follow-up by maximizing positive results. Extension of testing indications to contain the epidemic requires biologists to adapt their practices. A further study accurately describing clinical features would allow for a more appropriate prescription of tests.

Disclosure of interest

The authors declare that they have no competing interest.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki declaration and its later amendments.

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Interleukin-6 and severity of COVID-19 patients in Hefei, China

ARTICLE INFO

According to existing reports, the COVID-19 pandemic resulted in more than 20% of severe cases that required critical care, and the case fatality is around 2.84% [1]. In the present study, we analysed clinical and laboratory data from 75 patients with confirmed COVID-19 hospitalised in a designated hospital in Hefei, Anhui province, China, and investigated potential indicators for infection severity.

The most common laboratory abnormalities observed in this study were decreased total lymphocytes, prolonged APTT, elevated LDH, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Previous studies of COVID-19 patients in Wuhan suggested virus infection could induce a cytokine storm syndrome [2,3]. Here, most patients showed elevated inflammatory factors, e.g. CRP and ESR. Forty-nine patients were tested for IL-6, and 14 (28.57%) of them showed levels above the normal range, of which lymphocyte percentage, CD4$^+$, and CD8$^+$ T cell counts were significantly decreased and neutrophil percentage, CRP, and LDH levels increased significantly, compared with patients with normal IL-6 range.

Further analysis of severe/critical and non-severe (i.e., mild and moderate) groups demonstrated that the severe group had significantly increased IL-6, CRP, PCT, and LDH levels. On the contrary, the same group had significantly decreased lymphocyte percentage, CD4$^+$, and CD8$^+$ T cell counts although with higher number of total WBC and neutrophils (Fig. 1). PCT values were within normal range in both groups. This data indicated a potential correlation between increased IL-6 levels and severity of the viral infection and the resulting inflammation.

IL-6 is produced at the inflammation site and is the chief stimulator of the acute phase response [4]. A complex of IL-6 and sIL-6Rα can activate endothelial cells to secrete IL-8 and monocyte chemoattractant protein (MCP)-1, and induce expression of adhesion molecules [5]. IL-6 also elicits specific cellular and humoral immune responses, including end-stage B cell differentiation, immunoglobulin secretion, and T cell activation. Elevated IL-6 might lead to redistribution of T cells in the lung and respiratory tract in response to the viral infection observed post-mortem in COVID-19 patients [6].

Similarly to SARS-CoV, angiotensin converting enzyme II (ACE2) is also the cellular entry receptor of COVID-19 [7,8]. ACE2 is highly expressed in human lung tissues, the gastrointestinal tract, vascular endothelial cells, and arterial smooth muscle cells [9]. Therefore, all of these organs might be targets for virus attack. Our study showed that LDH levels were increased in 44% of patients and significantly increased in the patient with higher IL-6 production and liver and/or kidney dysfunction (Table 1). This data suggests strong evidence of multiple organ damage by the virus and predicts disease severity.

This study provides an assessment of the clinical and laboratory profiles of COVID-19 patients with various severity degrees in Hefei, China. Clinical manifestations of COVID-19 were non-specific. Hematological profiles including lymphocytes, LDH, CRP, and procalcitonin, especially IL-6, might be used
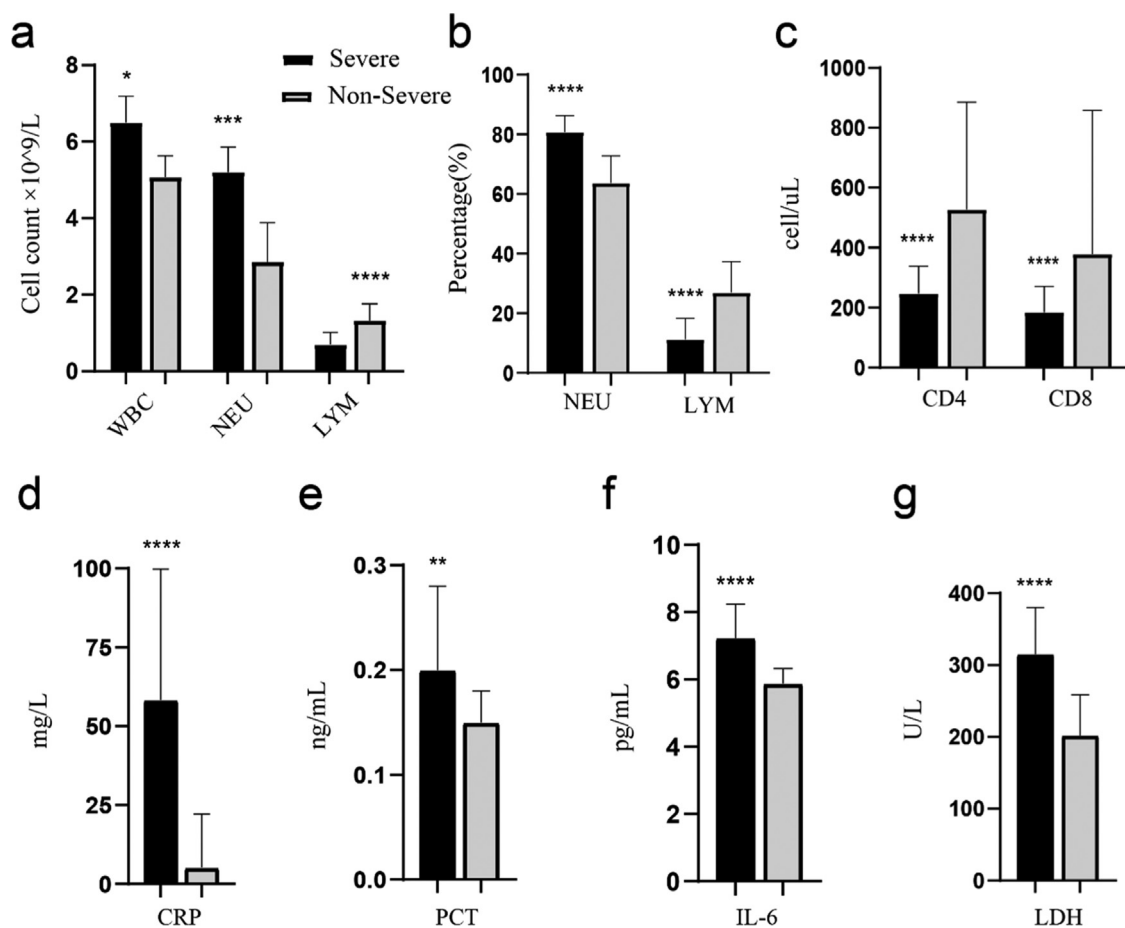
Fig. 1. Differences of laboratory findings between mild/moderate and severe/critical patients. (a) Absolute counts of WBC, neutrophils, and lymphocytes; (b) Percentage of neutrophils and lymphocytes; (c) CD4$^+$ and CD8$^+$ T cell counts; (d)–(f) Changes of infection indicators, CRP, PCT, and IL-6 in two groups; and (g) Detection of LDH levels. Data is presented as median (IQR) and analysed by Mann–Whitney test. All statistical analyses were performed using GraphPad Prism 8.3. *P* values indicate differences between mild/moderate and severe/critical patients (*$P < .05$, **$P < .005$, ***$P < .001$, ****$P < .0001$). $P < .05$ was considered statistically significant.
Différences des résultats de laboratoire entre les patients légers/modérés et sévères/critiques.

Table 1
Laboratory findings of patients with elevated and normal IL-6 level.
Comparaison des indices de laboratoire entre le groupe normal et le groupe élevé d'interleukine 6.

	Median (IQR)		P value
	Elevated IL-6 (*n* = 14)	Normal IL-6 (*n* = 35)	
Blood routine			
Leucocytes ($\times 10^9$ per L; normal range 3.5–9.5)	6.23 (4.13–6.86)	5.44 (3.9–6.63)	0.45
Neutrophils ($\times 10^9$ per L; normal range 1.8–6.3)	5.09 (3.36–5.66)	3.43 (1.81–4.75)	0.1055
Percentage of neutrophils (%; normal range 40–75)	78.02 (66.88–85.81)	70.54 (58.45–78.32)	0.0443*
Lymphocytes ($\times 10^9$ per L; normal range 1.1–3.2)	0.79 (0.53–1.11)	1.05 (0.67–1.79)	0.1055
Percentage of lymphocytes (%; normal range 20–50)	14.61 (8.52–24.03)	21.58 (14.15–32.59)	0.0264*
CD4 (cell/uL; normal range 410–1590)	322 (138.5–420.5)	511.6 (242.8–816.5)	0.0367*
CD8 (cell/uL; normal range 238–1250)	153.4 (119.2–228.4)	305.4 (179.6–651.8)	0.0021*
CD4/CD8 (normal range 0.9–3.6)	1.57 (0.930–2.46)	1.41 (0.53–1.78)	0.2081
Blood biochemistry			
Alanine aminotransferase (IU/L; normal range 7–40)	27.5 (13.5–43.75)	23 (16.00–47)	0.9782
Aspartate aminotransferase (IU/L; normal range 13–40)	27 (21.75–39.50)	28 (20–38)	0.6028
Total bilirubin (μmol/L; normal range 3.4–21.0)	13.45 (9.38–16.45)	14.3 (10.7–18.3)	0.5217
Serum creatinine (μmol/L; normal range 41–81)	72.5 (59.75–81.75)	67 (60–79)	0.5727
Creatine kinase (IU/L; normal range 22.0–269.0)	86.2 (66.95–240.3)	92.85 (56.45–144.3)	0.6619
Lactate dehydrogenase (U/L; normal range 120–250)	318 (252.5–408.8)	230 (177.8–319.3)	0.027*
Troponin I (ug/L; normal range 0–0.3)	0.26 (0.09–0.77)	0.08 (0.07–0.29)	0.0955
Infection-related biomarkers			
C-reactive protein (mg/L; normal range 0–8.0)	76.45 (21.53–110.5)	9.0 (3.26–23.10)	0.0003*
Erythrocyte sedimentation rate (mm/h; normal range 0–15)	69 (19.50–115.4)	29.10 (13.40–62.25)	0.127
Procalcitonin (ng/mL; normal range 0–0.5)	0.23 (0.17–0.29)	0.15 (0.11–0.18)	0.0017*

Note: data is presented as median (IQR) or *n* (%). Statistical analysis: Mann–Whitney test. *P* values indicate differences between patients with elevated and normal IL-6 level.
IL-6: interleukin-6.
* *P* < .05 was considered statistically significant.

as indicators for disease severity and guidance for COVID-19 treatment.

Ethical statement and approval

The study was approved by the Ethics Committee of the First Affiliated Hospital of USTC. All procedures performed in studies involving human participants complied with the 1964 Helsinki declaration and its later amendments.

Funding

Contribution

ZZ, MY, JJX, YY, and CD collected the clinical and laboratory data and drafted the article. YG and XM revised the final article and take responsibility for data integrity.

Disclosure of interest

The authors declare that they have no competing interest.

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