and Treatment Protocol for Novel

Coronavirus Infection-Induced Pneumonia version 5 (trial)". In the fifth edition of the diagnosis and treatment protocol, clinical diagnosis was included in the Hubei Province diagnostic criteria, whereby suspected cases with pneumonia imaging characteristics were clinically diagnosed. The 142 cases included in this study were divided into two groups according to different admission times. As the First People's Hospital of Jingzhou only established the isolation ward on January 23, 2020, the time of the first group was from January 23 to February 3 of 2020, and the second group was from February 4 to February 15 of 2020. Of the cases included in this study, 22 were clinically diagnosed, with 9 in the first group and 13 in the second group. All clinically diagnosed cases were determined by the new coronavirus expert group in strict accordance with the fifth edition of the treatment protocol. Each group of patients was divided into common, severe and critical types, as follows: (1) common - fever, respiratory tract infection symptoms, etc., with imaging indicating pneumonia; (2) severe (any of the following conditions)-I, respiratory distress, respiratory rate (RR) ≥ 30 breaths/min; II, oxygen saturation $\leq 93\%$ at rest; III, partial pressure of oxygen (PaO₂)/fraction of inspired oxygen (FiO₂) ≤ 300 mmHg (1 mmHg = 0.133 kPa); (3) critical (any of the following conditions) - I, respiratory failure and a requirement for mechanical ventilation; II, shock; III, concomitant failure of other organs and requirement for intensive care unit (ICU) monitoring and treatment.

Data Collection

The personal data, clinical data and laboratory results of the patients included in the study were collected from electronic medical records. Personal data included sex, age, epidemiological history, hospital stay, time from symptom onset to hospital admission and comorbidities [hypertension, cerebrovascular disease, chronic obstructive pulmonary disease (COPD), cancer, diabetes, chronic liver or kidney disease]. Laboratory data included routine blood tests, liver function, myocardial function and CRP. Disease prognoses were also collected.

Statistical Analysis

Continuous variables are expressed as medians and categorical variables as counts and percentages. All analyses were performed with SPSS software, version 23.0 (IBM Corp., Armonk, NY, USA).

Results

Epidemiological Characteristics and Clinical Features

Of the 142 patients, 72 were male and 70 female, with a median age of 48 years. All patients were divided into two groups according to admission time. In the first group, 67 patients were admitted from January 23 to February 3 of 2020; in the second group, 75 patients were admitted from February 4 to February 15 of 2020. There was no significant difference in age or sex between the two groups ($p > 0.05$). The hospital stay in the first group was significantly longer than that in the second group (26 [9-39] vs. 20 [6-30] $p=0.000$). There was also no significant difference in the time from symptom onset to hospital admission between the two groups ($p > 0.05$) or differences in comorbidities (hypertension, diabetes, chronic obstructive pulmonary

disease (COPD), cancer, cerebrovascular disease and chronic liver or kidney disease) ($p > 0.05$). In terms of clinical manifestations, fever was the most common symptom, and the proportion of all patients with fever was 66.2%, mostly 37.3-38.0 degrees Celsius. The proportion of patients with fever in the first group was significantly higher than that in the second group (79.1% compared with 54.7%, $p=0.002$). The proportion of chills, dyspnea and ocular symptoms in the first group was also significantly higher than that in the second group (16.4% vs. 5.3% $p=0.032$, 17.9% vs. 4% $p=0.007$, and 6.0% vs. 0% $p=0.032$, respectively). Although the first group exhibited slightly more sputum production, chest distress, digestive and fatigue or muscle pain than the second group, there was no significant difference ($p > 0.05$); despite more asymptomatic cases in the second group, the difference was not significant ($p > 0.05$) (Table I).

Table I. Epidemiological data and clinical features of COVID-19 patients upon hospital admission.

	All patients (n = 142)	Group 1 (n = 67)	Group 2 (n = 75)	p
Sex				0.495
Male	72 (50.7%)	36 (53.7%)	36 (48%)	
Female	70 (49.3%)	31 (46.3%)	39 (52%)	
Age	48 (14-83)	49 (22-83)	48 (14-78)	0.918
Time from symptom onset to hospital admission	5 (1-25)	6 (1-20)	5 (1-25)	0.398
Hospital stay	24 (6-39)	26 (9-39)	20 (6-30)	0.000
Comorbidities				
Hypertension	31 (21.8%)	12 (17.9%)	19 (25.3%)	0.283
Cerebrovascular disease	4 (2.8%)	0	4 (5.3%)	0.055
Diabetes	7 (4.9%)	4 (6.0%)	3 (4%)	0.602
COPD	4 (2.8%)	1 (1.5%)	3 (4%)	0.367
Malignant tumor	6 (4.2%)	2 (3%)	4 (5.3%)	0.487
Chronic liver or kidney disease	8 (5.6%)	3 (4.5%)	5 (6.7%)	0.572
Clinical manifestations				
Fever	94 (66.2%)	53 (79.1%)	41 (54.7%)	0.002
T < 37.3	46 (32.4%)	14 (20.9%)	32 (42.7%)	0.006
37.3-38.0	55 (38.7%)	30 (44.8%)	25 (33.3%)	0.162
38.1-39.0	39 (27.5%)	23 (34.3%)	16 (21.3%)	0.083
> 39	2 (1.4%)	0	2 (2.7%)	0.178
Chills	15 (10.6%)	11 (16.4%)	4 (5.3%)	0.032
Cough	81 (57.0%)	40 (59.7%)	41 (54.7%)	0.545
Sputum production	26 (18.3%)	15 (22.4%)	11 (14.7%)	0.235
Chest distress	17 (12.0%)	11 (16.4%)	6 (8%)	0.123
Dyspnea	15 (10.6%)	12 (17.9%)	3 (4%)	0.007
Fatigue or muscle pain	67 (47.2%)	37 (55.2%)	30 (40%)	0.070
Digestive symptoms	31 (21.8%)	17 (25.4%)	14 (18.7%)	0.334
Ocular symptoms	4 (2.8%)	4 (6.0%)	0	0.032
Asymptomatic	7 (4.9%)	1 (1.5%)	6 (8%)	0.074

Categorical variables were analyzed using the chi-square test, and the results are presented as numbers (percentages). Continuous variables with normal distributions were analyzed using independent samples *t*-tests, and the results are expressed as medians.

Laboratory Indices

A retrospective analysis was conducted on 142 patients with laboratory indicators, such as routine blood tests, C-reactive protein levels, liver function and heart function. The main abnormalities in routine blood tests were regarding white blood cell and lymphocyte counts and lymphocyte percentages. The proportion of patients with reduced white blood cell counts among all patients was 16.9%, which was significantly higher in the first group than in the second group (23.9% vs. 10.7%, $p=0.036$). There was no significant difference in white blood cell counts between the two groups ($p>0.05$). Among the 142 patients, 50% showed decreased lymphocyte counts, and the proportion of patients with decreased lymphocyte counts in the first group was significantly higher than that in the second group (71.6% compared with 30.7%, $p=0.000$). In addition, the lymphocyte count in the first group was significantly lower than that in the second group (0.94 [0.24-2.42] compared with 1.365 [0.22-3.62] $p=0.000$). Lymphocytic percentage reduction occurred in 55 of the 142 patients, accounting for 38.7% of the total. The proportion of patients with a reduced lymphocyte percentage in the first group was significantly higher than that in the second group (49.3% compared with 29.7%, $p=0.015$). The normal lymphocyte percentage in blood is 20%-50%, and we divided the lymphocyte percentage reduction into three levels according to the severity (mild: lymphocyte percentage from 15.1%-19.9%, moderate: lymphocyte percentage from 10.1%-15%, severe: lymphocyte percentage $\leq 10\%$). The proportion of each level between the two groups is depicted in Figure 1.

In some of the 142 patients, neutrophil, platelet, red blood cell and hemoglobin levels were

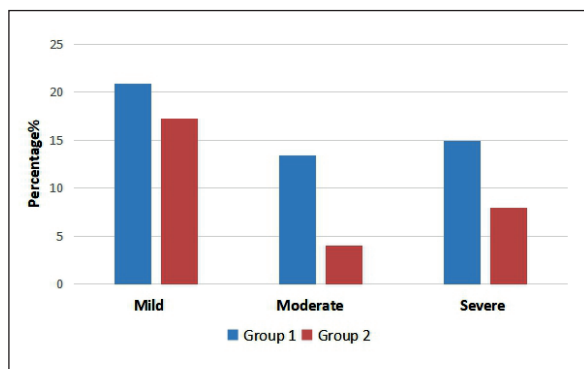


Figure 1. Severity comparison of lymphocyte percentage reduction the two groups.

decreased, but with no significant difference between the two groups. The level of C-reactive protein was increased in 47.9% of all patients, and the proportion of patients with a C-reactive protein count increase in the first group was significantly higher than that in the second group (60% compared with 38.7%, $p=0.020$). Some patients presented abnormal liver function and myocardial enzyme levels on admission, but there was no significant difference between the two groups ($p>0.05$) (Table II).

Disease Prognosis

Of the 142 patients, 84.6% were diagnosed with the common type and had a good prognosis. There were 22 cases of the severe or critical type, accounting for 15.5% of the total; 10 patients expired, with an overall mortality rate of 7.0%. In the first group, 13 patients (19.4%) were in the severe or critical type, among whom 6 died, with a mortality rate of 9%. For the second group, 9 patients had the severe or critical type, accounting for 12%. Among them, 4 patients died, with a mortality rate of 5.33% (Figure 2).

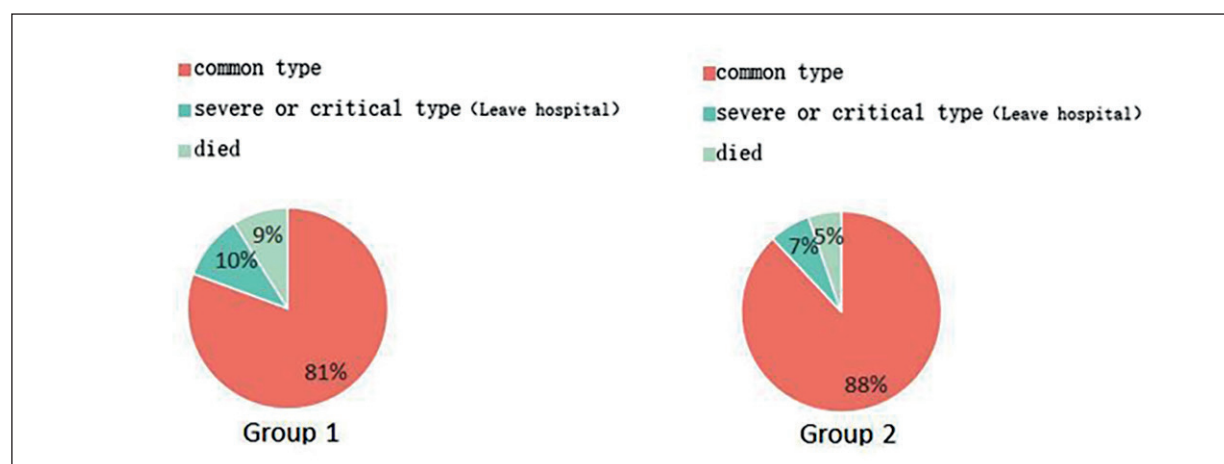
The proportions of severe or critical type and mortality in the first group were slightly higher than those in the second group, but with no significant difference (Table III).

Discussion

Coronaviruses are a group of enveloped viruses with non-segmented, single-stranded, and positive-sense RNA genomes. According to the International Committee on Taxonomy of Viruses, Coronaviruses are classified under the order *Nidovirales*, family *Coronaviridae*, subfamily *Coronavirinae*. Based on early serological and genomic evidence, *Coronavirinae* is divided into four genera: *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus*, and *Deltacoronavirus*⁷. The emergence of two zoonotic, highly pathogenic HCoV has occurred over the last 15 years: severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV)⁸. The recent emergence of a novel coronavirus (2019-nCoV), which is causing an outbreak of unusual viral pneumonia in patients worldwide, is another warning of the risk that CoVs pose to public health. 2019-nCoV is a novel member of *Betacoronavirus* that was isolated from the lower respiratory tract of patients with COVID-19.

Table II. Laboratory findings for COVID-19 patients upon hospital admission.

	All patients (n = 142)	Group 1 (n = 67)	Group 2 (n = 75)	p
Blood routine				
White blood cell count	24 (16.9%)	16 (23.9%)	8 (10.7%)	0.036
White blood cell count, $\times 10^9/L$	5.25 (1.9-19)	4.8 (1.9-14.51)	5.45 (2.6-19)	0.057
Lymphocyte count	71 (50%)	48 (71.6%)	23 (30.7%)	0.000
Lymphocyte count, $\times 10^9/L$	1.08 (0.22-3.62)	0.94 (0.24-2.42)	1.365 (0.22-3.62)	0.000
Lymphocyte percentage	55 (38.7%)	33 (49.3%)	22 (29.7%)	0.015
Neutrophil count	16 (11.3%)	10 (14.9%)	6 (8%)	0.193
Red blood cell count	54 (38.0%)	30 (44.8%)	24 (32%)	0.117
Platelet count	29 (20.4%)	13 (19.4%)	16 (21.3%)	0.776
Hemoglobin	43 (30.3%)	23 (34.3%)	20 (26.7%)	0.321
C-reactive protein	68 (47.9%)	39 (60%)	29 (38.7%)	0.020
C-reactive protein count, mg/L	10.73 (0.05-236.12)	12.76 (0.34-231.75)	5.28 (0.05-236.12)	0.895
Liver function				
ALT	23 (16.2%)	11 (16.9%)	12 (16%)	0.946
ALT count, U/L	16 (3-168)	18 (3-168)	14 (3-106)	0.513
AST	17 (12.0%)	7 (10.8%)	10 (13.3%)	0.597
AST count, U/L	23 (12-112)	23 (12-99)	24 (12-112)	0.737
LDH	34 (23.9%)	17 (26.2%)	17 (22.7%)	0.706
LDH count, U/L	201 (108-784)	204 (108-784)	194.5 (117-560)	0.491
Myocardial enzyme				
CK	17 (12.0%)	8 (12.3%)	9 (12%)	0.991
CK count, U/L	70 (13.92-402)	74.5 (23-382)	68 (13.92-402)	0.891
CK-MB	21 (14.8%)	12 (18.5%)	9 (12%)	0.285
CK-MB count, U/L	11 (6-59)	13 (6-31)	10 (5-59)	0.102

**Figure 2.** Comparative analysis of disease prognosis in the two groups.**Table III.** Disease prognosis of COVID-19 patients.

	All patients (n = 142)	Group 1 (n = 67)	Group 2 (n = 75)	p
Common type	120 (84.6%)	54 (80.6%)	66 (88%)	0.224 (1.481)
Severe or critical type	22 (15.5%)	13 (19.4%)	9 (12%)	
Mortality	10 (7.0%)	6 (8.96%)	4 (5.33%)	0.400 (0.709)

Comparative analysis of genome sequences has revealed that 2019-nCoV is closely related (with 88% identity) to two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses, bat-SL-CoVZC45 and bat-SL-CoVZXC21, collected in 2018 in Zhoushan, eastern China, but is more distant from SARS-CoV (approximately 79%) and MERS-CoV (approximately 50%)⁹. These data suggest that 2019-nCoV is derived from wild bats, with another animal acting as an intermediate host between bats and humans¹⁰. Similar to SARS, 2019-nCoV is able to enter cells via binding of the S protein on the virus surface to angiotensin-converting enzyme 2 (ACE2) on the host cell surface¹¹. Studies^{12,13} have shown that the affinity between the new coronavirus S protein and cellular ACE2 is 10 to 20 times that of SARS; the basic infection number R_0 is as high as 3.77. Therefore, compared to SARS, the transmission capacity of 2019-nCoV is stronger and the incidence is higher. At present, the number of infected cases worldwide has exceeded 100,000, whereas the total number of SARS cases is just more than 8,000. Although COVID-19 is more transmissible, it is less virulent than SARS and has a much lower mortality rate¹⁴. Regardless, COVID-19 is more variable than SARS, and some patients have become positive again for viral RNA after being discharged from the hospital. It is still unknown whether the virus will disappear as SARS did or whether it will evolve to a flu-like virus and persist as the number of passages in humans increases. Zavascki and Falci¹⁵ have shown that the symptoms of COVID-19 have changed and become more subtle. In this study, 142 patients who had been discharged from the hospital or expired were studied retrospectively to investigate the epidemiological history, clinical characteristics and prognosis of COVID-19. We expected to discover the disease evolution characteristics and provide new ideas for disease prevention and control. The patients were divided into two groups according to the time of admission. Among all the patients, males and females accounted for 50.7% and 49.3%, respectively, with a median age of 48 years. There was no significant difference in age or sex between the two groups.

The main clinical manifestations of most patients were fever, dry cough and fatigue, and a few patients displayed symptoms such as chills, sputum production and gastrointestinal symptoms. Additionally, a small number of patients,

especially those with the severe type, had dyspnea¹⁶. In this study, the main clinical manifestations of the two groups were consistent with the literature, but the clinical symptoms of the second group on admission were less common than were those of the first group. In particular, the proportion of patients with fever, chills and dyspnea was significantly less than in the first group. Furthermore, a small number of patients were admitted to the hospital without any symptoms and were only identified during clinical examination as close contacts of diagnosed patients. This phenomenon was more common in the second group, showing that the clinical symptoms of hospitalized patients are changing and are more subtle as the number of virus passages increases and with the constant adaptation of the virus to the host. Therefore, these changing factors should be considered in disease diagnosis, treatment and prevention to prevent misdiagnosis. At the same time, asymptomatic patients may also become a source of infection, and how to achieve early detection, early isolation and early treatment is crucial for controlling the epidemic. In addition, 4 patients in the first group had eye discomfort; despite no clear evidence that the virus can be transmitted through the conjunctiva, it is important to take effective prevention and control measures in ophthalmology during the novel coronavirus outbreak¹⁷. Comorbidities are important indices for evaluating the prognosis of patients, and older patients with comorbidities are more likely to develop the severe type¹⁸. In this study, there was no significant difference in the incidence of comorbidities between the two groups.

Laboratory examination is crucial for the diagnosis of COVID-19. In the early stage, the total number of peripheral blood white blood cells was normal or decreased, and the lymphocyte count or percentage was decreased. In some patients, liver enzymes and myocardial enzymes are elevated, and C-reactive protein and blood sedimentation are elevated in most patients¹⁹. According to autopsy and hospitalized patient biopsy results, the spleen becomes significantly shrunk, the number of lymphocytes in the spleen is significantly decreased, and the number of lymphocytes in lymph nodes is decreased, as is the number of myeloid cells²⁰. This indicates that infection by this virus destroys the body's immune organs and causes bone marrow hematopoietic inhibition. In this study, 16.9% of

the 142 patients had decreased white blood cell counts, and 50% and 38.7% had decreased lymphocyte counts and lymphocyte percentages, respectively. The proportion of patients in the first group with decreased white blood cells and lymphocytes was significantly higher than that in the second group, and the median lymphocyte count in the first group was significantly lower than that in the second group. Lymphocytes play a crucial role in maintaining the body's immune homeostasis and inflammatory response, and a decrease in lymphocytes can be used as an indicator of the severity and prognosis of COVID-19. Indeed, the protection, maintenance and promotion of lymphocyte levels may have a good effect on the prevention and treatment of COVID-19²¹. In our study, 47.9% of the patients showed increased C-reactive protein levels, and the proportion of patients in the first group was significantly higher than that in the second group. In general, attention should be paid to changes in routine blood tests in hospitalized patients admitted at different time periods, treatment plans should be adjusted in a timely manner, and patients should receive different personalized treatments. In this study, only a small number of patients showed abnormal liver function and myocardial enzyme levels when they were admitted to the hospital. This indicates that most of the patients did not have obvious abnormal organ function when they were admitted. Regardless, some patients will develop progressive hepatic and cardiac dysfunction with the development of the disease^{22,23}.

Compared with SARS, COVID-19 has a higher incidence but a lower mortality rate, which is less than 4% in China, though mortality is slightly higher in Hubei Province, at approximately 4.5%. The total mortality of the 142 patients in this study was 7.0%. Because the First People's Hospital in Jingzhou is a designated hospital for the treatment in severe and critical patients, the mortality rate of the patients in this study was higher than the total mortality rate of Hubei Province.

Conclusions

The mortality and severe type rates of the first group were slightly higher than those of the second group, but there was no significant difference. Factors affecting the prognosis of patients included age, comorbidities, the highest body

temperature on admission, C-reactive protein level, lymphocyte count and percentage²⁴. Close monitoring of a patient's indicators and timely treatment intervention will effectively reduce the rates of the severe type and mortality.

Conflict of Interest

The Authors declare that they have no conflict of interests.

Ethical Approval

The study was approved by the Institutional Ethics Committee of the First Hospital of Jingzhou, and written informed consent was obtained from all participants.

Authors' Contribution

Weirong Liu and Guojin Zuo carried out the studies, participated in collecting the data, and drafted the manuscript. Yi Qin performed the statistical analysis and participated in its design. Weirong Liu and Guojin Zuo participated in the acquisition, analysis, or interpretation of the data and drafted the manuscript. All authors read and approved the final manuscript.

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