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Dear Editor,

The newly emergent Coronavirus disease 2019 (COVID-19) causes severe viral pneumonia in humans and poses a serious threat to public health worldwide, with cases reported from all 6 permanently inhabited continents. Effective clinical management, based on comprehensive laboratory findings, is critical for improving the survival rates of COVID-19 patients. By now, clinical and epidemiological characteristics of COVID-19 in cities outside of Wuhan, such as Beijing[1] and Wenzhou[2] were described. However, it is currently unknown whether there are any markers that can be informative of mild vs. severe disease. The objective of this study is to describe the comprehensive clinical characteristics of confirmed patients with COVID-19 and explore the potential markers correlating with prognosis.

We collected data from 119 hospitalized patients confirmed by quantitative reverse transcription-polymerase chain reaction (qRT-PCR) with throat swab specimens in Xiangyang, Hubei Province, between January and February 2020. The severe cases in this study refer to the patients who had enrolled to the intensive care unit (ICU) and received a treatment more than 3 days. While the other confirmed cases were distributed to the mild group. As a control, we collected the laboratory results of 20 healthy subjects (normal cases) examined by the same laboratory department during early December 2019, when COVID-19 was not yet prevalent in Xiangyang. The epidemiological, clinical, laboratory and disease outcome data were obtained from data collection forms and electronic medical records. Information was collected on the date of illness onset, visits to clinical facilities, and hospital admissions. The date of disease onset was defined as the day when the symptom was first noticed. Laboratory tests were conducted at admission, including a complete blood count and serum biochemistry.

As shown in Table 1, we found that 85% (101) of cases were infected by another COVID-19 patient, 46% (55) of the patients were categorized as collective cases, and 30% (36) of patients were also diagnosed with a pre-existing medical condition. After hospital admission, 16.8 % (20) of these patients progressed to severe disease, 4.2% (5) of the patients had complications such as respiratory failure and

distress, and 2.5% (3) patients succumbed to COVID-19. Fever was the most common symptom (86%, 102 cases), followed by fatigue (75%, 89 cases) and dry cough (63%, 75 cases). Headache and diarrhea were also reported among 14% (17) and 12% (14) cases, respectively.

Laboratory findings showed that decreased lymphocyte counts (Figure 1A), as well as elevated levels of fibrinogen (FIB，Figure 1B) and D-dimer (Figure 1C), may be early markers contributing to disease severity. Decreased albumin (Figure 1D) and elevated CK (Figure 1E) levels among severe patients indicate liver damage and shown as indicators of prognosis. Increased lactate dehydrogenase (LDH, Figure 1F) and α-hydroxybutyrate dehydrogenase (HBDH, Figure 1G) levels, indicative of heart damage, were detected in COVID-19 patients. Kidney damage in the COVID-19 patients was evidenced by urinary occult blood, increased C1q (Figure 1H) and β2-MG (Figure 1I) in COVID-19 patients.

In the study, we analyzed 119 cases of COVID-19 patients from a local hospital, in which 101 people had no residence or travel history to Wuhan, meaning most of the subjects in this study are non-first-generation cases. While some studies for clinical examinations have been published, many were not comprehensive and the studies took place in Wuhan[3-6]. Especially in the early stages of the outbreak, due to the overwhelmed medical system and lack of adequate medical resources and staff in Wuhan, clinical studies and laboratory examination results may not be reflective of the true nature of COVID-19 in patients. Indeed, this is reflected in the case fatality rates inside (4%) and outside of Wuhan (2.5%, according to our study). While other studies suggest that men are more susceptible to SARS-CoV-2 infection, there were no significant differences in susceptibility to the virus between men and women, even though women had more mild disease cases. The results in this study support the suggestion that there are no significant differences in the levels of ACE2 (the receptor for SARS-CoV-2) expression between genders[7]. As ACE2 is more highly expressed in elderly people, they theoretically would account for a higher percentage of the COVID-19 patients in this study.

Biomarkers that serve as reliable prognostic indicators predicting progression to mild vs. severe disease are urgently needed to enhance the quality of clinical care. In this study, we explored the possibility of identifying a marker from a routine comprehensive laboratory examination. Consistent with other studies, we found that decreased lymphocyte counts and increased D-dimer concentrations might be an indication of a negative prognosis. In addition, we provide several newly discovered bio-markers: decreased albumin as well as elevated CK, LDH and HBDH levels serve as indicators of a negative prognosis for COVID-19; urinary occult blood, increased C1q and β2-MG were observed in COVID-19 patients, indicated kidney damage.

The damage of SARS-CoV-2 to various major tissues and organs of the body during COVID-19 is an important area of investigation. In this study, we found that this virus can cause damage to the liver, heart and kidney, in which abnormal renal indicators may be caused by immunopathological damage. These findings are consistent with recent studies that the virus can damage multiple major organs including liver[8-9] kidney and heart[9]. The exact mechanism of this viral or immune-induced damage should be investigated in future studies.

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Figure legends

Figure 1A. Routine blood examination, coagulation function, damage on organ functions of COVID-19 patients and healthy people. (A) The counts of lymphocytes, (B) fibrinogen (FIB) and (C)D-dimer are shown as indicators of coagulation function, (C) Liver function tests of albumin and (D) Creatine kinase (CK), (E) Myocardial damage as indicated by lactate dehydrogenase (LDH) and (F) α-hydroxybutyrate dehydrogenase (HBDH). *P<0.05, **P<0.01 and ***P<0.001.

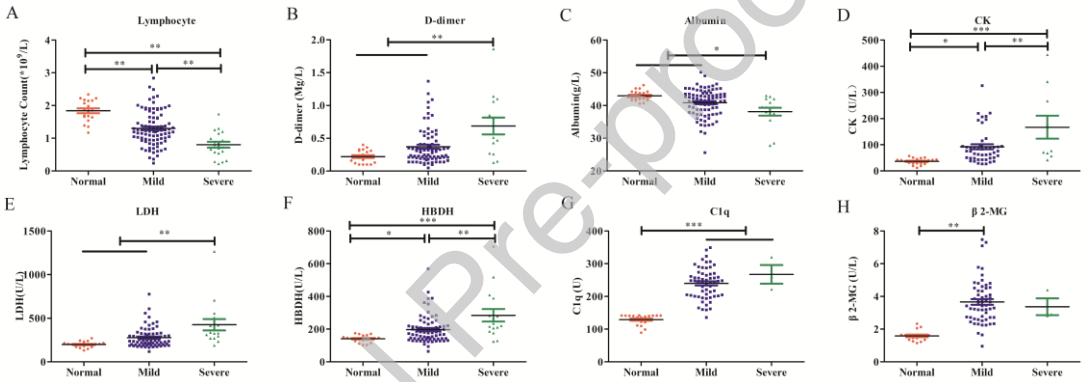

Table 1. Personal and clinical characteristics of patients with COVID-19 (n = 119)

Characteristics	No. (%)		
	All patients (n=119)	Mild disease (n=99)	Severe disease (n=20)
Median (IQR) age (Y)	49 (38-61)	45 (34-57)	67.5 (60-77)
Age groups (Y):			
≤18	7 (6)	7 (7)	0 (0)
19-40	35 (30)	35 (35)	0 (0)
41-65	55 (46)	46 (46)	9 (45)
≥66	22 (18)	11 (11)	11 (55)
Gender			
Female	63 (53)	55 (56)	8 (40)
Male	56 (47)	44 (44)	12 (60)
Co-morbidities	36 (30)	18 (18)	17 (85)
Hypertension	23 (19)	10 (10)	13 (65)
Diabetes	12 (10)	7 (7)	5 (25)

Cardiovascular disease	7 (6)	3 (3)	4 (20)
Renal diseases	2 (2)	1 (1)	1 (5)
Liver disease	2 (2)	2 (2)	0 (0)
Travel history to Wuhan			
Yes	18 (15)	15 (15)	3 (15)
No	101 (85)	84 (85)	17 (85)
Cluster cases	55 (46)	47 (47)	8 (40)
Signs and symptoms			
Fever	102 (86)	86 (86)	16 (80)
Fatigue	89 (75)	75 (75)	14 (70)
Dry cough	75 (63)	63 (53)	13 (65)
Expectoration	22 (18)	16 (16)	6 (30)
Headache	17 (14)	15 (15)	2 (10)
Diarrhea	14 (12)	11 (11)	3 (15)
Pharyngalgia	11 (9)	10 (10)	1 (5)
Palpitation	6 (5)	4 (4)	2 (10)
Nausea and vomiting	4 (3)	3 (3)	1 (5)
Rhinobyon	3 (3)	2 (2)	1 (5)
Routine urinalysis			
Urine protein	21（18）	21（18）	0（0）
Urinary occult blood	14（12）	14（12）	0（0）
Symptom onset to hospital admission, median (IQR), days	5 (3-7)	5(3-7)	5 (4-9)
Symptom onset to laboratory confirmation via qRT-PCR, median (IQR), days	6 (4-9)	6 (4-8)	7 (5-11)
Symptom onset to negative detection via qRT-PCR, median (IQR), days	21 (18-24)	19 (15-21)	25 (23-27)

Abbreviations: IQR, interquartile range; Y, year.