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BRIEF REPORT

Characteristics of laboratory indexes in COVID-19 patients with non-severe symptoms in Hefei City, China: diagnostic value in organ injuries

Tao Li[1,2] · Lianzi Wang[1] · Huihui Wang[1] · Yufeng Gao[3] · Xianwei Hu[4] · Xuemei Li[1] · Shubing Zhang[1] · Yuanhong Xu[1] · Wei Wei[2]

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Abstract

This study compared the laboratory indexes in 40 non-severe COVID-19 patients with those in 57 healthy controls. In the peripheral blood system of non-severe symptom COVID-19 patients, lymphocytes, eosinophils, basophils, total procollagen type 1 amino-terminal propeptide, osteocalcin N-terminal, thyroid-stimulating hormone, growth hormone, and insulin-like growth factor–binding protein 3 significantly decreased, and total protein, albumin, alanine transaminase, alkaline phosphatase, γ-glutamyl transferase, activated partial thromboplastin time, prothrombin time, fibrinogen, D-dimer, fibrinogen degradation products, human epididymal protein 4, serum ferritin, and C-reactive protein were elevated. SARS-CoV-2 infection can affect hematopoiesis, hemostasis, coagulation, fibrinolysis, bone metabolism, thyroid, parathyroid glands, the liver, and the reproductive system.

Keywords SARS-CoV-2 · COVID-19 · Organ injury · Laboratory index · Diagnostic value

Introduction

Since the unexplained viral pneumonia was reported in Wuhan in December 2019 [1], local, national, and international transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2] has enabled it to spread rapidly to 188 regions and countries around the world with more than 7 million confirmed infections and 402,699 deaths [3]. At present, there are many reports on the clinical characteristics of patients with severe disease and those who die [4–6]; however, there are few reports describing the clinical characteristics of non-severe patients. In this study, the clinical characteristics and laboratory indexes of 40 patients with non-severe COVID-19 treated in our hospital are described. Additionally, we explored the characteristics and changing trends in these laboratory indexes.

Subjects and methods

Subjects

This was a cross-sectional study that recruited 40 COVID-19 patients from the First Affiliated Hospital of Anhui Medical University in Hefei City, China, from 26 January 2020 to 8

✉ Tao Li
limedical1974@126.com

✉ Yuanhong Xu
xyhong1964@163.com

✉ Wei Wei
wwei@ahmu.edu.cn

1 Department of Clinical Laboratory, The First Affiliated Hospital of Anhui Medical University, No.218 Jixi road, Shushan District, Hefei 230032, Anhui Province, China

2 Institute of Clinical Pharmacology, Key Laboratory of Anti-inflammatory and Immune Medicine, Ministry of Education, Anhui Collaborative Innovation Center of Anti-inflammatory and Immune Medicine, Anhui Anti-inflammatory and Immune Medicine Innovation Team, Anhui Medical University, No. 81 Meishan road, Shushan District, Hefei 230032, Anhui Province, China

3 Department of Infectious Diseases, The First Affiliated Hospital of Anhui Medical University, Hefei 230032, China

4 Department of Respiratory and Critical Care Medicine, The First Affiliated Hospital of Anhui Medical University, Hefei 230032, China

March 2020, diagnosed on the basis of results from the nucleic acid reverse transcription polymerase chain reaction (RT-PCR) test as well as the pathological changes observed in computed tomography (CT) images, and 57 healthy individuals from the healthy examination center at the First Affiliated Hospital of Anhui Medical University over the same period, matched to the COVID-19 patients based on age and gender.

Biochemical measurements

Blood specimen collection

Two-milliliter blood samples were collected for all included participants after fasting for at least 8 h. It was left standing for 30 min and centrifuged for 5 min at 2352*g* within 2 h. The serum was subsequently used to measure the different levels of biochemical markers, and abbreviations for the various biochemical markers are shown in Table 1.

Furthermore, screening tests by serology for other pathogens were also conducted on the COVID-19 patients. These tests were conducted to identify the hepatitis C virus antibody, the *Treponema pallidum* antibody, the human immunodeficiency virus antibody, the hepatitis B surface antigen, the hepatitis B surface antibody, the hepatitis B e-antigen, the hepatitis B e-antibody, the hepatitis B core antibody, the serum IgM antibody for Q fever and rickettsia, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, parainfluenza (including subtypes 1, 2, and 3), respiratory syncytial virus, influenza A and B viruses, *Legionella pneumophila*, and adenovirus.

Outcomes measures

The COVID-19 patients and controls were assessed at four different time points based on the number of hospital admission days: time 1, the 1st day of admission; time 2, the 4th day of admission; time 3, the 7th day of admission; time 4, the 10th day of admission. All patients received four serological examinations.

Statistical analysis

SPSS (version 19) was used for the statistical analyses of the data. Two-sample *t* tests were used to analyze the differences in the continuous variables between two groups. One-way ANOVA was to analyze the differences in the continuous variables between multiple groups; thereafter, the SNK-*q* test was used to make comparisons between all of the groups. All continuous variables are expressed as means ± standard deviations (SD). Chi-squared tests (χ^2) were used for comparisons between categorical variables. *p* values less than 0.05 were considered statistically significant. Statistical charts were drawn using GraphPad Prism 8.

Table 1 Laboratory indexes and their abbreviation name

Full name	Abbreviation name
25-Hydroxy vitamin D_3	25(OH)D_3
Activated partial thromboplastin time	APTT
Alanine transaminase	ALT
Albumin	ALB
Albumin/globulin ratio	A/G
Aspartate aminotransferase	AST
Basophil counts	BASO#
Calcium	Ca
C-reactive protein	CRP
Creatine phosphokinase	CK
Creatine phosphokinase-MB	CK-MB
Creatinine	CRE
D-dimer	D-D
Eosinophil counts	EO#
Estimated glomerular filtration rate	eGFR
Fibrinogen	FIB
Fibrinogen degradation products	FDP
Free 3,5,3′-triiodothyronine	FT3
Globulin	GLB
Growth hormone	GH
Human epididymal protein 4	HE4
Insulin-like growth factor–binding protein 3	IGFBP-3
Interleukin 1 beta	IL-1β
Interleukin 8	IL-8
Lymphocyte counts	LYMPH#
Monocyte counts	MONO#
Myoglobin	MY
Osteocalcin N-terminal in the middle	N-MID OC
Parathyroid hormone	PTH
Progastrin-releasing peptide	ProGRP
Prothrombin time	PT
Serum ferritin	SF
Thyroid-stimulating hormone	TSH
Total procollagen type 1 amino-terminal propeptide	P1NP
Total protein	TP
Urea	UREA
α-Hydroxybutyrate dehydrogenase	α-HBDH

Results

Changes in white blood cells in peripheral blood

The LYMPH, EO, and BSO counts in patients with COVID-19 were significantly lower, compared with the controls on the 1st, 4th, 7th, and 10th days of admission, while the MONO counts were significantly higher in COVID-19 patients (Fig. 1a–d). LYMPH, EO, and BSO all presented upward trends.

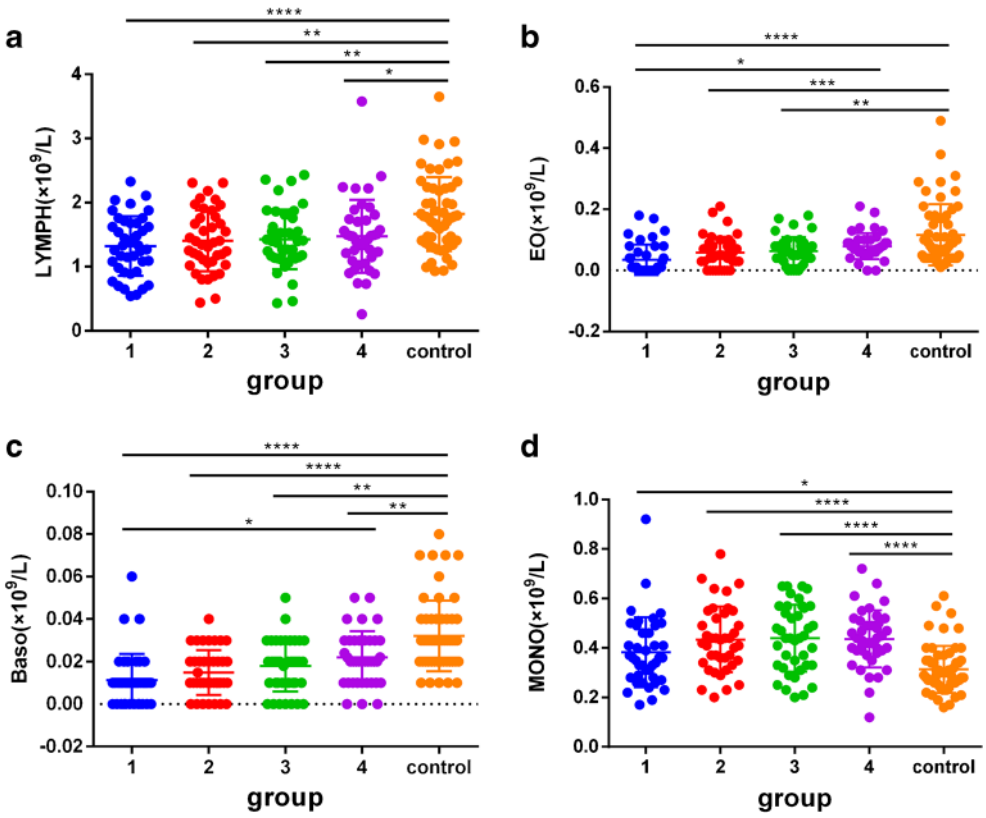

Fig. 1 The LYMPH, EO, BSO, and MONO counts in patients with COVID-19 (**a**–**d**)

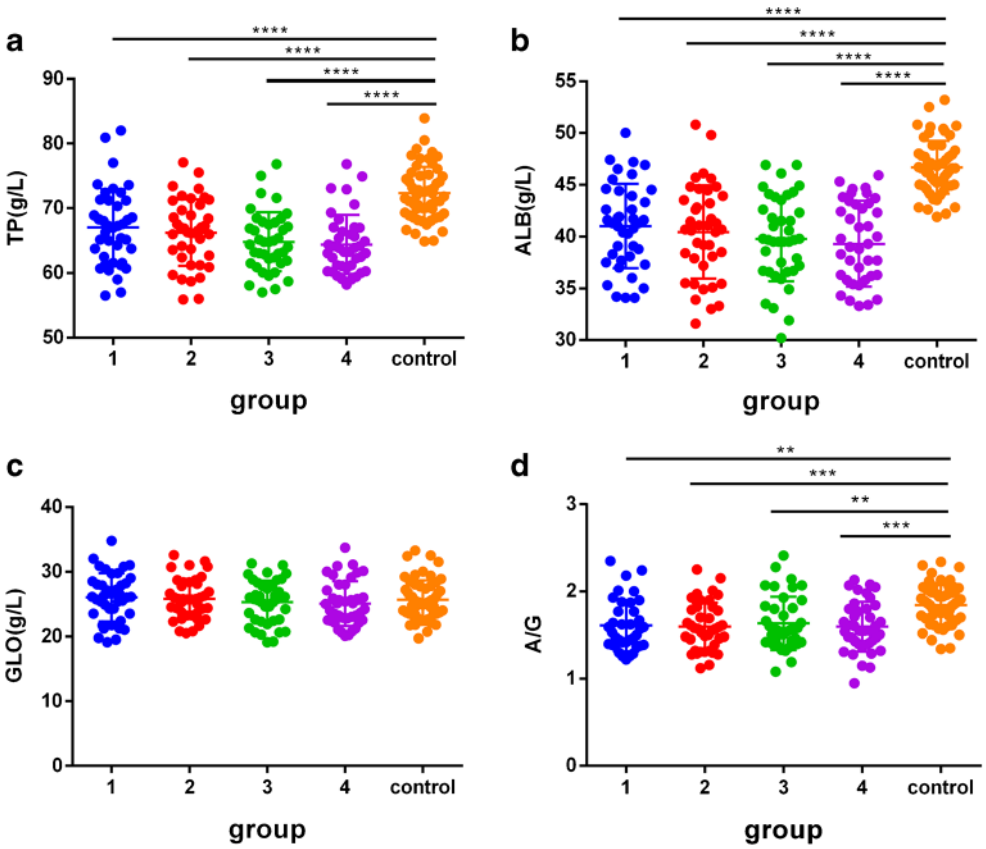

Fig. 2 TP, ALB, GLO, and A/G concentrations (**a**–**d**)

Table 2 Baseline characteristics of laboratory tests in patients with COVID-19 (mean ± SD)

	COVID-19 ($n = 40$)	Control ($n = 57$)	t	p
Age (years)	43.85 ± 12.84	47.77 ± 11.46	− 1.578	0.118
LYMPH ($\times 10^9$/L)	1.31 ± 0.463	1.82 ± 0.577	− 4.505	0.000
MONO ($\times 10^9$/L)	0.37 ± 0.137	0.31 ± 0.095	2.411	0.018
EO ($\times 10^9$/L)	0.03 ± 0.048	0.12 ± 0.10	− 5.522	0.000
BSO ($\times 10^9$/L)	0.01 ± 0.013	0.03 ± 0.0167	− 6.354	0.000
TP (g/L)	67.0 ± 5.673	72.3 ± 4.078	− 5.207	0.000
ALB (g/L)	41.0 ± 4.067	46.7 ± 2.551	− 7.543	0.000
GLO (g/L)	26.0 ± 3.681	25.6 ± 3.031	− 0.566	0.573
A/G	1.61 ± 0.292	1.81 ± 0.332	− 3.048	0.003
ALT (U/L)	24 ± 13.386	21 ± 7.748	1.266	0.211
AST (U/L)	25 ± 12.013	20 ± 6.779	2.451	0.018
CRE (μmol/L)	70.58 ± 15.41	58.80 ± 11.68	3.955	0.000
eGFR (mL/(min·1.73 m^2))	107.76 ± 15.37	114.93 ± 10.76	− 2.467	0.017
UREA (mmol/L)	4.191 ± 1.211	4.781 ± 1.101	− 2.429	0.017
D-D (μg/mL)	0.50 ± 0.495	0.22 ± 0.112	3.155	0.003
APTT (s)	38.52 ± 3.619	35.50 ± 3.691	3.802	0.000
FDP (μg/mL)	2.08 ± 1.343	1.06 ± 0.564	4.222	0.000
FIB (g/L)	4.14 ± 1.129	2.73 ± 0.791	6.390	0.000
PT-INR	1.03 ± 0.0602	0.98 ± 0.060	3.836	0.000
PT (s)	13.5 ± 0.691	13.0 ± 0.617	3.640	0.000
P1NP (ng/mL)	42.92 ± 17.718	55.90 ± 18.552	− 3.185	0.002
N-MID OC (ng/mL)	8.84 ± 5.367	12.06 ± 4.4630	− 3.002	0.004
PTH (pg/mL)	44.71 ± 19.026	38.64 ± 10.099	1.674	0.102
25(OH)D_3 (ng/mL)	13.82 ± 4.356	23.71 ± 8.236	− 7.407	0.000
GH (ng/mL)	0.53 ± 0.569	1.53 ± 2.358	− 3.023	0.004
IGFBP-3 (μg/mL)	3.40 ± 0.980	4.73 ± 1.123	− 5.424	0.000
TSH (μIU/mL)	2.13 ± 0.948	2.75 ± 1.358	− 2.446	0.017
FT3 (pmol/L)	4.57 ± 0.825	5.29 ± 0.913	− 3.678	0.000
Ca (mmol/L)	2.17 ± 0.122	2.31 ± 0.109	− 5.373	0.000
ProGRP (pg/mL)	9.97 ± 4.651	13.95 ± 4.805	− 3.753	0.000
HE4 (pmol/L)	55.58 ± 22.655	37.77 ± 13.427	4.062	0.000
SF (μg/L)	475.85 ± 478.382	178.20 ± 136.845	3.442	0.002
IL-1β (pg/mL)	5.00 ± 0.000*	13.90 ± 13.417	− 5.007	0.000
IL-8 (pg/mL)	6.99 ± 3.53	330.62 ± 552.55	− 4.442	0.000
CRP (mg/L)	17.10 ± 21.125	0.99 ± 0.631	4.638	0.000

*Because the concentrations of IL-1β in patients and IL-10 in controls are below the lower limit of the measurement range, we use the lower limit value of the measurement range as statistical data

Analyses of liver, skeletal muscle, and myocardial indexes

TP and ALB decreased significantly compared with the controls and showed a progressive downward trend, but GLO was increased, which led to the decrease of A/G (1.655 ± 0.305 VS 1.844 ± 0.223, $p = 0.004$) (Fig. 2a–d). Overall, 62.5% of the patients had a transient increase in ALT and/or AST (Table 2); eight of them had a simultaneous increase in α-HBDH, MY, CK, or CK-MB suggesting that these patients had liver injuries and some patients had skeletal muscle injuries (Table 2).

Analyses of biochemical indexes of renal function

There were abnormalities in CRE, eGFR, UREA, and Ca^{2+} in COVID-19 patients (Figs. 3a–c). In the process of continuous monitoring, the expression of CRE in patients with COVID-19 were significantly lower than those in the controls on the 1st, 4th, and 7th days of admission, and showed an overall downward trend (Fig. 3a). The expression of Ca^{2+} in patients with COVID-19 were significantly lower than those in the controls on the 1st, 4th, 7th and 10th days of admission, and showed an overall upward trend (Fig. 3d).

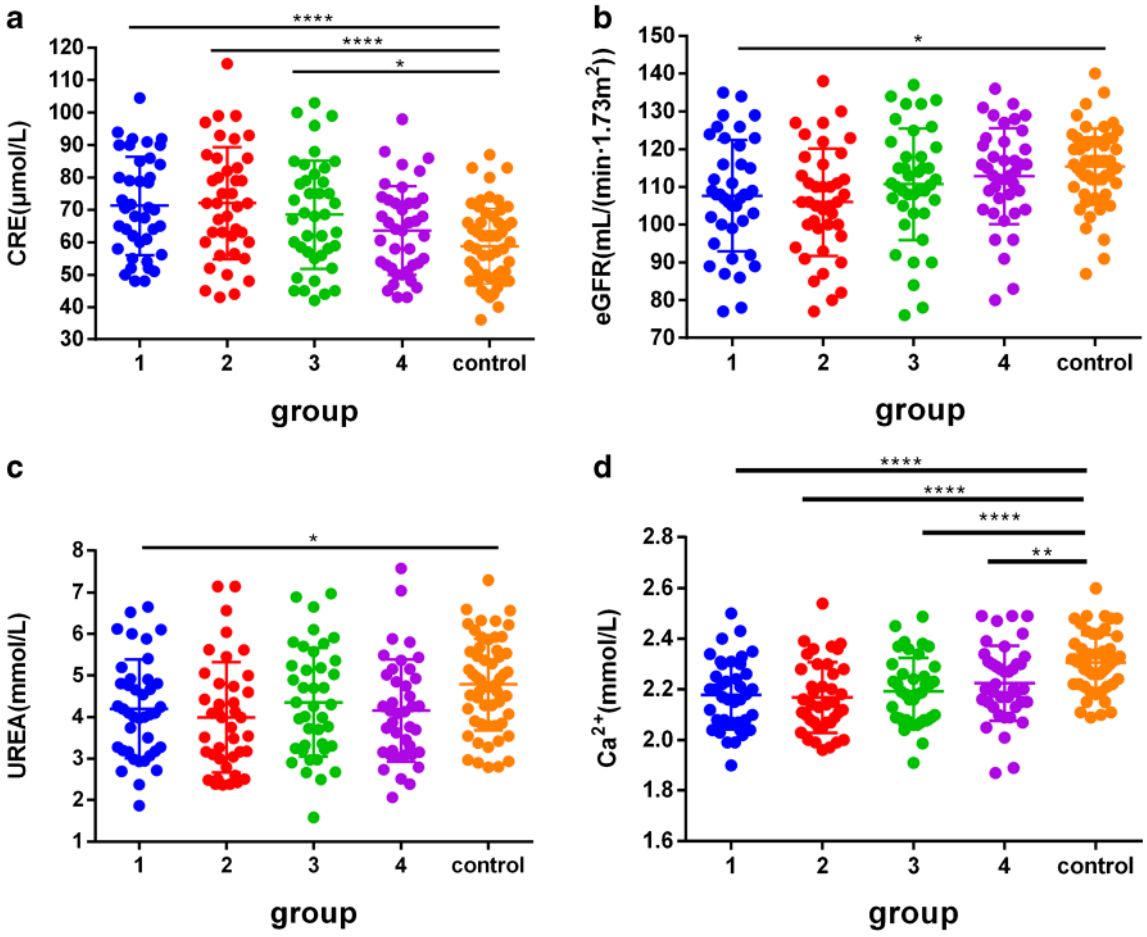

Fig. 3 Abnormalities in CRE, eGFR, UREA, and Ca2+ in COVID-19 patients (**a**–**d**)

Analyses of hemostasis, coagulation, and fibrinolysis-related systems

APTT and PT for COVID-19 patients were significantly longer than those in controls, and FDP, D-D, FIB, and PT-INR were higher compared with those in the controls (Table 2 and Fig. 4a–f). The expression of FIB in patients with COVID-19 were significantly higher as compared with those in the controls on the 1st, 4th, 7th, and 10th days of admission, and 50% of the patients' results were higher than the reference range (Table 2).

Analyses of thyroid axis and growth hormone axis–related markers, the parathyroid gland, and bone metabolism–related markers

The expression of PTH was elevated in COVID-19 patients on the 4th, 7th, and 10th days of admission (Table 2 and Fig. 5a). The expression of TSH, FT3, P1NP, N-MID OC, 25(OH)D_3, GH, and IGFBP-3 in COVID-19 patients decreased compared with those in controls (Fig. 5b–h).

Analyses of carbohydrate antigens, other cellular antigens, and cytokines

The expression of HE4, SF, and CRP significantly increased in COVID-19 patients during the early stages of the disease (Fig. 6b–d). However, the expression of ProGRP, IL-1β, and IL-8 significantly decreased in COVID-19 patients compared with those in controls (Fig. 6a, e, f).

Discussion

Our study found that in the early stages of disease, LYMPH, EO, and BSO counts were lower in COVID-19 patients than in controls. In acute infection or inflammation, the number of circulating EOs decreases rapidly and continuously [7]. It is worth noting that two eosinophil granule proteins, eosinophil cationic protein (ECP) and eosinophil-derived neurotoxin (EDN), neutralize most viruses [8]. The decreasing ESO in COVID-19 patients may be caused by the SARS-CoV-2 virus attacking ECP and

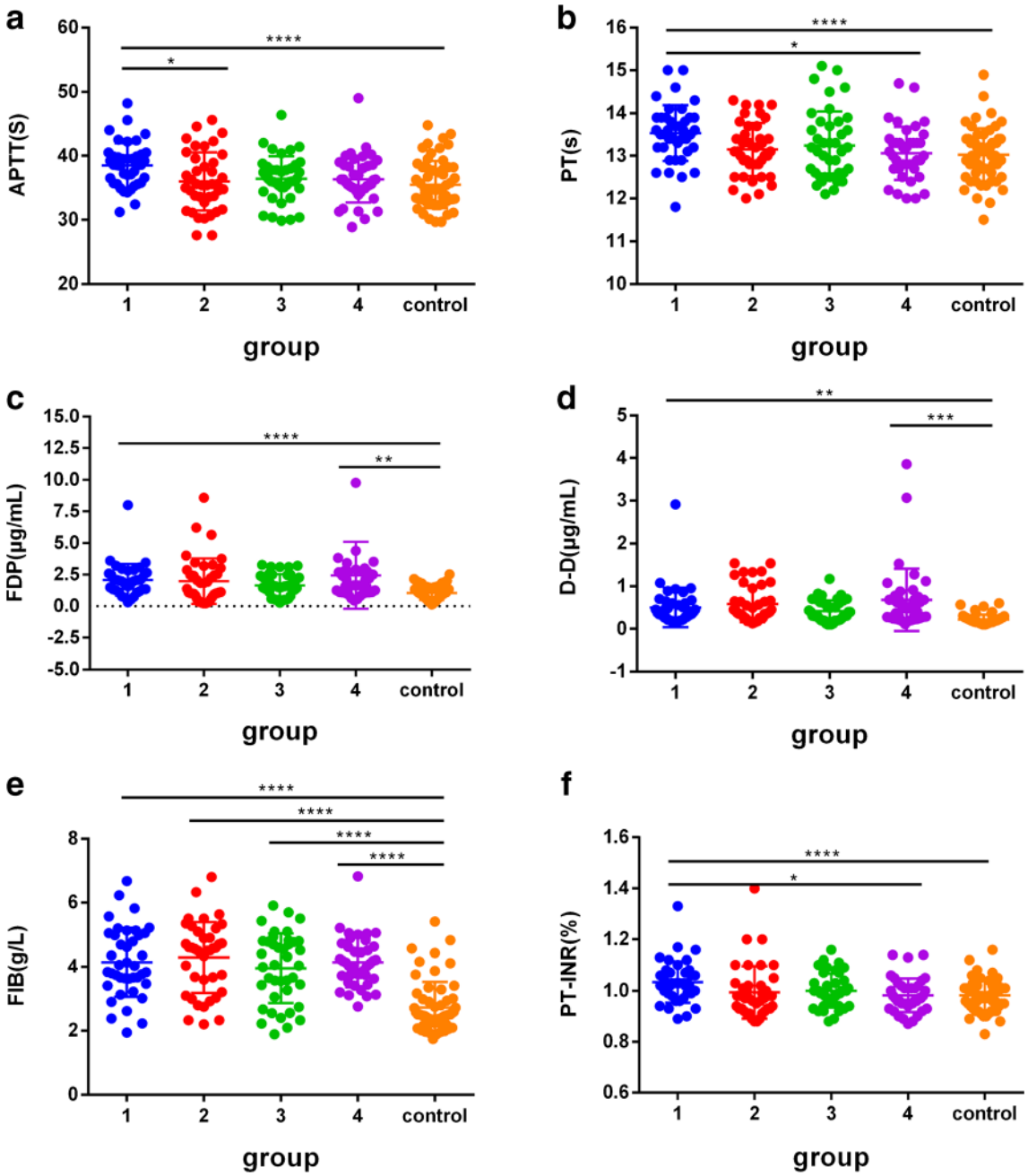

Fig. 4 APTT and PT duration and FDP, D-D, FIB, and PT-INR concentrations (**a**–**f**)

EDN. Besides, both BSO and EO can produce IL-4, which is an important cytokine to stimulate the proliferation of activated B and T cells [9]. Therefore, the decrease of EO and BSO counts in COVID-19 patients may further lead to the decrease of LYMPH counts. Impairment of liver function caused by SARS-CoV-2 has also been reported in many studies recently [10, 11]. Our results showed that the serum TP and ALB of patients decreased significantly while the level of GLO increased, leading to the abnormal frequency of A/G in the early stages of the disease. Additionally, the discovery that eight COVID-19 patients had a simultaneous increase in α-HBDH, MY, CK, or CK-MB suggested that we should pay attention to patients with different degrees of skeletal muscle injuries.

It has been reported that the human kidneys are a specific target for SARS-CoV-2 infection [12]. Our results showed that there were abnormalities in CRE, eGFR, and UREA in COVID-19 patients, mainly in CRE. In the process of continuous monitoring, we also found that the CRE levels on the 1th, 4th, and 7th day of admission in COVID-19 patients were

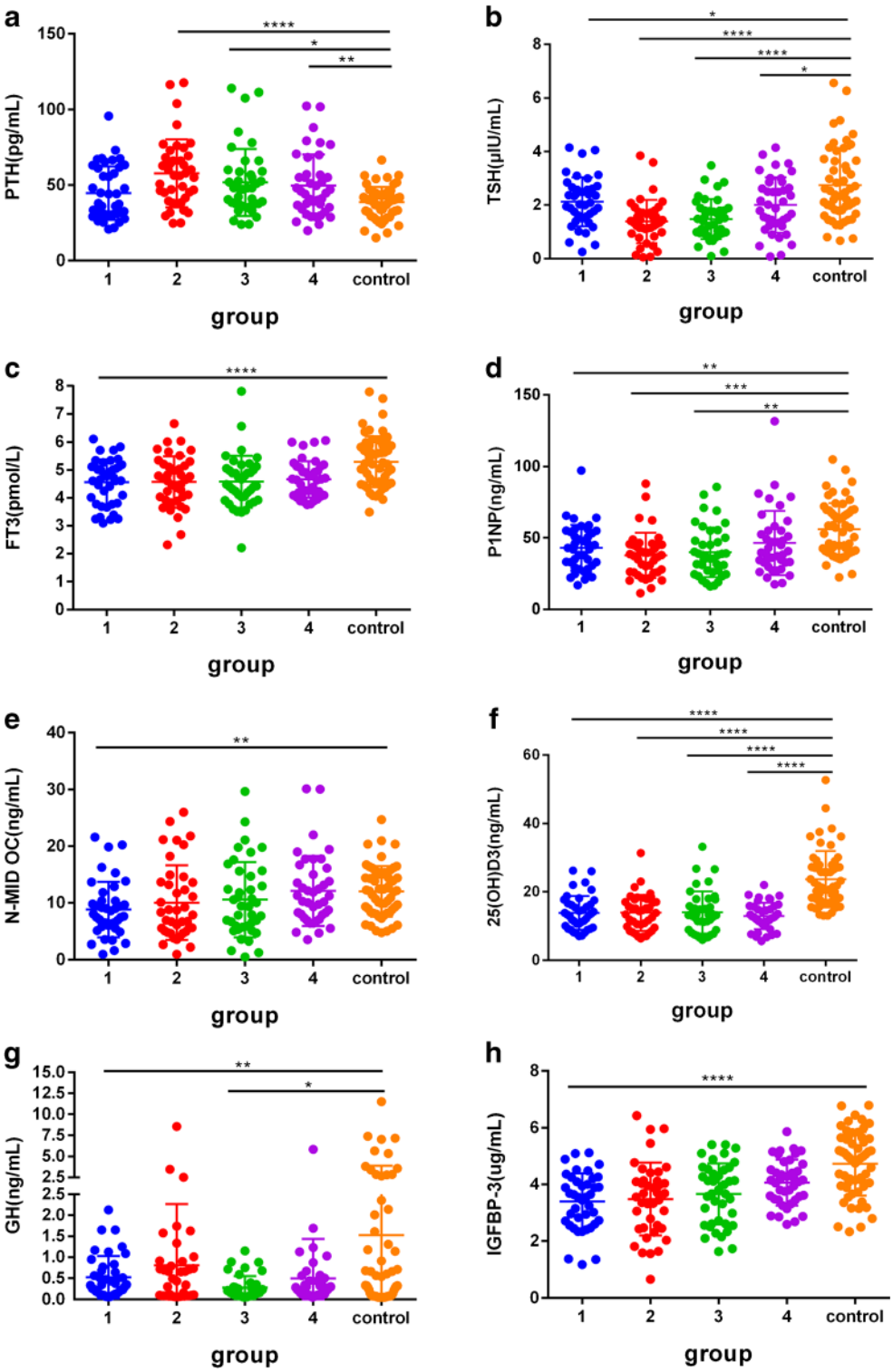

Fig. 5 The expression of TSH, FT3, P1NP, N-MID OC, 25(OH)D3, GH, and IGFBP-3 in COVID-19 patients (**a**–**h**)

significantly higher than those in the controls suggesting that SARS-CoV-2 virus might infect the kidneys of the patients, with the potential to cause renal damage.

Our results also showed that the APTT of COVID-19 patients were longer than that of controls, and the indexes of FDP, D-D, and FIB were higher than those of the control, suggesting that SARS-CoV-2 has an important effect on the hematopoietic system and hemostasis. Coagulation abnormalities such as prolonged PT and APTT, increased fibrin degradation products, and disseminated intravascular coagulation (DIC) require continuous vigilance and timely interventions.

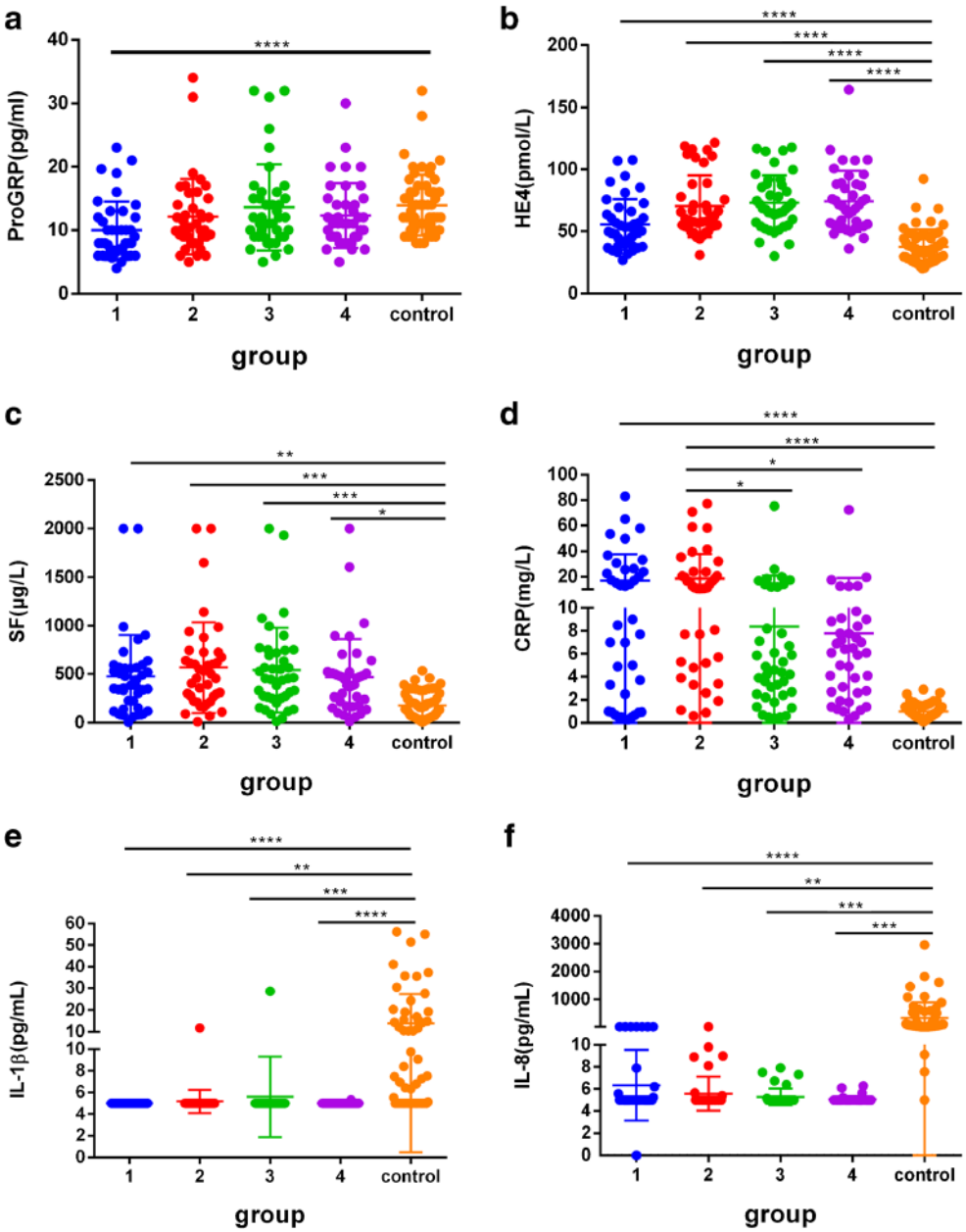

Fig. 6 The expression of HE4, SF, CRP, ProGRP, IL-1β, and IL-8 in COVID-19 patients (**a**–**f**)

We found that N-MID OC, PINP, and TSH were significantly decreased, while PTH increased in COVID-19 patients. Some studies have already highlighted that SARS-CoV-2 can affect thyroid function [13, 14]. Therefore, thyroid damage caused by SARS-CoV-2 also needs further exploration. We found that GH and IGFBP-3 significantly decreased in the serum of COVID-19 patients, suggesting that SARS-CoV-2 may invade the central nervous system. Baig et al. reported that the detection of SARS-CoV-2 in the cerebrospinal fluid of COVID-19 patients suggests that the CNS may be invaded by SARS-COV-2 [13].

Inflammatory infection can promote the synthesis of ferritin and lead to an increase in ferritin. Our study showed that SF and CRP abnormally increased in COVID-19 patients. An analysis of the data from 21 COVID-19 patients showed that the performance of SF in the patients significantly differed from that in the healthy control, which is consistent with our findings [5]. SF needs to be further studied to assist in the diagnosis of SARS-CoV-2 infection or to be used to monitor disease activity, and response to treatment in SARS-CoV-2 patients.

This study had some limitations. First, our sample size was small thus limiting the validity of our findings. Second, the cross-sectional survey used in this study limited our ability to identify etiological factors associated with COVID-19 patients. Third, we were unable to obtain all the clinical and treatment information of the subjects enrolled in the study, which limited us to having an analysis combined with clinical feature and limited us in explaining the phenomenon

caused by SARS-CoV-2. In further studies, we could focus on the specific biochemical marker difference in COVID-19 patients, and try to figure out the mechanism.

Conclusions

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection can affect hematopoiesis, hemostasis, coagulation, fibrinolysis, bone metabolism, thyroid and parathyroid glands, the liver, and the reproductive system.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflicts of interest.

Ethics approval This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Ethics Committee of the First Affiliated Hospital of Anhui Medical University approved this study and waived informed consent as a retrospective observational study.

Informed consent This study was a retrospective study, so formal consent was not required.

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