


# Manifestations of blood coagulation and its relation to clinical outcomes in severe COVID-19 patients: Retrospective analysis

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## Funding information

This work was supported by the National Natural Science Foundation of China (81801984), the China Postdoctoral Science Foundation (2019M664008), and the Military Medical Science and Technology Youth Cultivation Project (20QNYP092).

## Abstract

**Introduction:** Characteristics of blood coagulation and its relation to clinical outcomes in COVID-19 patients are still rarely reported. We aimed to investigate the blood coagulation function and its influences on clinical outcomes of patients with syndrome coronavirus 2 (SARS-CoV-2) infection.

**Methods:** A total of 71 severe patients with confirmed SARS-CoV-2 infection who were treated in Wuhan First Hospital from February 12 to March 20, 2020, were enrolled. The blood coagulation data in these patients and in 61 healthy controls were collected. The patients with COVID-19 were divided into two groups: the aggravated group and the nonaggravated group, respectively, basing on whether the patients' conditions turned to critically ill or not after admission.

**Results:** Compared with healthy controls, patients with COVID-19 had significant performances with coagulation dysfunction, including dramatically elevated values of FIB, PT, APTT, INR, FDP, and D-Dimers but markedly reduced AT value ( $P < .05$ ). Importantly, more noteworthy coagulation disorders similar to the differences between patients and controls were found in the aggravated patients with conditions deterioration after admission than those in the nonaggravated patients without conditions deterioration ( $P < .05$ ). Moreover, the aggravated patients possessed a longer hospital stay and a higher mortality compared with the nonaggravated patients ( $P < .001$ ). The coagulation parameters of COVID-19 patients were widely and closely related to the indexes of liver function and inflammation ( $P < .05$ ), indicating the coagulation dysfunction of these patients may be caused by liver injury and inflammatory storm.

**Conclusion:** Severe patients with SARS-CoV-2 infection often possess coagulation dysfunction on admission. A certain correlation exists in coagulation disorder and adverse clinical outcome among severe COVID-19 patients.

## KEYWORDS

blood coagulation, clinical outcome, COVID-19, inflammation, liver function

## 1 | INTRODUCTION

Since early December 2019, pneumonia cases with unknown cause emerged in Wuhan<sup>1</sup>; then, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was identified as the causative agent of this mysterious pneumonia.<sup>2</sup> At the time of writing this paper, a total number of more than two million confirmed cases with coronavirus disease 2019 (COVID-19) have been identified, spanning 181 countries and regions of the whole world.

Patients infected by SARS-CoV-2 are generally classified as mild, severe, and critical types in accordance with the severity of clinical symptoms.<sup>3</sup> According to previous study,<sup>1,4-6</sup> the severe or critical patients with COVID-19 markedly appear to have clinical manifestations of coagulation dysfunction. However, the correlations between coagulation and clinical outcomes, and the factors leading to coagulation dysfunction of COVID-19 patients were not fully elaborated. In this study, the complete coagulation parameters of severe COVID-19 patients and its influence on clinical outcomes were shown and analyzed, which may be helpful for formulating appropriate therapeutic strategy on coagulopathy of COVID-19.

## 2 | MATERIALS AND METHODS

### 2.1 | Patients

All consecutive severe patients (N = 71) with confirmed SARS-CoV-2 infection who had been tested by real-time RT-PCR for viral infection and had conducted a test of coagulation function within 3 days on admission and were treated in Wuhan First Hospital from February 12 to March 20, 2020, were enrolled. The study was approved by the Hospital Ethics Committee, and oral informed consent was obtained from each of the patients. The patients enrolled in this study were treated according to WHO interim guidance,<sup>7</sup> and patients' conditions and clinical outcomes were determined by reference to the notice on the issuance of strategic guidelines for diagnosis and treatment of COVID-19.<sup>8</sup> A patient was categorized as severe case if any of the bellowed clinical scenes appeared: (a) respiratory rate  $\geq 30$ /min; (a) oxygen saturation  $\leq 93\%$ ; and (c) arterial partial pressure of oxygen (PaO<sub>2</sub>)/ fraction of inspired oxygen (FiO<sub>2</sub>)  $\leq 300$  mmHg (1 mmHg = 0.133 kPa). A patient was categorized as critically ill case if any of the bellowed clinical scenes appeared: (a) with acute respiratory distress syndrome (ARDS) and needing mechanical ventilation either invasively or noninvasively; (b) shock; and (c) complication of organ functional failure and need intensive care unit support. All enrolled patients were severe cases with COVID-19 on admission and then were divided into two groups, the aggravated group and the nonaggravated group, respectively, basing on whether the patients' conditions turned to critically ill or not after admission.

### 2.2 | Data collection

The general information (age, sex, initial symptoms, coexisting disorders), clinical, laboratory, and radiological characteristics data of the enrolled patients on admission were extracted from electronic medical records. For coagulation data, the first results of patients within 3 days on admission were shown and analyzed. The measurement process of coagulation function was conducted with Sysmex CS5100 Automatic Blood Coagulation Analyzer (Sysmex) using corollary reagents (Siemens). The coagulation function was assessed by the parameters of fibrinogen (FIB, normal range 2-4 g/L), activated partial thromboplastin time (APTT, normal range 20-40 seconds), prothrombin time (PT, normal range 9-13 seconds), thrombin time (TT, normal range 14-21 seconds), international normalized ratio (INR, normal range 0.7-1.3), D-Dimers (D-D, normal range 0-0.55 mg/L), fibrin/FIB degradation products (FDP, normal range 0-5 mg/L), and antithrombin (AT, normal range 75%-141%). FIB, APTT, PT, and TT were tested using the clot-based method. D-D and FDP were tested using the method of immunoturbidimetry method. AT was tested using the method of chromogenic substrate. For other laboratory data (liver function test, lactate dehydrogenase [LDH, normal range 114-250 U/L], and C-reactive protein [CRP, normal range 0-5 mg/L]), the relevant results were tested using Beckman Coulter Chemistry Analyzer AU5800 (Beckman) and corollary reagents (Beckman), and were recorded and analyzed based on the test time closest to coagulation test. The liver function was assessed by the parameters of alanine aminotransferase (ALT, normal range 7-45 U/L), aspartate aminotransferase (AST, normal range 13-35 U/L), total bilirubin (TBiL, normal range 2-24  $\mu$ mol/L), and direct bilirubin (DBiL, normal range 0-7  $\mu$ mol/L). In addition, the coagulation test results obtained from 61 healthy controls who had conducted physical examinations in Wuhan First Hospital in February 2019 were used as a reference.

### 2.3 | Statistical analysis

Continuous variables were described as the means and standard deviations or medians and interquartile ranges (IQR) values. Categorical variables were expressed as the counts and percentages. Independent group *t* tests were applied to continuous variables that were normally distributed; otherwise, the Mann-Whitney test was used. Categorical variables were compared using the Chi-square tests, while the Fisher exact test was used when the data were limited. Statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) version 22.0 software. A two-sided  $\alpha$  of less than 0.05 was considered statistically significant.

## 3 | RESULTS

### 3.1 | Demographics and patient characteristics

The clinical characteristics of the 71 patients with COVID-19 enrolled in this study are shown in Table 1. The median age

Characteristics	All patients (N = 71)	Aggravated (N = 17)	Nonaggravated (N = 54)	P value
Age, Median (IQR) – year	65.0 (56.5-71.5)	68.0 (62.0-72.0)	65.0 (56.0-71.0)	.169
Sex				
Male	38 (53.5)	10 (58.8)	28 (51.9)	.615
Female	33 (46.5)	7 (41.2)	26 (48.1)	
Onset of symptom to hospital admission – day	12.0 (7.0-21.0)	12.0 (10.0-17.5)	11.5 (7.0-21.0)	.622
CT findings of ground-glass opacity and/or patchy shadowing	69 (97.2)	17 (100)	52 (96.3)	>.99
Initial symptoms				
Fever	48 (67.6)	13 (76.5)	35 (64.8)	.370
Dry cough	33 (46.5)	4 (23.5)	29 (53.7)	.030
Chest tightness	15 (21.1)	3 (17.6)	12 (22.2)	.950
Fatigue	13 (18.3)	3 (17.6)	10 (18.5)	>.99
Chest pain	4 (5.6)	1 (5.9)	3 (5.6)	>.99
Shortness of breath	3 (4.2)	0 (0.0)	3 (5.6)	>.99
Dyspnea	2 (2.8)	0 (0.0)	2 (3.7)	>.99
Vomiting	2 (2.8)	1 (5.9)	1 (1.9)	.424
Chill	1 (1.4)	0 (0.0)	1 (1.9)	>.99
Diarrhea	1 (1.4)	0 (0.0)	1 (1.9)	>.99
Headache	1 (1.4)	1 (5.9)	0 (0.0)	.239
Nausea	1 (1.4)	0 (0.0)	1 (1.9)	>.99
Dizziness	1 (1.4)	0 (0.0)	1 (1.9)	>.99
Anorexia	1 (1.4)	0 (0.0)	1 (1.9)	>.99
Coexisting disorders				
Hypertension	22 (31.0)	6 (35.3)	16 (29.6)	.660
Diabetes	15 (21.1)	3 (17.6)	12 (22.2)	.950
Cardiovascular disease	11 (15.5)	3 (17.6)	8 (14.8)	>.99
Chronic respiratory disease	4 (5.6)	1 (5.9)	3 (5.6)	>.99
Hepatopathy	4 (5.6)	2 (11.8)	2 (3.7)	.241
Cerebrovascular disease	1 (1.4)	1 (5.9)	0 (0.0)	.239
Malignancy	1 (1.4)	0 (0.0)	1 (1.9)	>.99
Clinical outcomes				
Length of hospital stay – day	27.0 (19.0-33.0)	34.0 (31.5-35.0)	23.0 (18.8-31.0)	<.001
Mortality	4 (5.6)	4 (23.5)	0 (0.0)	<.001

Note: Data are median (IQR) or n (%). P values comparing patients in the aggravated group and in the nonaggravated group are from Chi-square test, Fisher's exact test, or Mann-Whitney U test. Aggravated, patients in the aggravated group; Nonaggravated, patients in the nonaggravated group.

**TABLE 1** Demographic and baseline characteristics of 71 enrolled COVID-19 patients

was 65.0 years (IQR, 56.5-71.5), and 38 (53.5%) of the patients were men. The median time from illness onset to hospital admission of these patients was 12.0 days (IQR, 7.0-21.0).

On admission, most (97.2%) of the patients possessed a typical CT finding of ground-glass opacity and/or patchy shadowing. Of these patients, the most common initial symptoms were

fever (48 [67.6%]), dry cough (33 [46.5%]), and chest tightness (78 [32.8%]). Hypertension (22 [31.0%]), diabetes (15 [21.1%]), and cardiovascular disease (11 [15.5%]) were the most common coexisting disorders. According to whether the patients' conditions worsened further or not after admission, the enrolled patients were divided into two groups: the aggravated group and the nonaggravated group, respectively (Table 1). Between the two group patients, no statistical differences were found in baseline characteristics except for initial symptoms of dry cough ( $P < .05$ ). In addition, patients in the aggravated group evidently had a longer hospital stay (34.0 days [IQR, 31.5-35.0] vs 23.0 days [IQR, 18.8-31.0];  $P < .001$ ) and a higher mortality (23.5% vs 0.0%;  $P < .001$ ) compared with patients in the nonaggravated group.

### 3.2 | Comparison of blood coagulation between COVID-19 patients and healthy controls

The differences of hemostasis function between COVID-19 patients and healthy controls were shown on account of the assessment of eight parameters (Table 2). The FIB value of COVID-19 patients was higher than that of healthy controls (3.96 g/L [IQR, 3.42-4.17] vs 2.89 g/L [IQR, 2.50-3.26];  $P < .001$ ), which indicates blood of COVID-19 patients is in hypercoagulable state in comparison with healthy individuals. However, the values of APTT (26.30 seconds [IQR, 24.10-28.90] vs 24.10 seconds [IQR, 21.75-26.15];  $P < .001$ ), PT (11.60 seconds [IQR, 11.00-12.10] vs 11.00 seconds [IQR, 10.65-11.50];  $P < .001$ ), and INR (1.03 [IQR, 0.97-1.08] vs 0.97 [IQR, 0.94-1.02];  $P < .001$ ) were simultaneously found to be higher in COVID-19 patients compared with healthy controls. Importantly, the FDP (3.20 mg/L [IQR, 1.90-8.00] vs 0.90 mg/L [IQR, 0.55-1.10];  $P < .001$ )

**TABLE 2** Comparison of coagulation function between COVID-19 patients and healthy controls

Parameters	Patients (N = 71)	Controls (N = 61)	P value
FIB, g/L	3.96 (3.42-4.17)	2.89 (2.50-3.26)	<.001
APTT, s	26.30 (24.10-28.90)	24.10 (21.75-26.15)	<.001
PT, s	11.60 (11.00-12.10)	11.00 (10.65-11.50)	<.001
TT, s	18.00 (17.10-19.00)	18.00 (17.20-18.45)	.340
INR	1.03 (0.97-1.08)	0.97 (0.94-1.02)	<.001
FDP, mg/L	3.20 (1.90-8.00)	0.90 (0.55-1.10)	<.001
D-D, mg/L	0.55 (0.30-3.24)	0.29 (0.18-0.46)	<.001
AT, %	83.00 (76.50-90.20)	86.90 (80.45-92.70)	.032

Note: Data are median (IQR). P values comparing the COVID-19 patients and the healthy controls are from Mann-Whitney U test. Patients = patients with COVID-19.

Abbreviations: APTT, activated partial thromboplastin time; AT, antithrombin; Controls, healthy controls; D-D, D-Dimers; FDP, fibrin/fibrinogen degradation products; FIB, fibrinogen; INR, international normalized ratio; PT, prothrombin time; TT, thrombin time.

and D-D (0.55 mg/L [IQR, 0.30-3.24] vs 0.29 mg/L [IQR, 0.18-0.46];  $P < .001$ ) values were both higher in COVID-19 patients than those in controls, whereas the AT value was lower in COVID-19 patients than that in controls (84.0% [IQR, 76.50-90.20] vs 86.9% [IQR, 80.45-92.70];  $P < .05$ ). Nevertheless, no difference could be observed in the TT value between the two group patients ( $P > .05$ ). Taken the data above all, significant differences can be concurrently found in parameters representing the functions of coagulation, fibrinolysis, and anticoagulation between COVID-19 patients and healthy individuals.

### 3.3 | Comparison of laboratory findings on admission and clinical outcomes between the aggravated and nonaggravated patients

To make clear the relationship between blood coagulation on admission and clinical outcomes of severe COVID-19 patients, several hematological findings in laboratory were shown and compared between the aggravated and nonaggravated patients (Table 3). For coagulation function test, the values of APTT (30.40 seconds [IQR, 24.30-34.65] vs 26.10 seconds [IQR, 24.10-28.43];  $P < .05$ ), PT (12.00 seconds [IQR, 11.75-12.80] vs 11.50 seconds [IQR, 10.90-11.83];  $P < .001$ ), and INR (1.07 [IQR, 1.05-1.14] vs 1.02 [IQR, 0.96-1.05];  $P < .001$ ) were simultaneously found to be higher in the aggravated patients compared with patients in the nonaggravated group. However, no statistical differences were found in the percentage values of APTT, PT, and INR above their normal ranges between two group patients ( $P > .05$ ). The FDP (13.00 mg/L [IQR, 5.50-65.05] vs 2.40 mg/L [IQR, 1.70-5.00];  $P < .001$ ) and D-D (5.95 mg/L [IQR, 1.23-20.08] vs 0.44 mg/L [IQR, 0.25-1.19];  $P < .001$ ) values were both higher in the aggravated patients than those in the nonaggravated patients, whereas the AT value was lower in the aggravated patients than that in the nonaggravated patients (76.10% [IQR, 63.40-81.35] vs 84.25% [IQR, 79.48-91.95];  $P < .001$ ). In addition, significant differences could be found in the percentage values of FDP and D-D above their normal ranges ( $P < .001$ ) and AT below the normal range between two group patients ( $P < .01$ ). Notably, the values of FIB and TT did not differ in these two group patients ( $P > .05$ ).

For liver function test and diagnostic enzyme indexes, the values of AST, TBiL, DBiL, LDH, and CRP of patients in the aggravated group were significantly higher than those of patients in the nonaggravated group ( $P < .05$ ), but no difference was observed in the ALT value between two group patients. Moreover, the percentage values of AST, LDH, and CRP above their normal ranges were, respectively, higher in the aggravated patients than those in the nonaggravated patients ( $P < .05$ ). The percentage values of ALT, TBiL, and DBiL above their normal ranges in the aggravated patients were, respectively, equal to those in the nonaggravated patients ( $P > .05$ ).

**TABLE 3** Laboratory findings on admission and clinical outcomes of COVID-19 patients

Parameters	Aggravated (N = 17)	Nonaggravated (N = 54)	P value
<b>Coagulation function test</b>			
FIB (g/L; normal range 2.00-4.00)	3.84 (3.51-4.40)	3.96 (3.42-4.17)	.532
Increased	8 (47.1)	19 (35.2)	.379
APTT (s; normal range 20.00-40.00)	30.40 (24.30-34.65)	26.10 (24.10-28.43)	.027
Increased	0 (0.0)	0 (0.0)	>.99
PT (s; normal range 9.00-13.00)	12.00 (11.75-12.80)	11.50 (10.90-11.83)	<.001
Increased	3 (17.6)	3 (5.6)	.144
TT (s; normal range 14.00-21.00)	17.20 (16.95-19.35)	18.10 (17.30-19.00)	.200
INR (normal range 0.70-1.30)	1.07 (1.05-1.14)	1.02 (0.96-1.05)	<.001
Increased	1 (5.9)	0 (0.0)	.239
FDP (mg/L; normal range 0.0-5.0)	13.00 (5.50-65.05)	2.40 (1.70-5.00)	<.001
Increased	14 (82.4)	13 (24.1)	<.001
D-D (mg/L; normal range 0.00-0.55)	5.95 (1.23-20.08)	0.44 (0.25-1.19)	<.001
Increased	15 (88.2)	18 (33.3)	<.001
AT (%; normal range 75.0-141.0)	76.10 (63.40-81.35)	84.25 (79.48-91.95)	<.001
Decreased	7 (41.2)	5 (9.3)	.007
<b>Liver function test</b>			
ALT (U/L; normal range 7-45)	25.00 (15.50-112.00)	24.50 (13.75-40.00)	.217
Increased	7 (41.1)	12 (22.2)	.220
AST (U/L; normal range 13-35)	38.00 (24.50-88.50)	23.00 (17.75-35.00)	.003
Increased	9 (52.9)	12 (22.2)	.016
TBiL ( $\mu$ mol/L; normal range 2.0-24.0)	14.30 (11.45-18.55)	11.30 (8.58-15.03)	.036
Increased	2 (11.8)	3 (5.6)	.587
DBiL ( $\mu$ mol/L; normal range 0.0-7.0)	2.80 (1.30-4.45)	1.50 (1.08-2.35)	.026
Increased	1 (5.9)	1 (1.9)	.424
<b>Diagnostic enzyme index</b>			
LDH (U/L; normal range 114-250)	382.00 (271.00-515.00)	180.00 (157.00-218.00)	<.001
Increased	14 (82.4)	6 (11.1)	<.001
CRP (mg/L; normal range 0.00-5.00)	73.20 (31.50-128.00)	3.11 (3.11-12.45)	<.001
Increased	16 (94.1)	19 (35.2)	<.001

Note: Data are median (IQR) or n (%). P values comparing patients in the aggravated group and in the nonaggravated group are from Chi-square test, Fisher's exact test, or Mann-Whitney U test.

Aggravated, patients in the aggravated group; Nonaggravated, patients in the nonaggravated group.

Abbreviations: ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; AT, antithrombin; CRP, C-reactive protein; DBiL, direct bilirubin; D-D, D-Dimers; FDP, fibrin/fibrinogen degradation products; FIB, fibrinogen; INR, international normalized ratio; LDH, lactate dehydrogenase; PT, prothrombin time; TBiL, total bilirubin; TT, thrombin time.

### 3.4 | Correlation analysis of blood coagulation with liver function and diagnostic enzymes in COVID-19 patients

Correlation analysis results of coagulation function parameters with liver function parameters and diagnostic enzyme indexes in COVID-19 patients are displayed in Table 4. FIB was positively correlated with TBiL, DBiL, LDH, and CRP. APTT merely had a positive relevance to CRP, while PT and INR were

simultaneously and positively correlated with AST, TBiL, DBiL, LDH, and CRP. TT had a positive relevance to ALT and a negative relevance to CRP. FDP and D-D were positively correlated with AST, TBiL, DBiL, LDH, and CRP, while AT owned a negative relevance to AST, LDH, and CRP. Overall, the coagulation parameters have a close connection to the indexes of liver function and inflammatory factors, which implies the coagulation of COVID-19 patients may be influenced by liver function and inflammation.

**TABLE 4** Correlation analysis of coagulation function parameters with indexes of liver function and diagnostic enzyme in COVID-19 patients

Parameters	ALT (U/L)	AST (U/L)	TBiL ( $\mu\text{mol/L}$ )	DBiL ( $\mu\text{mol/L}$ )	LDH (U/L)	CRP (mg/L)
FIB, g/L	0.122	0.142	0.285 <sup>*</sup>	0.297 <sup>*</sup>	0.353 <sup>**</sup>	0.397 <sup>***</sup>
APTT, s	-0.075	0.121	0.085	0.072	0.122	0.496 <sup>***</sup>
PT, s	0.111	0.255 <sup>*</sup>	0.327 <sup>**</sup>	0.302 <sup>*</sup>	0.462 <sup>***</sup>	0.675 <sup>***</sup>
TT, s	0.273 <sup>*</sup>	0.161	-0.222	-0.143	-0.119	-0.445 <sup>***</sup>
INR	0.110	0.254 <sup>*</sup>	0.328 <sup>**</sup>	0.303 <sup>*</sup>	0.461 <sup>***</sup>	0.675 <sup>***</sup>
FDP, mg/L	0.123	0.351 <sup>**</sup>	0.277 <sup>*</sup>	0.378 <sup>**</sup>	0.674 <sup>***</sup>	0.635 <sup>***</sup>
D-D, mg/L	0.147	0.271 <sup>*</sup>	0.270 <sup>*</sup>	0.332 <sup>**</sup>	0.613 <sup>*</sup>	0.476 <sup>***</sup>
AT, %	-0.091	-0.271 <sup>*</sup>	-0.194	-0.194	-0.498 <sup>***</sup>	-0.470 <sup>***</sup>

Note: Data are *r* values. The values of *r* and *P* comparing parameters of coagulation function and indexes of liver function and diagnostic enzyme are from Spearman's correlation analysis.

Abbreviations: ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; AT, antithrombin; CRP, C-reactive protein; DBiL, direct bilirubin; D-D, D-Dimers; FDP, fibrin/fibrinogen degradation products; FIB, fibrinogen; INR, international normalized ratio; LDH, lactate dehydrogenase; PT, prothrombin time; TBiL, total bilirubin; TT, thrombin time.

\**P* < .05.

\*\**P* < .01.

\*\*\**P* < .001.

## 4 | DISCUSSION

In this study, the coagulation function results between severe COVID-19 patients and healthy individuals were compared. The test parameters showed that FIB values in COVID-19 patients were significantly higher than those in controls, and that values of APTT, PT, and INR were simultaneously higher in COVID-19 patients than those in controls. These results imply that severe patients with COVID-19 possess coagulation dysfunction. This seemingly contradictory result can be explained by that the functions of coagulation, anticoagulation, and fibrinolysis in most of the severe cases with COVID-19 are simultaneously and negatively affected.<sup>6,9,10</sup> Compared with healthy controls, the dramatically elevated values of FDP and D-D and significantly reduced values of AT in severe COVID-19 patients also confirm this conclusion. Overall, our results also bring into correspondence with those of previous studies. Thus, we reinforce the suggestion that the coagulation of severe patients with SARS-CoV-2 infection is a matter of particular concern.

To make clear the relations of monitoring of coagulation on admission with clinical outcomes, the enrolled COVID-19 patients were, respectively, divided into the aggravated group and the non-aggravated group according to whether the patients' conditions aggravated or not after admission. The routine hemostasis tests showed that similar differences with COVID-19 patients and healthy controls were observed in the values of all coagulation parameters except for FIB value between patients in the aggravated group and in the nonaggravated group. It is likely that COVID-19 patients with conditions deterioration after admission possess more significant coagulation dysfunction on admission than those patients without conditions deterioration. The results give us an important idea that the coagulation function of COVID-19 patients on admission may

have a close connection with their clinical outcomes, and that early monitoring of coagulation function may be essential for establishing an accurate therapeutic strategy, especially for coagulation disorders and preventing disease progression.

The liver is responsible for the synthesis and transport of many coagulation factors and anticoagulants,<sup>11,12</sup> and inflammation also acts as a significant role in coagulation regulation cascade network.<sup>13,14</sup> CRP is a kind of acute protein which rises sharply in the plasma when the body is infected or damaged, and it is a nonspecific and momentous marker of inflammation. LDH widely exists in human organs and tissues, and it is able to reflect the inflammation and injury residing in liver. The correlation analysis results demonstrated that all of the coagulation parameters had a direct connection with CRP value, prompting inflammation existing in COVID-19 patients probably, and primarily lead to coagulation disorders. Furthermore, the close correlation between liver function indexes, LDH, and coagulation function parameters also indicates that coagulation dysfunction may be related to liver injury of COVID-19 patients. Therefore, we speculate that different clinical outcomes caused by coagulation function may be due to the different degree of organ damage (especially liver) and the different intensity of inflammatory response in COVID-19 patients.<sup>1,15,16</sup>

Unfortunately, the number of patients infected by SARS-CoV-2 is globally exhibiting a rapid and constant progression. Although the mortality of this emerging infectious disease seems not high, severe or critical patients still possess a high risk of developing ARDS and getting poor clinical outcomes. Most of the severe or critical patients with COVID-19 often possess coagulation disorders, which points out that coagulation function may play an important role in disease progression. Thus, accurate diagnosis of coagulation and timely treatment of coagulopathy at the early stage of disease progression may be essential for preventing the deterioration of patients' conditions and improving the otherwise unfavorable clinical outcomes.

## CONFLICT OF INTEREST

The authors declare that no conflict of interest exists.

## AUTHOR CONTRIBUTIONS

LL, SW, and YH.Z. conceived the study and designed experimental procedures; LH, HC, SL,YX, JL, and YZ collected patients' data and performed statistical analysis. LL, SW, YH.Z., and LH wrote the paper. All authors reviewed and approved the final version.

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**How to cite this article:** Zhang Y, He L, Chen H, et al. Manifestations of blood coagulation and its relation to clinical outcomes in severe COVID-19 patients: Retrospective analysis. *Int J Lab Hematol*. 2020;42:766-772. <https://doi.org/10.1111/ijlh.13273>