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Hematological characteristics of patients with novel coronavirus pneumonia in intensive care unit

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ABSTRACT

Background: Toward the end of December 2019, a novel type of coronavirus (2019-nCoV) broke out in Wuhan, China. Here, the hematological characteristics of patients with severe and critical 2019-nCoV pneumonia in intensive care unit (ICU) were investigated, which may provide the necessary basis for its diagnosis and treatment.

Methods: We collected data on patients with confirmed 2019-nCoV pneumonia in the ICU of Leishenshan Hospital in Wuhan from February 25 to April 2, 2020. Real-time reverse-transcription polymerase chain reaction was used to confirm the presence of 2019-nCoV, and various hematological characteristics were analyzed.

Results: All patients tested positive for 2019-nCoV using nasopharyngeal swabs or sputum after admission, and interstitial pneumonia findings were noted on chest computed tomography. Sex, age and comorbidities were not significantly different between the severe and critical groups. In terms of prognosis, the survival rate of patients in the severe group reached 100%, whereas that of patients in the critical group was only 13.33% after positive treatment. Furthermore, lymphocyte percentage, blood urea nitrogen, calcium, D-dimer, myohemoglobin, procalcitonin, and IL-6 levels were high-risk factors for disease progression in critical patients. Finally, lymphocyte percentage and blood urea nitrogen, calcium, myohemoglobin, and IL-6 levels were closely associated with patient prognosis.

Conclusions: 2019-nCoV pneumonia should be considered a systemic disease. Patients with more complications were more likely to develop critical disease. Lymphocyte percentage and blood urea nitrogen, calcium, myohemoglobin, and IL-6 levels can be monitored to prevent progression critical disease.

1. Introduction

In December 2019, a novel coronavirus (2019-nCoV) infection had been reported in Wuhan, China. This infectious disease spread rapidly to other parts of the country and then to several countries abroad. Thereafter, the Chinese Center for Disease Control (CDC) announced the inclusion of the disease into national "class B" and adopted "class A" prevention and control measures [1]. According to the national CDC official website (<http://2019ncov.chinacdc.cn/nCoV/>), a total of 84,547

patients were diagnosed with this disease and 4,645 patients had died as of May 27, 2020.

During the initial stages of 2019-nCoV pneumonia, severe acute respiratory infection symptoms occur, with some patients rapidly developing acute respiratory distress syndrome, acute respiratory failure, and other serious complications [2]. As a result, most patients with severe 2019-nCoV pneumonia require hospital admission or treatment in the intensive care unit (ICU) [3]. To date, several investigations have established the characteristics of patients with coronavirus disease 2019

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(COVID-19), including epidemiological, clinical, laboratory, and radiological characteristics; treatment; and clinical outcomes [2,4,5]. However, the findings of these studies were mainly focused on the general population, and the clinical characteristics of patients with varying degrees of severity of this disease in the ICU are less known.

In this study, we analyzed the hematological characteristics of patients with 2019-nCoV pneumonia admitted to the ICU of Leishenshan Hospital in Wuhan and explored the clinical significance of changes in blood routine examination, blood biochemistry examination, coagulation function, myocardial injury markers, and inflammatory markers.

2. Materials and Methods

2.1. Patient characteristics

A total of 51 patients with severe and critical 2019-nCoV pneumonia (severe and critical groups, respectively) who were admitted to the ICU of Leishenshan Hospital in Wuhan from February 25 to April 2, 2020, were enrolled in this retrospective analysis. The sex and age of each patient were recorded. We also recorded the comorbidities of each enrolled patient in detail, including the history of chronic systemic diseases (cardiovascular, respiratory, endocrine, liver, kidney, cerebrovascular), malignancies and autoimmune diseases to explore the impact of different comorbidities on critical patients with COVID-19. According to the Diagnosis and Treatment Program of 2019 New Coronavirus Pneumonia (seventh edition) in China, the 51 patients were divided into two groups: severe ($n = 21$) and critical ($n = 30$). The severe group met any of the following criteria: (1) dyspnea or respiratory rate of ≥ 30 /min; (2) oxygen saturation of $\leq 93\%$ at rest; (3) arterial pressure of oxygen/oxygen concentration of < 300 mmHg; and (4) chest imaging showing $> 50\%$ lesion progression within 24–48 h. The critical group met any of the following criteria: (1) respiratory failure and mechanical ventilation; (2) shock state; and (3) combined with other organ failure. This study was approved by the Ethics Committee of the Fifth People's Hospital of Shanghai of Fudan University and Shanghai Jiao Tong University, and written informed consent was obtained from the patients before enrollment when their data were collected.

2.2. Test methods

Under limosis condition, vein blood samples were obtained early in the morning after admission to the hospital to examine blood routine parameters, blood biochemistry parameters (including liver function, renal function, and electrolyte levels), coagulation function, myocardial injury markers, and inflammatory markers [such as serum inflammatory factor interleukin-6 (IL-6)]. Among these indicators, IL-6 was detected by enzyme-linked immunosorbent assay.

2.3. Statistical treatment

Statistical analyses were performed using SPSS version 21.0 (SPSS Inc., Chicago, USA). The demographic and clinical characteristics of patients with severe and critical 2019-nCoV pneumonia were compared using the χ^2 test and Student's *t*-test. Multivariate logistic regression analysis was performed to correct the significant *P*-value. Differences with *P*-values of < 0.05 were considered significant.

3. Results

A total of 51 patients admitted to the ICU, 21 patients with severe 2019-nCoV pneumonia and 30 patients with critical 2019-nCoV pneumonia, were included in this study. The demographic and clinical characteristics of the patients with 2019-nCoV pneumonia are shown in Table 1. There was no statistically significant difference between the two groups at different age stages ($P = 0.548$). In terms of overall comorbidity, 12 (57.1%) severe patients and 20 (73.3%) critical patients had

Table 1

The basic characteristics of the patients of 2019-nCoV pneumonia.

	Severe cases (n =21)	Critical cases (n=30)	<i>P</i> value
Age			
< 40 years	0 (0%)	1 (3.3%)	0.548
40-60 years	4 (19%)	8 (26.7%)	
> 60 years	17 (81%)	21 (70%)	
Sex			
Male	13 (61.9%)	16 (53.3%)	0.543
Female	8 (38.1%)	14 (46.7%)	
Comorbidities			
Hypertension	12 (57.1%)	22 (73.3%)	0.227
Diabetes	9 (42.9%)	14 (46.7%)	0.461
Cardiovascular disease	4 (19%)	7 (23.3%)	0.714
Chronic obstructive pulmonary disease	3 (14.3%)	6 (20%)	0.598
Chronic kidney disease	3 (14.3%)	1 (3.3%)	0.152
Chronic liver disease	1 (4.8%)	2 (6.7%)	0.776
Malignant tumour	1 (4.8%)	2 (6.7%)	0.776
Autoimmune disease	0 (0%)	2 (6.7%)	0.227
Cerebrovascular disease	1 (4.8%)	1 (3.3%)	0.796
Number of comorbidity			
1	3 (14.3%)	8 (26.7%)	0.29
2	8 (38.1%)	10 (33.3%)	0.726
≥ 3	5 (23.8%)	6 (20%)	0.745
Prognosis			
Survival rate	1 (4.8%)	8 (26.7%)	0.043
	21 (100%)	4 (13.33%)	

chronic diseases, including hypertension, diabetes, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, chronic liver disease, malignant tumor, autoimmune disease, and cerebrovascular disease. The differences in age, sex, and comorbidity were not significantly different between the two groups ($P = 0.924, 0.543,$ and 0.227 , respectively). However, the number of patients in the critical group was significantly higher than that in the severe group for > 3 comorbidities (4.8% vs. 26.7%).

By comparing the differences in blood routine characteristics, blood biochemistry characteristics, coagulation function, myocardial injury markers, and inflammatory markers between severe and critical patients, most of these indicators were found to be significantly different (Table 2). White blood cell count, neutrophil percentage, lymphocyte percentage, red blood cell count, and hemoglobin levels were significantly different between the two groups ($P = 0.012, 0.000, 0.000, 0.012,$ and 0.009 , respectively), whereas no remarkable difference was observed in the platelet count ($P = 0.079$). In terms of the severity of anemia, the incidences of moderate and severe anemia were higher in the critical group than in the severe group (19.05% vs. 46.67%, 0% vs. 6.66%). In terms of blood biochemistry characteristics, significant differences were noted in serum albumin, blood urea nitrogen, creatinine, blood sodium, and blood calcium levels between the two groups ($P = 0.009, 0.000, 0.000, 0.012,$ and 0.043 , respectively). In terms of blood sodium level, severe patients showed hyponatremia as the main characteristic (38.1% vs. 10%), whereas critical patients showed hypernatremia (36.67% vs. 9.52%). No significant differences were observed in serum alanine aminotransferase and aspartate aminotransferase, blood potassium, and blood chlorine levels between the two groups ($P = 0.357, 0.694, 0.371,$ and 0.127 , respectively). In terms of coagulation function, significant differences were noted in prothrombin time, activated partial thromboplastin time, and D-dimer levels between the two groups ($P = 0.001, 0.002,$ and 0.023 , respectively), whereas no significant difference was observed in fibrinogen levels ($P = 0.561$). In terms of myocardial injury markers, creatine kinase, creatine kinase isoenzyme, lactate dehydrogenase, hypersensitive troponin I, myohemoglobin, and brain natriuretic peptide levels were significantly higher in critical patients than in severe patients ($P = 0.000, 0.014, 0.048, 0.038, 0.000,$ and 0.042 , respectively). Finally, significant differences were noted in terms of inflammatory marker levels, including hypersensitive C-reactive protein, procalcitonin, and IL-6 levels, between the two groups ($P = 0.000, 0.000,$ and 0.000 , respectively).

Table 2
Hematologic examination of patients with 2019-nCoV pneumonia in ICU ward.

	Reference value	Severe (n=21)	Critical (n=30)	P value
Blood testing				
White blood cell count ($\times 10^9/L$)	3.5-9.5	8.24 \pm 2.89	11.11 \pm 4.44	0.012
Neutrophil percentage (%)	40-75	78.52 \pm 8.92	89.09 \pm 6.17	0.000
Lymphocyte percentage (%)	20-50	12.76 \pm 6.91	5.84 \pm 4.51	0.000
Red blood cell count ($\times 10^{12}/L$)	4.3-5.8	3.72 \pm 0.76	3.13 \pm 0.81	0.012
Hemoglobin (g/L)	120-160	113.09 \pm 21.46	93.83 \pm 27.28	0.009
Mild	90-120	17 (80.95%)	14 (46.67%)	0.04
Moderate	60-89	4 (19.05%)	14 (46.67%)	
Severe	<59	0 (0%)	2 (6.66%)	
Platelet count ($\times 10^9/L$)	125-350	231.52 \pm 83.68	187.9 \pm 86.87	0.079
Liver function				
Alanine aminotransferase (U/L)	9-50	73.90 \pm 41.26	71.93 \pm 53.89	0.357
Aspartate aminotransferase (U/L)	15-40	43.57 \pm 26.63	47.17 \pm 35.20	0.694
Albumin (g/L)	40-55	30.94 \pm 3.53	28.26 \pm 3.44	0.009
Renal function				
Blood urea nitrogen (mmol/L)	3.6-9.5	6.26 \pm 2.95	13.47 \pm 6.74	0.000
Creatinine (μ mol/L)	64-104	58.87 \pm 20.86	123.27 \pm 75.75	0.000
Electrolytes				
Potassium (mmol/L)	3.5-5.3	4.20 \pm 0.64	4.37 \pm 0.71	0.371
Sodium (mmol/L)	137-147	141.8 \pm 5.00	146.18 \pm 9.90	0.043
Normal		11 (52.38%)	16 (53.33%)	0.017
Hypernatremia		2 (9.52%)	11 (36.67%)	
Hypонатremia		8 (38.10%)	3 (10%)	
Chlorine (mmol/L)	99-110	105.89 \pm 4.41	109.72 \pm 10.65	0.127
Calcium (mmol/L)	2.11-2.52	2.01 \pm 0.12	1.93 \pm 0.13	0.040
Normal		5 (23.81%)	1 (3.33%)	0.026
Hypocalcemia		16 (76.19%)	29 (96.67%)	
Blood glucose (mmol/L)	3.9-6.1	10.27 \pm 4.15	12.07 \pm 4.96	0.235
Coagulation function				
Prothrombin time (s)	9-13	12.41 \pm 0.94	14.11 \pm 2.20	0.001
Normal		16 (76.19%)	9 (30%)	0.001
Prolonged		5 (23.81%)	21 (70%)	
Activated partial thromboplastin time (s)	20-40	28.38 \pm 5.57	38.64 \pm 13.34	0.002
Normal		20 (95.24%)	21 (70%)	0.025
Prolonged		1 (4.76%)	9 (30%)	
Fibrinogen (g/L)	2-4	4.01 \pm 1.25	4.27 \pm 1.96	0.561
D-dimer (g/L)	0-0.55	4.89 \pm 3.72	8.16 \pm 6.19	0.023
Myocardial injury marker				
Creatine kinase (U/L)	0-171	128.05 \pm 79.49	305.73 \pm 205.92	0.000
Creatine kinase isoenzyme (U/L)	0-4.97	3.21 \pm 2.35	5.50 \pm 3.42	0.014
Lactate dehydrogenase (U/L)	125-243	322.33 \pm 129.24	413.93 \pm 176.70	0.048
Hypersensitive troponin (mg/L)	0-0.04	0.155 \pm 0.131	0.271 \pm 0.253	0.038
Myohemoglobin (mg/L)	0-65	476.13 \pm 324.72	51.00 \pm 26.08	0.000
Brain natriuretic peptide (ng/mL)	0-100	262.76 \pm 188.95	535.54 \pm 405.52	0.002
Inflammatory marker				
Hypersensitive C-reactive protein (mg/L)	0-4	34.22 \pm 27.73	82.30 \pm 39.24	0.000

Table 2 (continued)

	Reference value	Severe (n=21)	Critical (n=30)	P value
Procalcitonin (mg/L)	0-0.05	0.221 \pm 0.199	0.895 \pm 0.713	0.000
Interleukin-6 (mg/L)	0-7	9.72 \pm 7.66	652.45 \pm 498.84	0.000

Furthermore, multivariate logistic regression analysis revealed that lymphocyte percentage and blood urea nitrogen, blood calcium, D-dimer, myohemoglobin, procalcitonin, and IL-6 levels were high-risk factors for progression into critical disease ($P = 0.008, 0.011, 0.021, 0.037, 0.005, 0.012,$ and $0.035,$ respectively; odds ratio [OR] = 3.342, 1.468, 2.012, 1.931, 2.382, 1.712, and 2.743, respectively) (Table 3).

Of the seven risk factors shown in Table 4, lymphocyte percentage and blood urea nitrogen, calcium, myohemoglobin, and IL-6 levels were closely related to the prognosis of patients ($P = 0.001, 0.04, 0.038, 0.000,$ and $0.023,$ respectively).

4. Discussion

Coronavirus is a large family of viruses that are known to cause diseases ranging from common colds to Middle East respiratory syndrome and severe acute respiratory syndrome [6,7]. The current 2019-nCoV emerged in December 2019, with a cluster of patients identified with connections to Huanan Seafood Market in Wuhan, China. People infected with 2019-nCoV exhibited symptoms of viral pneumonia, such as fever, difficulty in breathing, and bilateral lung infiltration in the most severe cases.

We found no significant differences in age, sex, and overall comorbidities between severe and critical patients; however, the number of patients in the critical group was significantly higher than that in the severe group for > 3 comorbidities. This indicated that the higher the number of complications, the higher the risk of patients developing critical disease.

In blood routine characteristics, the white blood cell count of patients with 2019-nCoV infections should be normal or reduced [4,8]; however, we found that the white blood cell count of critical patients was significantly higher than that of severe patients, even by $> 20 \times 10^9/L$ in some critical patients. With significantly elevated

Table 3
Logistic regression analysis of risk factors.

Factors	β	SE	P	OR	OR 95%CI
White blood cell count	0.520	0.363	0.102	0.898	0.268–1.923
Neutrophil percentage	0.712	0.226	0.072	1.112	0.234–1.118
Lymphocyte percentage	1.238	0.294	0.008	3.342	0.423–6.121
Red blood cell count	0.415	0.198	0.133	0.911	0.321–1.876
Hemoglobin	0.684	0.331	0.111	0.887	0.228–1.546
Albumin	0.534	0.274	0.068	1.213	0.454–1.923
Blood urea nitrogen	0.832	0.385	0.011	1.468	0.884–4.006
Creatinine	0.772	0.218	0.084	1.302	0.684–2.157
Sodium	0.345	0.112	0.134	0.767	0.235–0.979
Calcium	0.648	0.234	0.021	2.012	0.302–2.897
Prothrombin time	0.328	0.172	0.156	0.843	0.138–0.885
Activated partial thromboplastin time	0.188	0.198	0.147	0.659	0.254–0.818
D-dimer	0.893	0.224	0.037	1.931	0.484–3.915
Creatine kinase	0.565	0.321	0.221	0.778	0.313–0.881
Creatine kinase isoenzyme	0.471	0.228	0.189	0.587	0.196–0.923
Lactate dehydrogenase	0.688	0.149	0.161	0.612	0.222–0.856
Hypersensitive troponin	0.718	0.256	0.078	1.045	0.318–2.516
Myohemoglobin	1.767	0.618	0.005	2.382	0.324–3.248
Brain natriuretic peptide	0.535	0.233	0.236	0.664	0.225–1.113
Hypersensitive C-reactive protein	0.811	0.312	0.072	0.887	0.322–1.234
Procalcitonin	0.918	0.219	0.012	1.712	0.518–3.126
Interleukin-6	0.875	0.523	0.005	2.743	0.459–3.953

Table 4
Correlation between risk factors and prognosis.

Factor	Reference value	Survived	Death	P value
Lymphocyte percentage (%)	20–50	10.91 ± 7.04	5.22 ± 3.79	0.001
Blood urea nitrogen (mmol/L)	3.6–9.5	8.22 ± 6.36	16.81 ± 12.35	0.040
Calcium (mmol/L)	2.11–2.52	2.00 ± 0.11	1.93 ± 0.14	0.038
D-dimer (g/L)	0–0.55	4.93 ± 3.48	7.71 ± 6.87	0.082
Myohemoglobin (mg/L)	0–65	103.58 ± 75.41	336.87 ± 270.95	0.000

hypersensitive C-reactive protein, procalcitonin, and IL-6 levels in critical patients, we considered that higher white blood cell counts were associated with mixed viral infections and even leukemia-like responses in some patients. The difference between neutrophil and lymphocyte percentages was significant between the two groups, which is consistent with the results of a previous study [9]. Patients with low lymphocyte percentage seemed to have severe disease; the reason may be related to the decreased immunity caused by the decreased lymphocyte percentage. Unlike the observations of a previous study [10], the incidence of anemia was higher in critical patients than in severe patients, particularly the incidences of moderate and severe anemia in the present study. Some patients even need blood transfusion, suggesting an association with systemic depletion due to severe infections in critical patients. No difference was observed in the platelet count between the two groups. Even in critical patients, the increase or decrease in platelet counts was only slightly significant, indicating that the effect of 2019-nCoV pneumonia on platelets was not significant. To our surprise, our conclusions were different from some previous studies [11,12]. Through the two meta-analyses of the influence on platelet counts in COVID-19 patients, we found that different studies had different responses to COVID-19 platelets. Remarkably, not all the patients were detected with thrombocytopenia, but many studies were still on platelet normality and advancement. Platelet decline could occur during severe infection, and COVID-19 was no exception. The mechanism might be related to the microcirculation disturbance caused by severe pneumonia, especially the appearance of disseminated intravascular coagulation and extensive pulmonary coagulation. We found that the platelet counts in critically ill patients were decreased than in patients with overall severe decreased platelet counts, which was still within the normal range. However, critically ill patients of coagulant function were obviously abnormal with an increase of most apparent D-dimer. Therefore, we hypothesized that systemic inflammatory response syndrome in critically ill patients seriously affected the coagulation function and various vital organs' functions in the early stage. The platelets didn't have enough time to show a decline before the death of patients.

In terms of blood biochemistry characteristics, serum alanine aminotransferase, aspartate aminotransferase, and albumin levels were used to evaluate liver function in our study. Mild liver function injury was found in both the groups, but no significant difference was noted. Most of the changes in liver function characteristics were temporary and reversible, indicating that liver function injury might be caused by several factors such as immunity, inflammation, and drugs [13]. In this study, the patients' albumin levels often decreased as the disease progressed and even reached a level below the lower limit of the reference range, which is inconsistent with the results of another study [14]; the albumin levels of the two groups decreased at varying degrees, especially in critical patients, indicating that the consumption of the body due to viral pneumonia was significant. Severe hypoproteinemia can also lead to a series of secondary changes, such as systemic swelling, multiple serosal effusion, and cachexia.

In terms of renal function analysis, blood urea nitrogen and creatinine levels were significantly increased in critical patients, illustrating that renal function damage was prevalent in these patients. However, a

recent study indicated that COVID-19 does not result in acute kidney injury [15], possibly due to the following reasons: (1) 2019-nCoV pneumonia with hypotension can lead to insufficient renal perfusion and cause prerenal kidney injury; (2) the highly expressed angiotensin-converting enzyme 2 in the kidney tissues had a strong affinity for 2019-nCoV, which may directly mediate virus-induced kidney injury [16] and (3) viral infection caused by immune response, secondary bacterial infection, and even the occurrence of sepsis could cause the release of a large number of pro-inflammatory factors in response to kidney damage.

In an early study on COVID-19, some evidence has suggested the presence of electrolyte disorders upon patient's presentation, including sodium, potassium, chloride, and calcium abnormalities [17]. In the present study, the two groups had different electrolyte disorders, with no difference noted in blood potassium and chlorine levels and significant difference noted in blood sodium and calcium levels. Among these electrolyte disorders, in terms of blood sodium levels, hyponatremia was prevalent in the severe group, whereas the critical group was characterized by hypernatremia. Therefore, the incidence of hypernatremia in critical patients was obviously increased in our study. However, compared with hyponatremia, hypernatremia was more harmful and difficult to manage because it can easily cause hyperosmotic state, cell dehydration, organ function damage, and even death. In terms of blood calcium levels, the two groups showed varying degrees of decreases, with the critical group showing a more obvious decrease. Accompanied by tissue and organ ischemia and hypoxia, severe infection in critical patients could result in changes in cell membrane permeability and a decrease in the activity depending on the adenosine triphosphate function of calcium pumps, eventually leading to accumulation of intracellular calcium and a decrease in blood calcium levels [18]. The reduced blood calcium levels indicated a severe disease and poor prognosis.

The blood glucose levels of severe and critical patients were significantly increased, but not significantly different between the two groups. There was also no significant difference in blood glucose levels between the patients with and without diabetes, which indicated that the patients in both groups were severely stressed. This finding showed that we can control blood glucose within a controllable range through active hypoglycemic treatment, which has great clinical implications for both the control of pulmonary infections and protection of visceral function.

In terms of coagulation function analysis in the two groups, we found that prothrombin time, activated partial thromboplastin time, and D-dimer level were significantly increased in critical patients, whereas fibrinogen level was not different between the two groups. This suggested that conventional coagulation parameters evaluated during the course of 2019-nCoV pneumonia were significantly associated with disease severity. Our conclusions are slightly different from those reported by other scholars [19,20], showing a significantly increased D-dimer level in severe patients. Hence, we reinforce the suggestion that routine monitoring of hematological characteristics is useful in establishing an accurate therapeutic strategy and preventing disease progression and even death.

We found that the levels of the six myocardial injury markers were increased in critical patients, with the most significant difference noted in myoglobin level. Our current data demonstrated that patients in the critical group were more susceptible to heart failure. Hypersensitive troponin I is reported to be one of the best laboratory parameters inflecting cardiac injury for predicting the severity of 2019-nCoV pneumonia [21]. It should be noted that the elevated hypersensitive troponin I levels in patients with 2019-nCoV infection are only indicative of myocardial injury that was probably secondary to severe hypoxemia. Another important laboratory parameter is myoglobin [22]. At the time of myocardial injury, myoglobin is the first biomarker to enter the blood, with diffusion rates higher than those of hypersensitive troponin I. Therefore, the degree of myocardial injury can be considered as an important predictor of the severity and prognosis of severe infection. For patients with positive hypersensitive troponin I and myoglobin results, we must select the appropriate respiratory support strategy to

improve oxygenation and wait for the recovery of myocardial injury.

Similar to that reported by other studies in terms of inflammatory markers [5,23], abnormal laboratory findings include elevated hyper-sensitive C-reactive protein, procalcitonin, and IL-6 levels, indicating sustained inflammatory responses after 2019-nCoV infection. These inflammatory responses can induce mitochondrial damage and glucose utilization disorders and promote functional damage in vital organs such as the lungs, heart, liver, and kidney. In addition, hypersensitive C-reactive protein, procalcitonin, and D-dimer levels and neutrophil percentage were significantly higher in the critical group than in the severe group, which may represent more prominent inflammation in critical patients.

We also screened high-risk hematological indicators, including lymphocyte percentage, blood urea nitrogen, calcium, D-dimer, myohemoglobin, procalcitonin, and IL-6 levels, for critical patients using multivariate logistic regression analysis. However, lymphocyte percentage and blood urea nitrogen, calcium, myohemoglobin, and IL-6 levels were closely related to the prognosis of all patients, as revealed by analysis of these high-risk factors mentioned above.

A review of different studies showed that the use of specific hematological markers in ICU patients with severe diseases may lead to different results. Atieh et al. conducted a meta-analysis of 2988 patients with COVID-19 (including 484 severe patients) included in 19 articles, and the results showed that lymphopenia; mild thrombocytopenia; increased erythrocyte sedimentation rate and D-dimer, C-reactive protein, lactate dehydrogenase, alanine transaminase, aspartate aminotransferase levels; and decreased albumin levels have important value in diagnosing the severity of new coronary pneumonia, whereas leukocytosis; neutrophilia; lymphopenia; thrombocytopenia; increased D-dimer, C-reactive protein, procalcitonin, lactate dehydrogenase, alanine transaminase, aspartate aminotransferase, total bilirubin, and creatinine levels; and decreased fibrinogen and albumin levels had important significance in the prognosis of COVID-19 [24]. Regarding blood markers for predicting diagnosis and prognosis, most studies on hematological indicators have reached the same conclusion, and only some studies on hematological indicators have examined certain variables. The reasons for consideration of specific variables may include the following: (1) the population of the study is different: most studies focus on comparing mild and severe patients, while this study focuses on the comparison between severe and critical patients admitted to the ICU and (2) the hematological indicators of the study are different: different studies are limited to the analysis of specific hematological indicators. The present study basically examined most of the indicators that can be monitored, and multifactor logistic regression analysis was used to screen out high-risk diagnostic factors. Simultaneously, in view of the difficult conditions under the COVID-19 severe pandemic, the number of patients we enrolled in the group was limited, which also may have influenced our results.

In summary, this study established the laboratory characteristics of 51 patients with 2019-nCoV pneumonia who were admitted to the ICU. We conclude that 2019-nCoV pneumonia involves multiple systems, in addition to the respiratory system. 2019-nCoV pneumonia had influence on blood routine characteristics, blood biochemistry characteristics, coagulation function, myocardial markers, and inflammatory markers to some extent. In critical patients, the abnormal increase in several hematological characteristics indicates serious damage; some of these characteristics were closely related to disease prognosis. Therefore, further study is warranted to gain better understanding of these risk factors, which may ultimately help guide efforts aimed at reducing the fatality rate.

CRediT authorship contribution statement

YD, ZL and JJ designed the experiments and reviewed the manuscript. YD and ZL performed the experiments. YD, JJ, TS, YD, LQ, WH, QH, JF, RJ and XC collected and analyzed the data. HJ and ZJ edited the

manuscript. All authors read and approved the final manuscript.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study was approved by the Ethics Committee of the Fifth People's Hospital of Shanghai of Fudan University and Shanghai Jiao Tong University, and written informed consent was obtained from the patients before enrolment when their data were collected.

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References

- [1] L. Chen, H.G. Liu, W. Liu, J. Liu, K. Liu, J. Shang, Y. Deng, S. Wei, [Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia], *Zhonghua Jie He He Hu Xi Za Zhi* 43 (2020) 203-208. 10.3760/cma.j.issn.1001-0939.2020.03.013.
- [2] N. Chen, M. Zhou, X. Dong, J. Qu, F. Gong, Y. Han, Y. Qiu, J. Wang, Y. Liu, Y. Wei, J. Xia, T. Yu, X. Zhang, L. Zhang, Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study, *Lancet* 395 (2020) 507-513. S0140-6736(20)30211-7 [pii] 10.1016/S0140-6736(20)30211-7.
- [3] J. Phua, L. Weng, L. Ling, M. Egi, C.M. Lim, J.V. Divatia, B.R. Shrestha, Y.M. Arabi, J. Ng, C.D. Gomersall, M. Nishimura, Y. Koh, B. Du, Intensive care management of coronavirus disease 2019 (COVID-19): challenges and recommendations, *Lancet Respir Med* 8 (2020) 506-517. S2213-2600(20)30161-2 [pii] 10.1016/S2213-2600(20)30161-2.
- [4] C. Huang, Y. Wang, X. Li, L. Ren, J. Zhao, Y. Hu, L. Zhang, G. Fan, J. Xu, X. Gu, Z. Cheng, T. Yu, J. Xia, Y. Wei, W. Wu, X. Xie, W. Yin, H. Li, M. Liu, Y. Xiao, H. Gao, L. Guo, J. Xie, G. Wang, R. Jiang, Z. Gao, Q. Jin, J. Wang, B. Cao, Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China, *Lancet* 395 (2020) 497-506. S0140-6736(20)30183-5 [pii] 10.1016/S0140-6736(20)30183-5.
- [5] D. Wang, B. Hu, C. Hu, F. Zhu, X. Liu, J. Zhang, B. Wang, H. Xiang, Z. Cheng, Y. Xiong, Y. Zhao, Y. Li, X. Wang, Z. Peng, Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China, *JAMA* (2020). 2761044 [pii] 10.1001/jama.2020.1585.
- [6] L.E. Gralinski, V.D. Menachery, Return of the Coronavirus: 2019-nCoV, *Viruses* 12 (2020). v12020135 [pii] 10.3390/v12020135.
- [7] N. Zhu, D. Zhang, W. Wang, X. Li, B. Yang, J. Song, X. Zhao, B. Huang, W. Shi, R. Lu, P. Niu, F. Zhan, X. Ma, D. Wang, W. Xu, G. Wu, G.F. Gao, W. Tan, A Novel Coronavirus from Patients with Pneumonia in China, *N. Engl. J. Med.* 382 (2020) (2019) 727-733, <https://doi.org/10.1056/NEJMoa2001017>.
- [8] W.J. Guan, Z.Y. Ni, Y. Hu, W.H. Liang, C.Q. Ou, J.X. He, L. Liu, H. Shan, C.L. Lei, D. S.C. Hui, B. Du, L.J. Li, G. Zeng, K.Y. Yuen, R.C. Chen, C.L. Tang, T. Wang, P. Y. Chen, J. Xiang, S.Y. Li, J.L. Wang, Z.J. Liang, Y.X. Peng, L. Wei, Y. Liu, Y.H. Hu, P. Peng, J.M. Wang, J.Y. Liu, Z. Chen, G. Li, Z.J. Zheng, S.Q. Qiu, J. Luo, C.J. Ye, S. Y. Zhu, N.S. Zhong, Clinical Characteristics of Coronavirus Disease 2019 in China, *N. Engl. J. Med.* 382 (2020) (2019) 1708-1720, <https://doi.org/10.1056/NEJMoa2002032>.
- [9] Z. Xu, L. Shi, Y. Wang, J. Zhang, L. Huang, C. Zhang, S. Liu, P. Zhao, H. Liu, L. Zhu, Y. Tai, C. Bai, T. Gao, J. Song, P. Xia, J. Dong, J. Zhao, F.S. Wang, Pathological findings of COVID-19 associated with acute respiratory distress syndrome, *Lancet Respir Med* 8 (2020) 420-422. S2213-2600(20)30076-X [pii] 10.1016/S2213-2600(20)30076-X.
- [10] T. Chen, D. Wu, H. Chen, W. Yan, D. Yang, G. Chen, K. Ma, D. Xu, H. Yu, H. Wang, T. Wang, W. Guo, J. Chen, C. Ding, X. Zhang, J. Huang, M. Han, S. Li, X. Luo, J. Zhao, Q. Ning, Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study, *BMJ* 368 (2020), m1091, <https://doi.org/10.1136/bmj.m1091>.
- [11] D. Bashash, F.S. Hosseini-Baharanchi, M. Rezaie-Tavirani, M. Safa, N. Akbari Dilmaghani, M. Faranoush, H. Abolghasemi, The Prognostic Value of Thrombocytopenia in COVID-19 Patients; a Systematic Review and Meta-Analysis, *Archives of academic emergency medicine* 8 (2020) e75.
- [12] G. Lippi, M. Plebani, B.M. Henry, Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis, *Clinica chimica acta; international journal of clinical chemistry* 506 (2020) 145-148. 10.1016/j.cca.2020.03.022.
- [13] G. Zhang, J. Zhang, B. Wang, X. Zhu, Q. Wang, S. Qiu, Analysis of clinical characteristics and laboratory findings of 95 cases of 2019 novel coronavirus

- pneumonia in Wuhan, China: a retrospective analysis, *Respir. Res.* 21 (2020) 74, <https://doi.org/10.1186/s12931-020-01338-8> [pii].
- [14] Y. Zhou, Z. Zhang, J. Tian, S. Xiong, Risk factors associated with disease progression in a cohort of patients infected with the 2019 novel coronavirus, *Ann Palliat Med* 9 (2020) 428-436. *apm.2020.03.26* [pii] 10.21037/apm.2020.03.26.
- [15] L. Wang, X. Li, H. Chen, S. Yan, D. Li, Y. Li, Z. Gong, Coronavirus Disease 19 Infection Does Not Result in Acute Kidney Injury: An Analysis of 116 Hospitalized Patients from Wuhan, China, *Am J Nephrol* 51 (2020) 343-348. 000507471 [pii] 10.1159/000507471.
- [16] Y. Liu, Y. Yang, C. Zhang, F. Huang, F. Wang, J. Yuan, Z. Wang, J. Li, C. Feng, Z. Zhang, L. Wang, L. Peng, L. Chen, Y. Qin, D. Zhao, S. Tan, L. Yin, J. Xu, C. Zhou, C. Jiang, L. Liu, Clinical and biochemical indexes from 2019-nCoV infected patients linked to viral loads and lung injury, *Sci. China Life Sci.* 63 (2020) 364-374, <https://doi.org/10.1007/s11427-020-1643-8> [pii].
- [17] G. Lippi, A.M. South, B.M. Henry, Electrolyte imbalances in patients with severe coronavirus disease 2019 (COVID-19), *Ann. Clin. Biochem.* 57 (2020) (2019) 262-265, <https://doi.org/10.1177/0004563220922255>.
- [18] R.T. Sankaran, J. Mattana, S. Pollack, P. Bhat, T. Ahuja, A. Patel, P.C. Singhal, Laboratory abnormalities in patients with bacterial pneumonia, *Chest* 111 (1997) 595-600. S0012-3692(15)46808-4 [pii] 10.1378/chest.111.3.595.
- [19] N. Tang, D. Li, X. Wang, Z. Sun, Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia, *J. Thromb. Haemost.* 18 (2020) 844-847, <https://doi.org/10.1111/jth.14768>.
- [20] H. Han, L. Yang, R. Liu, F. Liu, K.L. Wu, J. Li, X.H. Liu, C.L. Zhu, Prominent changes in blood coagulation of patients with SARS-CoV-2 infection, *Clin. Chem. Lab. Med.* (2020), <https://doi.org/10.1515/cclm-2020-0188/j/cclm.ahead-of-print/cclm-2020-0188/cclm-2020-0188.xml> [pii].
- [21] R.H. Du, L.R. Liang, C.Q. Yang, W. Wang, T.Z. Cao, M. Li, G.Y. Guo, J. Du, C.L. Zheng, Q. Zhu, M. Hu, X.Y. Li, P. Peng, H.Z. Shi, Predictors of mortality for patients with COVID-19 pneumonia caused by SARS-CoV-2: a prospective cohort study, *Eur Respir J* 55 (2020). 13993003.00524-2020 [pii] 10.1183/13993003.00524-2020.
- [22] S. Shi, M. Qin, B. Shen, Y. Cai, T. Liu, F. Yang, W. Gong, X. Liu, J. Liang, Q. Zhao, H. Huang, B. Yang, C. Huang, Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China, *JAMA Cardiol* (2020). 2763524 [pii] 10.1001/jamacardio.2020.0950.
- [23] J.J. Zhang, X. Dong, Y.Y. Cao, Y.D. Yuan, Y.B. Yang, Y.Q. Yan, C.A. Akdis, Y. D. Gao, Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China, *Allergy* (2020), <https://doi.org/10.1111/all.14238>.
- [24] A. Pourbagheri-Sigaroodi, D. Bashash, F. Fateh, H. Abolghasemi, Laboratory findings in COVID-19 diagnosis and prognosis, *Clinica chimica acta; international journal of clinical chemistry* 510 (2020) 475-482. 10.1016/j.cca.2020.08.019.