RESEARCH ARTICLE

Clinical laboratory characteristics in patients with suspected COVID-19: One single-institution experience

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Abstract

Objectives: Since December 2019, the outbreak of coronavirus disease 2019 (COVID-19) has become a worldwide pandemic. The aim of the study is to investigate the demographic, clinical, and laboratory characteristics in suspected COVID-19 patients in our institution.

Methods: In this retrospective study, we investigated suspected COVID-19 patients admitted to the University of Alabama at Birmingham with a request for an interleukin-6 send-out test, from March 28 to June 27, 2020. Patients' demographic, clinical, and laboratory characteristics were collected by chart review.

Results: Fifty patients suspected with COVID-19 were included in our study, of whom 24 patients were positive with severe acute respiratory syndrome coronavirus-2 infection and 26 were negative. During the observation period, 30 patients were discharged, 17 died during hospitalization, and three remained in hospital. Compared to non-COVID-19 patients, COVID-19 patients had older age, more comorbidities, and elevated levels of inflammation markers such as erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum ferritin, and lactate dehydrogenase (LDH). However, there was no significant difference in laboratory data between survivors and nonsurvivors in COVID-19 patients in our study.

Conclusion: This study indicated that potential risk factors of older age, multiple comorbidities, and high levels of ESR, CRP, serum ferritin, and LDH could help the clinician to identify potential COVID-19 patients. However, this data needs to be further validated in a larger population.

KEYWORDS
coronavirus disease 2019, infection, inflammation, severe acute respiratory syndrome coronavirus-2

1 | INTRODUCTION

Since December 2019, coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has dramatically spread around the world. By June 24, 2020, there have been 9,129,146 confirmed cases of COVID-19 including 473,797 deaths globally per reports from the World Health Organization.

The most common symptoms for patients infected with COVID-19 are fever, dry cough, and fatigue. The majority of patients recovered gradually without hospitalization, however, about 5%–20% of patients with COVID-19 developed a critical illness that is characterized by acute respiratory distress syndrome (ARDS).[1-4] Available data suggested that in-hospital mortalities were highly associated with hematologic, biochemical, and immune biomarkers

particularly interleukin-6 (IL-6), D-dimer, interleukin-10 (IL-10), CD4+ T cells, CD8+ T cells, high sensitivity cardiac troponin I (hs-cTnI), lactate dehydrogenase (LDH), and lymphopenia.[4–8] Although multiple studies regarding the laboratory data in COVID-19 patients have been characterized in China, limited data are available in the United States.[6,9–11]

The aim of the study is to investigate the demographic, clinical outcome, and laboratory data in suspected COVID-19 patients admitted to our institution.

2 | METHODS

2.1 | Study design and patients

This study was approved by the Institutional Review Board of the University of Alabama at Birmingham. We retrospectively identified suspected COVID-19 patients admitted to our institution from March 28 to June 27, 2020 with a request for IL-6 send-out test. Patients with hematological malignancies and pregnant women were excluded to this study.

Laboratory testing for SARS-CoV-2 infection was done by using reverse transcription-polymerase chain reaction (RT-PCR) of nasopharyngeal or oropharyngeal swab samples. Testing was performed by the Department of Pathology at the University of Alabama at Birmingham, after which testing capacity was developed by the clinical microbiology laboratory.

2.2 | Data collection

Patients' demographic, clinical, and laboratory data were collected by chart review. The collected laboratory data included complete blood count with differentiation, coagulation profiles (prothrombin time [PT], partial thromboplastin time [PTT], fibrinogen, international normalized ratio [INR], and D-dimer), and biochemistry tests (blood urea nitrogen [BUN], creatinine, alkaline phosphatase [Alk phos], alanine aminotransferase [ALT], aspartate aminotransferase [AST], creatine kinase [CK], LDH, IL-6, C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], procalcitonin, hs-cTnI, and serum ferritin). The biochemistry tests were mainly performed on Beckman Coulter AU 5800 analyzer.

2.3 | Statistics

Descriptive analyses were performed for categorical variables and compared by Fisher's exact test or χ^2 test. Continuous variables were expressed as the mean ± SD and compared by independent sample t-test. p Value less than .05 was considered statistically significant. Data analysis was performed by IBM SPSS (Statistical Package for the Social Sciences, version 26).

3 | RESULTS

3.1 | Demographic and clinical characteristics of patients

A total of 50 patients were included in this study (27 males and 23 females) with a mean age of 66.60 (SD, 12.81; range, 34–83) years old. Twenty-four patients were confirmed positive for SARS-CoV-2 infection by RT-PCR, while 26 patients were negative for SARS-CoV-2 infection. Patients' demographic characteristics were summarized in Table 1. The mean age for COVID-19 patients was 65.38 (SD, 9.6; range, 47–83). The COVID-19 patients had older ages compared to non-COVID-19 patients with a mean age of 56.3 (SD, 14.0; range, 34–83; p = .011). The main symptoms at admission were fever, shortness of breath, ARDS, cough, and fatigue. Comorbidities including diabetes mellitus, hypertension, cardiac vascular disease (CAD), chronic obstructive pulmonary disease (COPD), and malignancies were significantly more common in the COVID-19 patients than non-COVID-19 patients (p < .05). For COVID-19 patients, 11 patients died during hospitalization, 11 patients were discharged, and two patients remained in hospital. For non-COVID-19 patients, 6 patients died, 19 patients were discharged, and 1 patient was still in the hospital.

3.2 | Clinical laboratory data

In the next step, we investigated the factors associated with SARS-CoV-2 infection by comparing the patients' laboratory data at admission between COVID-19 patients and non-COVID-19 patients. As shown in Table 2, the levels of ESR, CRP, serum ferritin, and LDH were significantly higher in COVID-19 patients compared to non-COVID-19 patients (p < .05). However, no significant differences were identified in other laboratory data including BUN, creatinine, Alk phos, ALT, AST, procalcitonin, hs-cTnI, CK, white blood cell (WBC), red blood cell, hemoglobin, platelet, neutrophils counts, lymphocytes counts, monocytes counts, IL-6, PT, PTT, INR, fibrinogen, and D-dimer between COVID-19 patients and non-COVID-19 patients.

3.3 | Inflammatory and cardiac markers for COVID-19 patients

An inflammatory laboratory panel was performed for suspected COVID-19 patients admitted to the University of Alabama. This inflammatory laboratory panel including inflammatory markers IL-6, ESR, CRP, LDH, serum ferritin, and cardiac markers hs-cTnI and CK. Table 3 further analyzed these markers between COVID-19 patients and non-COVID-19 patients based on the corresponding quantities and proportions. For COVID-19 patients, the levels of IL-6, ESR, and CRP were all above the normal values while for non-COVID-19

TABLE 1 The demographic and clinical characteristics of 50 suspected COVID-19 patients

Characteristics	All patients (n = 50)	COVID-19 status		p Value
		Negative (n = 26)	Positive (n = 24)	
Age, years (mean ± SD, median)	60.66 ± 12.81 (62)	56.31 ± 14.00 (60.5)	65.38 ± 9.60 (66.5)	.011*
Sex, n (%)				
Male	27 (54%)	12 (46.15%)	15 (62.5%)	.247
Female	23 (46%)	14 (53.85)	9 (37.5%)	
Race, n (%)				
White	13 (26%)	10 (38.46%)	3 (12.5%)	.054
Black	35 (70%)	16 (61.54%)	19 (79.17%)	
Other	2 (4%)	0 (0%)	2 (8.33%)	
Comorbidities, n (%)				
Diabetes	16 (32%)	5 (19.23%)	11 (45.83%)	.044*
Hypertension	32 (64%)	12 (46.15%)	20 (83.33%)	.006*
Cardiovascular disease	15 (30%)	12 (46.15%)	3 (12.5%)	.009*
COPD	15 (30%)	11 (42.31%)	4 (16.67%)	.048*
Malignancy	11 (22%)	9 (34.62%)	2 (8.33%)	.025*
Clinical outcome, n (%)				
Remained in hospital	3 (6%)	1 (3.85%)	2 (8.34%)	
Discharged	30 (60%)	19 (73.08%)	11 (45.83%)	.121
Died	17 (34%)	6 (23.07%)	11 (45.83%)	

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019.
*p < .05.

patients, the corresponding abnormal values for IL-6, ESR, and CRP were 14 (53.85%), 17 (68%), and 19 (73.1%). In the non-COVID-19 group, 16 (84.21%) patients had normal values of CK, while there was only 10 (47.62%) COVID-19 patients had normal CK values. Thus, the application of an inflammatory laboratory panel may be a good indication for COVID-19 patients.

3.4 | Disease evolution and prognosis of COVID-19 patients

A total of 24 COVID-19 patients were followed until discharge (two patients remained hospitalization), and the longest follow-up time was 57 days. The demographic characteristics and laboratory data of patients were compared between survivors and nonsurvivors (Table 4). The results showed that there was no significant difference identified between survivors and nonsurvivors. Interestingly, we found that survivors had a longer hospitalization time compared to nonsurvivors (26.91 ± 19.45 vs. 11.64 ± 6.48 days; p = .023).

4 | DISCUSSION

Our retrospective study identified several risk factors for patients who were hospitalized due to suspected SARS-CoV-2 infection. In particular, older age and comorbidities were associated with a higher prevalence of SARS-CoV-2 infection. Additionally, elevated levels of CRP, ESR, serum ferritin, and LDH were more commonly seen in COVID-19 patients.

Previous studies indicated that patients confirmed with SARS-CoV-2 infection had an older age compared to suspected patients.[4,12] Moreover, increased age was associated with death in patients with SARS-CoV-2 infection.[5] Opal et al.[13] found that the age-dependent defects in the functions of T-cells and B-cells cloud cause the deficiency in inhibiting viral replication combined with age-related excess production of type 2 cytokine, leading to a poor outcome. Consistent with previous studies, we observed that COVID-19 patients were older than non-COVID-19 patients. In general, old patients with more coexisting illness, for example, diabetes, hypertension, CAD, and COPD were more likely to infect SARS-CoV-2 and develop severe symptoms.[2,4,14–16] We also noticed that SARS-CoV-2 infected patients had more comorbidities than patients without SARS-CoV-2 infection.

Henry et al.[6] performed a meta-analysis involving 21 studies showed that inflammatory biomarkers including ESR, CRP, serum ferritin, IL-6, procalcitonin, and IL-2R were significantly elevated in patients with both severe and fetal COVID-19. Previous studies have shown that the main cause of rapid disease progression is the excessive inflammatory responses due to cytokine release syndrome.[9,17,18] Multiple studies have shown that higher concentrations of IL-6 were associated with the severity of COVID-19.[4,9,19] Furthermore, IL-6 blocking treatment (e.g., tocilizumab) may prevent the

TABLE 2 Laboratory data of suspected COVID-19 patients (n = 50)

Laboratory data	Normal range	COVID-19 status		p Value
		Negative (n = 26)	Positive (n = 24)	
BUN (mg/dl)	5–22	30.5 ± 19.19	26.75 ± 17.40	.474
Creatinine (mg/dl)	0.7–1.3	2.08 ± 1.94	1.40 ± 0.70	.113
Procalcitonin (ng/ml)	0–0.07	5.90 ± 20.17	3.34 ± 9.74	.58
CRP (mg/L)	0–10.90	90.84 ± 100.34	178.01 ± 99.52	.004*
Alk phos (Units/L)	37–117	103.19 ± 65.06	156.33 ± 301.29	.384
ALT (Units/L)	7–52	51.65 ± 87.55	40.88 ± 32.52	.573
AST (Units/L)	12–39	61.35 ± 80.73	92.63 ± 94.70	.214
LDH (Units/L)	120–240	407.40 ± 253.56	744.17 ± 615.75	.015*
CK (Units/L)	35–250	762.37 ± 2747.27	623 ± 787.40	.825
hs Troponin-I (ng/L)	3–20	293.24 ± 650.89	91.54 ± 187.18	.167
Serum ferritin (ng/ml)	23.9–336.2	354.80 ± 328.01	1294.79 ± 1624.0	.007*
WBC (×10⁹/L)	4.0–11.0	9.54 ± 6.65	9.37 ± 5.93	.927
RBC (×10⁹/L)	4.4–5.8	3.88 ± 0.97	4.27 ± 1.88	.352
Hb (g/dl)	13.5–17.0	11.10 ± 2.73	12.42 ± 5.28	.266
Platelet (×10⁹/L)	150–400	237.20 ± 141.77	204.23 ± 109.77	.365
Neutrophil (×10⁹/L)	1.4–8.03	7.77 ± 6.48	7.54 ± 5.37	.89
Lymphocytes (×10⁹/L)	0.60–5.72	1.06 ± 0.65	6.28 ± 26.15	.314
Monocytes (×10⁹/L)	0.16–1.43	0.58 ± 0.36	0.56 ± 0.43	.866
IL-6 (pg/ml)	≤5.0	31.65 ± 75.52	41.23 ± 44.13	.603
ESR (mm/hr)	0–10	36.62 ± 32.58	63.59 ± 32.11	.007*
PT (s)	12.0–14.5	17.41 ± 5.59	16.48 ± 3.52	.505
INR	N/A	1.44 ± 0.64	1.34 ± 0.38	.509
PTT (s)	25–35	32.95 ± 7.34	35.32 ± 12.93	.469
Fibrinogen (mg/dl)	220–498	462.17 ± 250.49	504.47 ± 12.93	.672
D-Dimer (ng/ml)	0–240	3565.30 ± 4861.12	5521 ± 7066.28	.28

Abbreviations: Alk phos, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CK, creatine kinase; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; hs Troponin-I, high sensitivity Troponin-I; IL-6, interleukin 6; INR, international normalized ratio; LDH, lactate dehydrogenase; PTT, partial thromboplastin time; PT, prothrombin time; RBC, red blood cell; WBC, white blood cell.

*p < .05.

TABLE 3 Data of inflammatory laboratory panel in suspected COVID-19 patient

COVID-19	Lab values	IL-6	ESR	CRP	LDH	Serum ferritin	hs Tn-I	CK
Negative	Within normal values, n (%)	12 (46.15%)	8 (32%)	7 (26.9%)	6 (24%)	15 (60%)	8 (30.77%)	16 (84.21%)
	Above normal vales, n (%)	14 (53.85%)	17 (68%)	19 (73.1%)	19 (76%)	10 (40%)	18 (69.23%)	3 (15.78%)
Positive	Within normal values, n (%)	0 (0%)	0 (0%)	0 (0%)	2 (8.33%)	9 (37.5%)	9 (37.5%)	10 (47.62%)
	Above normal vales, n (%)	22 (100%)	22 (100%)	23 (100%)	22 (91.67%)	15 (62.5%)	15 (62.5%)	11 (52.38%)

Abbreviations: CK, creatine kinase; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; hs Tn-I, high sensitivity Troponin-I; IL-6, interleukin 6; LDH, lactate dehydrogenase.

TABLE 4 Demographic, clinical, and laboratory characteristics in COVID-19 patients

Laboratory data	Normal range	Nonsurvivors (n = 11)	Survivors (n = 11)	p Value
Demographic				
Age, years (mean ± SD, median)		69.00 ± 10.01 (70)	65.09 ± 5.46 (62)	.269
Sex, n (%)				
Male		6 (54.5%)	7 (63.64%)	
Female		5 (45.5%)	4 (36.36%)	
Race, n (%)				
White		1 (0.09%)	2 (18.18%)	
Black		10 (90.91%)	7 (63.64%)	
Other		0 (0%)	2 (18.18%)	
Comorbidities, n (%)				
Diabetes		7 (63.64%)	4 (36.36%)	
Hypertension		10 (90.91%)	8 (72.73%)	
Cardiovascular disease		3 (27.27%)	0 (0%)	
COPD		4 (36.36%)	0 (0%)	
Malignancy		2 (18.18%)	0 (0%)	
Laboratory data				
BUN (mg/dl)	5–22	30.09 ± 18.19	20.45 ± 15.99	.202
Creatinine (mg/dl)	0.7–1.3	1.58 ± 0.77	1.09 ± 0.55	.1
Procalcitonin (ng/ml)	0–0.07	4.90 ± 14.12	0.65 ± 0.77	.331
CRP (mg/L)	0–10.90	190.32 ± 120.82	155.97 ± 85.16	.457
Alk phos (Units/L)	37–117	193.45 ± 434.02	79.82 ± 55.37	.399
ALT (Units/L)	7–52	40.91 ± 36.04	32.64 ± 25.54	.541
AST (Units/L)	12– 39	104.36 ± 114.07	53.73 ± 36.55	.176
LDH (Units/L)	120–240	618.00 ± 277.75	583.64 ± 501.76	.844
CK (Units/L)	35–250	598.50 ± 719.04	259.56 ± 215.27	.193
hs Troponin-I (ng/L)	3–20	46.27 ± 60.41	138.18 ± 268.84	.282
Ferritin (ng/ml)	23.9–336.2	968.27 ± 1285.54	874.36 ± 852.14	.842
WBC (×10⁹/L)	4.0–11.0	9.23 ± 8.13	9.40 ± 3.83	.951
RBC (×10⁹/L)	4.4–5.8	4.09 ± 0.86	4.47 ± 2.71	.658
Hb (g/dl)	13.5–17.0	11.61 ± 2.13	13.34 ± 7.61	.475
Platelet (×10⁹/L)	150–400	248.52 ± 123.22	189.24 ± 70.25	.181
Neutrophil (×10⁹/L)	1.4–8.03	7.39 ± 7.58	7.59 ± 2.95	.937
Lymphocytes (×10⁹/L)	0.60–5.72	12.69 ± 38.59	0.97 ± 0.67	.326
Monocytes (×10⁹/L)	0.16–.43	0.63 ± 0.48	0.53 ± 0.42	.634
IL-6 (pg/ml)	≤5.0	34.70 ± 34.70	48.70 ± 56.79	.514
ESR (mm/h)	0–10	68.0 ± 39.22	60.27 ± 30.08	.624
PT (s)	12.0–14.5	15.9 ± 2.85	15.34 ± 2.85	.547
INR	N/A	1.27 ± 0.3	1.21 ± 0.11	.521
PTT (s)	25–35	37.38 ± 12.14	31.11 ± 13.95	.342
Fibrinogen (mg/dl)	220–498	631.14 ± 260.46	372.83 ± 248.58	.096
D-Dimer (ng/ml)	0–240	5102.0 ± 7262.74	3270.31 ± 3834.39	.473
Hospital stay time (days)		11.64 ± 6.48	26.91 ± 19.45	.023*

Abbreviations: Alk phos, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CK, creatine kinase; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; IL-6, interleukin 6; INR, international normalized ratio; hs Troponin-I, high sensitivity Troponin-I; LDH, lactate dehydrogenase; PTT, partial thromboplastin time; PT, prothrombin time; RBC, red blood cell; WBC, white blood cell.

*p < .05.

development of severe disease in COVID-19 patients.[20–23] We observed elevated levels of ESR, CRP, serum ferritin, and LDH were associated with SARS-CoV-2 infection, however, IL-6 levels were neither correlated with SARS-CoV-2 infection nor mortality of

COVID-19 patients. Increased cardiac troponin level has been reported to be associated with severity and mortality in COVID-19 patients.[24] In this study, we observed the elevation of hs-cTnI level in both COVID-19 patients and non-COVID-19 patients. However,

there is no statistically significant difference between the two groups (Table 2). In addition, there is no statistically significant difference between the survivors and nonsurvivors of COVID-19 patients (Table 4). These discrepancies could be due to the small sample size.

Hematologic markers (WBC count, neutrophil count, lymphocyte count, and platelet count), biochemical markers (BUN, creatinine, and CK), and coagulation markers (D-dimer and PTT) were also reported to be correlated with severity and mortality of COVID-19 patients.[4–7,25] However, we did not find any association of these data in COVID-19 patients which could be due to a limited sample size.

Our study has some limitations. First, our institution is a large tertiary referral hospital, thereby many severe patients were transferred from outside hospitals without effective treatment contributing to poor clinical outcomes in some patients. Second, our study included a high percentage of black or African American patients who are known to have high rates of SARS-CoV-2 infection and mortality due to the high prevalence of cardiometabolic co-morbidities and socioeconomic vulnerabilities. Last but not the least, we only had 24 COVID-19 patients in our study, so our findings may be limited due to the small sample size.

5 | CONCLUSIONS

In summary, our study indicated that COVID-19 patients were associated with high levels of ESR, CRP, LDH, and serum ferritin. The inflammatory lab panel could be used as an indicator to evaluate COVID-19 infection, however, this needs to be further validated in a larger population.

CONFLICT OF INTERESTS
The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS
Fei Fei was involved in the data collection and manuscript preparation. John A. Smith was involved in the revision of the manuscript. Liyun Cao was involved in the preparation and revision of the manuscript.

DATA AVAILABILITY STATEMENT
The data that support the findings of this study are available on reasonable request from the corresponding author.

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