Original Article

Analysis of blood samples from 42 patients with varying degrees of infection during the epidemic of COVID-19: a retrospective study

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Background: Blood samples from 42 patients with coronavirus disease 2019 (COVID-19) with varying degrees of infection were examined to further explore the relationship between clinical features, immune factors and COVID-19, as well as the diagnostic and predictive values of clinical features and immune factors in severe disease progression.

Methods: This study included 42 nucleic acid-positive COVID-19 patients admitted to the First Hospital of Jiaxing from January 26, 2020 to February 21, 2020, who were divided into mild-moderate group and severe group based on respiratory rate, resting oxygen saturation and alveolar oxygen partial pressure/O_2 inhalation. On February 21, 2020, clinical data including sex, age, body mass index (BMI), past medical history, clinical symptoms, hematology indexes [white blood cell (WBC); neutrophil (NEUT); lymphocyte (LYM); C-reactive protein (CRP)] were collected. The chi-square test was used to compare the clinical data differences between the two groups, so as to perform comparative analysis in the context of serious disease development.

Results: There were 8 cases of severe disease, and 34 cases of mild and moderate symptoms. Comparative analysis showed that patients with advanced age (≥60 years, OR =5.800, P=0.0286), history of hypertension (OR =5.800, P=0.0286) and pulmonary lobe lesions (≥4, OR =6.273, P=0.0270) were more likely to develop serious diseases. In addition, according to clinical symptoms, chest pain was more prominent in patients with severe disease. Laboratory tests showed that levels of WBC (severe 4.96±1.76 *vs.* mild-moderate 5.45±2.01, P=0.5300), NEUT (severe 3.56±1.44 *vs.* mild-moderate 3.94±1.87, P=0.5945) and LYM (severe 0.91±0.25 *vs.* mild-moderate 1.11±0.51, P=0.2903) were normal or decreased, but CRP level (severe 31.03±9.38 *vs.* mild-moderate 12.53±15.73, P=0.0029) was obviously increased, especially in patients with severe disease, with statistically significant difference between groups.

Conclusions: Patients with hypertension and advanced age are more likely to develop deteriorate with COVID-19, and the number of lung lobes with lesions and chest pain may indicate disease progression. Notably, CRP level is significantly elevated in severe disease and it may be closely related to COVID-19 progression.

Keywords: Coronavirus disease 2019 (COVID-19); clinical features; C-reactive protein (CRP)

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Introduction

Beginning in December 2019, a group of patients with pneumonia of unknown etiology emerged in Wuhan, Hubei Province in central China. Genome sequencing revealed that the coronavirus disease was caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and the disease was initially known as 2019 novel coronavirus (2019-nCoV) but is now called coronavirus disease 2019 (COVID-19) worldwide. Research has found that SARS-CoV-2 is a positive-sense single-stranded RNA virus belonging to the coronavirus β (βCoV) genus (1). Additionally, evolutionary analysis shows that SARS-CoV-2 is intimately relevant to two SARS-like coronaviruses carried in bats, which have been named bat-SL-CoVZC45 and bat-SL-CoVZXC21, with a shared nucleotide profile ranging from 88% to 89% (2), whereas for SARS-CoV and MERS-CoV (Middle East respiratory syndrome coronavirus) that were discovered in 2002 and 2012, respectively, SARS-CoV-2 shares a nucleotide profile of 79% and 50% (2). As a great deal of research has shown that COVID-19 is highly contagious and that patients who develop severe disease are more to die, so it is vital to study clinical features of COVID-19 in the hunt for more efficient therapeutic regimens, especially for those who are apt to develop severe disease.

Due to increasing numbers of cases and disease progression, emerging research has focused on the clinical characteristics of COVID-19. Fever, dry cough, respiratory difficulties, myalgia, fatigue, decreased white blood cell (WBC) count and abnormal pulmonary CT scans are the prominent clinical manifestations in patients suffering from COVID-19, and patients in the severe stage of disease are mostly elderly (3). Ji *et al*. analyzed 425 patients with COVID-19 and found that 56% were male with a median age of 59 years and a median incubation period of 5.2 days; patients aged ≥60 years comprised approximately half of their cohort (4). A study of the clinical characteristics of 138 COVID-19 patients in Wuhan, China, showed that the patients in the intensive care unit had advanced age and most of them had complications (5). Similarly, a recent epidemiological and clinical study of 671 COVID-19 patients in Henan Province, China, found that significantly decreased lymphocyte percentage, longer hospitalization, advanced age, and being complicated with cardiovascular disease (including hypertension) were associated with the severity of COVID-19 (6). Although studies have analyzed the relationship between clinical features and disease severity in patients with COVID-19, most of the factors can be applied to other severe diseases as well. Hence, the factors that are more closely related to COVID-19 need to be determined, and their potential predictive values for the diagnosis and prognosis of COVID-19 await to be analyzed.

Therefore, this study analyzed the clinical features of patients with severe COVID-19 to further explore the factors that influence progression to severe COVID-19, so as to provide a reference for targeted treatment of the disease. We present the following article in accordance with the STROBE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-22-658/rc).

Methods

General information

Clinical data of 42 COVID-19 cases admitted to the First Hospital of Jiaxing between January 26, 2020 and February 21, 2020 were analyzed. Based on severity of disease, cases were divided group A with severe disease (n=8; median age, 55.63±16.86 years), and group B with mild/moderate disease (n=34; median age, 46.74±12.45 years). Underlying diseases of the patients included type 2 diabetes, hypertension, hepatitis and neoplasia.

The protocol was approved by ethics committee of the First Hospital of Jiaxing/Affiliated Hospital of Jiaxing University (No. LS2020-010). Written informed consent from all participants was obtained prior to screening. This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Criteria for disease diagnosis and classification

According to the diagnostic criteria provided by the Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (7th edition) (issued by China's National Health Commission on March 4, 2020), suspect cases meeting one of the following two etiological evidence were confirmed as positive: (I) SARS-CoV-2 from respiratory or blood specimens detected positive by real-time quantitative polymerase chain reaction (PCR); (II) viral gene identified by genetic sequencing shared increased homology with known SARS-CoV-2. Patients with COVID-19 can be classified as mild, moderate, severe and critical cases based on their clinical symptoms. For this study, patients fulfilling one of the following criteria were identified as "severe": (I) shortness of breath; respiratory rate ≥30/min; (II) figure oxygen saturation under resting conditions ≤93%; (III)

alveolar oxygen partial pressure/fraction of inspired O_2 ≤300 mmHg. If in severe cases the patients developed respiratory failure, shock or other organ failure, they were identified as critical cases.

Therapeutic regimen

Treatments were administered to patients according to the following standardized specifications: (I) recombinant interferon α2b (2 mL sterilized water for injection and a dose of 5 million U or equivalent for adults) was provided twice daily via nebulization; (II) Kaletra (lopinavir/ritonavir, AbbVie, 200 mg/50 mg/tablet) was given as two tablets twice daily; (III) Arbidol (Suzhou Pharmaceutical Factory of Jiangsu Wuzhong Pharmaceutical Group Corporation, Suzhou, China, 0.1 g/tablet) was administered as two tablets three times a day, with prezcobix (darunavir and cobicistat tablets, Janssen Ortho, LLC, Xi'an, China, 800 mg/150 mg/tablet) given as one tablet daily; (IV) infusion of immunoglobulin [Zhejiang Haikang Biological Products Co., Ltd., Wenzhou, China, 0.2–0.4 g/(kg·day)] and intravenous transfusion of 40 mg of methylprednisolone (methylprednisolone sodium succinate, Pfizer Manufacturing Belgium NV, Brussels, Belgium) once daily.

When body temperature returned to homeostasis for ≥3 days and respiratory function improved, treatment for inflammation was instituted using symptom reduction measures, including cough suppressants, antidiarrheals, supplements of potassium and various other vitamins or minerals. For patients who responded positively to treatment according to lung imaging and negative nucleic acid on two successive tests (respiratory specimens collected with a minimum interval of 1 day), they were discharged, or transferred to other departments for treatment of other underlying diseases.

Data collection

Relevant epidemiological and clinical data were collected for retrospective analysis: sex, age, body mass index (BMI), past medical history, clinical symptoms, hematology indexes [WBC; neutrophils (NEUT); lymphocytes (LYM); C-reactive proteins (CRP)].

Statistical analysis

SPSS Statistics 22.0 (7) was used for the statistical analysis of all collected data. Mean and standard deviation were used to express measurement data, with *t*-test conducted for group comparisons. Enumeration data are presented as percentages (%), with chi-square test performed for category association comparisons. P value of two-sided test was used for all statistics, and P<0.05 was considered as statistically significant difference.

Results

Clinical features

The BMI of all patients ranged from 18.5 to 29.9, so they were subdivided into normal (18.5–24.9) kg/m^2 and obese (25–29.9) kg/m^2. No statistical association (P>0.05) was observed between disease severity and sex or BMI (*Table 1*), which eliminated these factors as main causes for development of severe disease. Patients who had hypertension were statistically more likely to develop severe COVID-19 (P=0.0286). Additionally, increasing age (P=0.0286) and the number of lung lobes with lesions (P=0.0270) were statistically associated in both groups A and B. These results indicated that the disease was more likely to progress to a severe stage when patients had a medical history of hypertension and advanced age. In addition, patients with more lung lobes affected with lesions should undergo intensive monitoring.

Clinical features

As shown in *Table 2*, fever, cough, hemoptysis, chest pain and fatigue were the main clinical manifestations, with no statistical association reported between the two severity groups (P>0.05). Chest pain did exhibit a statistical association, with 1 case in group A and 0 in group B (P<0.05). The clinical data of the patient with chest pain were further analyzed to exclude the influence of other diseases. We speculate that chest pain might indicate the development of severe disease, with certain significance.

Analysis of laboratory results

The laboratory examinations mainly included the detection of inflammatory indexes such as WBC, NEUT, LYM and CRP in the blood. There was no statistical significance of WBC, NEUT and LYM in the two severity groups, with lower levels (P>0.05). However, the CRP levels in the two groups was noticeably elevated, and the elevation in severe cases relative to mild or moderate cases had statistical

Table 1 Comparative analysis of clinical features

Trait	Group A (n=8), severe disease, n (%)	Group B (n=34), mild/moderate disease, n (%)	P value	OR	95% CI
Sex					
Male	6 (75.0)	18 (52.9)	0.2566	2.667	0.470–15.136
Female	2 (25.0)	16 (47.1)			
BMI (kg/m^2)					
<25	4 (50.0)	19 (55.9)	0.7636	0.789	0.169–3.691
≥25	4 (50.0)	15 (44.1)			
Underlying disease					
Diabetes	2 (25.0)	3 (8.8)	0.2037	3.444	0.470–25.231
Hypertension	4 (50.0)	5 (14.7)	0.0286*	5.800	1.081–31.112
Hepatitis	0	2 (5.9)	0.4821	NA	NA
Other	1 (12.5)	1 (2.9)	0.2533	4.714	0.262–84.767
Age, years					
<60	4 (50.0)	29 (85.3)	0.0286*	5.800	1.081–31.112
≥60	4 (50.0)	5 (14.7)			
No. of lesion infiltrated lung lobes					
<4	2 (25.0)	23 (67.6)	0.0270*	6.273	1.085–36.249
≥4	6 (75.0)	11 (32.4)			

*, P<0.05 indicates a significant difference. BMI, body mass index; OR, odds ratio; 95 % CI, 95% confidence interval; NA, not available.

Table 2 Comparative analysis of clinical characteristics

Symptom	Group A (n=8), severe disease, n (%)	Group B (n=34), mild/moderate disease, n (%)	P value	OR	95% CI
Fever	7 (87.5)	26 (76.5)	0.4939	2.154	0.229–20.234
Cough	6 (75.0)	21 (61.8)	0.4821	1.857	0.325–10.617
Hemoptysis	0	3 (8.8)	0.3833	NA	NA
Chest pain	1 (12.5)	0	0.0369*	NA	NA
Chest distress	1 (12.5)	4 (11.8)	0.9539	1.071	0.103–11.130
Fatigue	3 (37.5)	6 (17.6)	0.2182	2.800	0.521–15.041

*, P<0.05 indicates a significant difference. OR, odds ratio; 95 % CI, 95% confidence interval; NA, not available.

significance (P<0.0029). We also speculate that a noticeably increased CRP level suggests the patient is more likely to develop severe COVID-19 (*Figure 1*).

Discussion

Coronavirus is one of the main pathogens responsible for human respiratory infections (8). Two highly pathogenic viruses, SARS-CoV and MERS-CoV, are known to cause SARS, and another four coronaviruses, HCoV-OC43, HCoV-229E, HCoV-NL63 and HCoV-HKU1, cause mild upper respiratory disease (8). SARS became a pandemic in 2002 with 8,422 infections occurring across 29 countries around the world (9). MERS first appeared in Middle

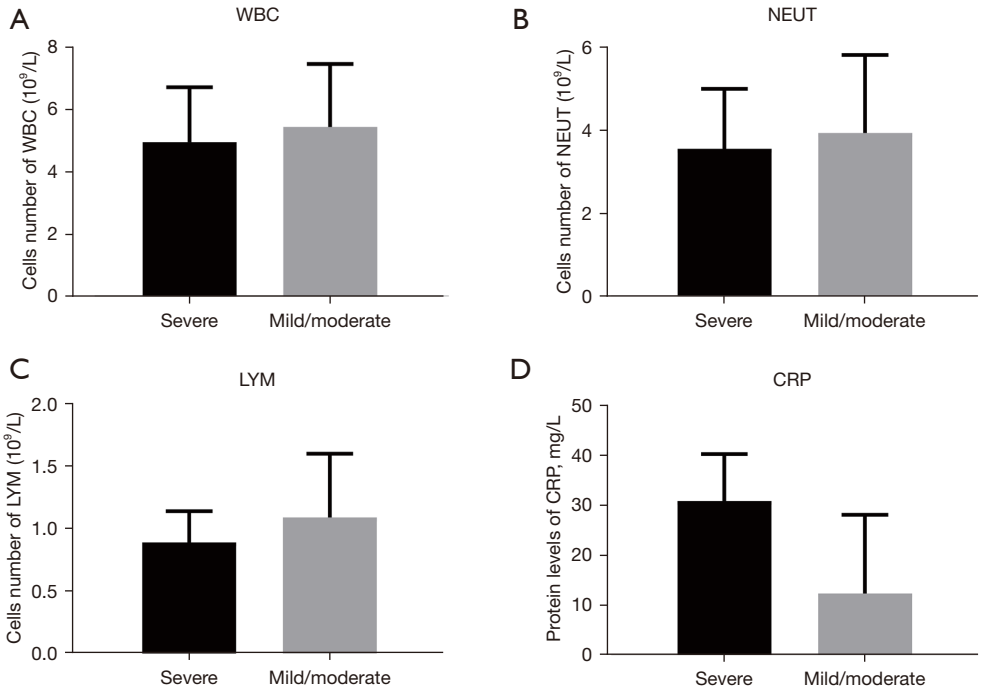

Figure 1 Comparison of routine hematology indexes for group A (severe) and group B (mild/moderate) including the total counts of (A) WBCs, (B) NEUTs, (C) LYMs and (D) CRP. WBC, white blood cell; NEUT, neutrophils; LYM, lymphocytes; CRP, C-reactive protein.

Eastern countries in 2012 and eventually appeared in China. The SARS-CoV-2 discovered most recently is different from these six other coronaviruses and is classified into the βCoV genus. A current study suggests that masked civets and civets may be intermediate hosts of SARS-CoV, and MERS-CoV can cross species barriers to infect humans after infecting dromedary camels (10). SARS-CoV and MERS-CoV both originate in bats and according to the latest data, SARS-CoV-2 most likely originated in bats as well, but spread through infected pangolins or other wild animals for sale in the South China Seafood Wholesale Market in Wuhan City, China, causing a persistent epidemic in humans (11). Based on the extensive research into SARS-CoV-2, we focused on factors that potentially might indicate disease progression by retrospectively analyzing the clinical data of 42 patients with COVID-19.

The average age of our subjects was 48.4 years, which concords with the average age of patients with COVID-19 ranging from 47 to 55.5 years in the published literature. It has also been reported that patients aged ≥60 years have a high risk of disease (12), and our study the most severe cases were patients of advanced age. Thus, severe disease is more likely in people with a weakened immune system, whether from age or underlying disease (13). Hypertension and diabetes are the most common complications in patients affected by COVID-19, and our study verified that patients with a history of hypertension were more likely to develop severe COVID-19. Clinical data show that patients with severe COVID-19 are significantly more likely to have hypertension and diabetes than those with mild COVID-19 (14). Past medical history is also relevant to severe disease development, and consistently, most of the patients with severe disease in our study had a past medical history.

SARS-CoV-2 infection shares many clinical characteristics with other βCoV infections, including fever, dry cough, respiratory difficulty, and bilateral ground-glass appearance on chest CT scan. Approximately 32.5% of patients infected with SARS-COV-2 (15) or 25% of patients infected with MERS-CoV (16) developed renal symptoms (e.g., diarrhea). Blood chemistry tests revealed that most patients had decreased WBC, NEUT and LYM, and there is evidence from prior research that a significant reduction of total LYM count is a reflection of a weakened immune system (coronavirus consumes immune cells) (17), and damage to T-cells might be responsible for disease deterioration. Other than the decreased hematological indexes above, there was a noticeably increased level of CRP in patients with severe disease, which corroborates

a previous report that patients with severe COVID-19 develop an especially severe inflammatory response (18).

Conclusions

In patients with COVID-19, age, hypertension, extent of lung lesions and chest pain are potential indicators of progression to severe disease. Furthermore, an abnormal elevation of CRP is more prominent in the development of severe disease and should be noted. Our findings provide certain reference for research on the clinical characteristics of patients with severe COVID-19. However, due to the limited sample size, our results are not precise enough and hence, further research is needed.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-22-658/rc

Data Sharing Statement: Available at https://apm.amegroups.com/article/view/10.21037/apm-22-658/dss

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-22-658/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by ethics committee of the First Hospital of Jiaxing/Affiliated Hospital of Jiaxing University (No. LS2020-010). Written informed consent from all participants was obtained prior to screening.

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