A 3-Week Dynamic Differences of Immunological Parameters in Severe and Non-severe COVID-19

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Abstract

Objective We aimed to compare the dynamic differences of immunological parameters in severe and non-severe COVID-19.

Methods In this study, the cytokine profiles and lymphocyte subsets of 70 patients (31 severe COVID-19 and 39 non-severe COVID-19) were longitudinally analyzed.

Results Compared with non-severe cases, severe cases had higher age (64 vs 36 years, $p < 0.001$), more common comorbidities (74.2% vs 15.4%, $p < 0.001$), and more frequently lymphopenia (0.7 vs $1.6 \times 10^9/L$, $p < 0.001$). Severe cases had markedly higher levels of IL-6, IL-8, and IL-10 than non-severe cases from baseline to 3 weeks after admission ($p < 0.001$). No significant differences were observed in the levels of IL-1 β , IL-2, IL-4, IL-5, IL-12P70, IL-17, TNF- α , IFN- α , and IFN- γ between the two groups during the follow-up ($p > 0.05$). The absolute numbers of CD3+, CD4+, CD8+, and CD45+ T cells were markedly lower in severe cases compared with that in non-severe cases from baseline to 3 weeks after admission ($p < 0.001$). The decrease of T lymphocyte subsets reached its peak from day 1 to 3 after admission, and gradually increased from day 4 to 21 in the non-severe group; however, reached its peak from day 4 to 7 after admission, and sustained at a low levels in the severe group.

Conclusion The dynamic changes of cytokine profiles and T lymphocyte subsets are related with the disease severity of patients with COVID-19.

Introduction

Since November 2019, the rapid outbreak of 2019 novel coronavirus disease (COVID-19), which caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global public health emergency. Person-to-person transmission of SARS-CoV-2 has been confirmed in hospital and family settings ^[1]. The number of confirmed cases and death cases has been quickly growing, and as of June 16th, 2020, there have been 7941, 791 confirmed cases and 434, 796 deaths globally ^[2]. The clinical characteristics of COVID-19 had been reported in numerous researches, which suggested that most patients with COVID-19 had a good prognosis, but there were still some patients developed to severe cases rapidly, and then resulting in death ^[3].

The key point in the disease progression of COVID-19 could be the depletion of antiviral defenses related to innate immune response as well as an elevated production of inflammatory cytokines ^[4]. Cytokines are a broad category of relatively small proteins (< 40 kDa) that are produced and released with the aim of cell signaling ^[5]. Recently, more and more data suggest that there are cytokine storms in severe patients with COVID-19, which is an important cause of death ^[6]. Huang et al analyzed the first 41 cases with COVID-19, and found that compared with non-ICU patients, ICU patients had higher plasma levels of cytokines, which could be associated with disease severity ^[7]. Chen et al analyzed 21 cases with COVID-19, and found that compared with moderate cases, severe cases had markedly higher levels of cytokines,

and markedly lower numbers of T lymphocytes, CD4 + T cells, and CD8 + T cells ^[8]. Ulhaq et al also presented the evidence that circulating IL-6 levels are closely linked to the severity of COVID-19 ^[9].

Although there are some reports on the baseline levels of immunological parameters in patients with COVID-19, the data about the dynamics of cytokines and T lymphocyte subsets in patients with COVID-19 is relatively few. In this study, we performed a 3-week dynamic comparison of immunological parameters between 31 severe and 39 non-severe cases with COVID-19. The results may help us extend our understanding of the risk factors associated with disease severity following the SARS-CoV-2 infection.

Methods

Study participants

From January 20th 2020 to June 10th 2020, a total of 31 severe cases with COVID-19 hospitalized in Shanghai Public Health Clinical Center, Shanghai, China, were enrolled into this study. As a comparison group, 39 non-severe cases with COVID-19 hospitalized in Shanghai Public Health Clinical Center from May 1th 2020 to May 14th 2020 were enrolled. All patients were confirmed infected with SARS-CoV-2 by the Chinese Center for Disease Control and Prevention.

Diagnostic criteria

Patients with COVID-19 were confirmed by the positive results of SARS-CoV-2 nucleotides tests in the nasopharyngeal or throat swab specimens using the real-time polymerase-chain-reaction (RT-PCR) methods ^[10]. According to the guidelines released by the National Health Commission of China, severe cases with COVID-19 were defined as at least one of the followings ^[11]: (1) Respiratory rates $\geq 30/\text{min}$; (2) Oxygen saturation $\leq 93\%$ in a resting state; (3) Oxygenation index ($\text{Pao}_2/\text{Fio}_2$) $\leq 300 \text{ mmHg}$; (4) Require mechanical ventilation; (5) Shock; (6) Combined with other organ failures and needed treatment in ICU.

Laboratory measurements

The SARS-CoV-2 nucleic acids were detected by RT-PCR methods using automatic magnetic extraction device and accompanying kit (Shanghai Bio-Germ) and screened with a semi-quantitative RT-PCR kit (Shanghai Bio-Germ) with amplification targeting the ORF1a/b and N gene. Conditions for the amplifications were 50 °C for 15 minutes, 95 °C for 3 minutes, followed by 45 cycles of 95 °C for 15 seconds and 60 °C for 30 seconds. The lymphocyte test kits (Becton Dickinson and Company, California, USA) were used for the lymphocyte subset analysis. Twelve plasma cytokines (IL-1 β , IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL-12P70, IL-17, TNF- α , IFN- α , and IFN- γ) were detected using the human cytokine kit II (Raisecare Ltd, Qingdao, China). All tests were performed according to the manufacturers' instructions.

Data collection

We retrospectively evaluated the medical records including clinical charts, nursing records, laboratory findings, radiological tests, and immunological results obtained from 70 enrolled patients with COVID-19. The data about demographics, epidemiological characteristics, clinical characteristics, laboratory findings, radiological manifestations, treatment, and clinical outcomes were obtained with data collection forms. The data of cytokine profiles and lymphocyte subsets were obtained from baseline to 3 weeks after admission. The data collection forms were reviewed independently by 2 researchers.

Statistical analyses

The normality test was performed for continuous variables using the Kolmogorov-Smirnov test. Normal distribution variables were expressed as mean $\pm$ standard deviation (SD) and compared using the T test. Non-normal distribution continuous variables were presented as medians [interquartile ranges (IQR)], and compared with the Mann-Whitney test. Categorical variables were showed as numbers (percentage), and compared by the chi-square test. All significance tests were two-tailed, and $p < 0.05$ was considered statistically significant. All statistical analyses were done using SPSS software version 15.0 (SPSS Inc. USA).

Results

Demographics and clinical characteristics of patients with COVID-19

Demographics and clinical characteristics of patients with COVID-19 are shown in Table 1. The mean age was 49 ± 20 years, 52 (74.3%) were men, and 29 (41.4%) patients had comorbidities, including hypertension (18 [25.7%]), diabetes (11 [15.7%]), cardiovascular disease (7 [10%]), chronic pulmonary disease (4 [5.7%]), cerebrovascular disease (2 [2.9%]), chronic kidney disease (2 [2.9%]), and malignancy (1 [1.4%]). The common symptoms were fever (37 [52.9%]), cough (32 [45.7%]), dyspnea (9 [12.9%]), and fatigue (8 [11.4%]). All patients received antiviral agents including Lopinavir/Ritonavir, Oseltamivir, Emtricitabine/Tenofovir, Interferon-alpha, Hydroxychloroquine, Arbidol, and Chinese medicine.

Table 1
Demographics and clinical characteristics of patients with COVID-19

	All (n = 70)	Severe (n = 31)	Non-severe (n = 39)	P value
Characteristics				
Age (years)	49 ± 20	64 ± 14	36 ± 14	< 0.001
Male, n (%)	52 (74.3%)	24 (77.4%)	28 (71.8%)	0.593
Any comorbidity, n (%)	29 (41.4%)	23 (74.2%)	6 (15.4%)	< 0.001
Hypertension	18 (25.7%)	16 (51.6%)	2 (5.1%)	< 0.001
Diabetes	11 (15.7%)	8 (25.8%)	3 (7.7%)	0.039
Cardiovascular disease	7 (10%)	7 (22.6%)	0	0.002
Chronic pulmonary disease	4 (5.7%)	3 (9.7%)	1 (2.6%)	0.203
Cerebrovascular disease	2 (2.9%)	2 (6.5%)	0	0.108
Chronic kidney disease	2 (2.9%)	2 (6.5%)	0	0.108
Malignancy	1 (1.4%)	1 (3.2%)	0	0.259
Symptoms				
Fever, n (%)	37 (52.9%)	26 (83.9%)	11 (28.2%)	< 0.001
Cough, n (%)	32 (45.7%)	15 (48.4%)	17 (43.6%)	0.689
Dyspnea, n (%)	9 (12.9%)	9 (29.0%)	0	< 0.001
Fatigue, n (%)	8 (11.4%)	6 (19.4%)	2 (5.1%)	0.063
Treatments				
Antiviral therapy	70 (100%)	31 (100%)	39 (100%)	
Corticosteroids	28 (40%)	26 (83.9%)	2 (5.1%)	< 0.001
Intravenous immunoglobulin	27 (38.6%)	27 (87.1%)	0	< 0.001
Thymosin-α1	35 (50%)	26 (83.9%)	9 (23.1%)	< 0.001
Hospital stays (days)	29 ± 23	42 ± 29	19 ± 7	< 0.001
The p values indicate differences between severe group and non-severe group. $p < 0.05$ was considered statistically significant.				

The mean age of severe cases was higher than non-severe cases (64 vs 36 years). Compared with non-severe cases, severe cases had more common comorbidity (74.2% vs 15.4%, $p < 0.001$), fever (83.9% vs 28.2%, $p < 0.001$), and dyspnea (29.0% vs 0, $p < 0.001$). More patients received corticosteroids (83.9% vs

5.1%, $p < 0.001$), intravenous immunoglobulin (87.1% *vs* 0, $p < 0.001$), and thymosin- α 1 (83.9% *vs* 23.1%, $p < 0.001$) therapy in severe group, compared with that in non-severe group. The mean hospital stays of severe cases is significant longer than that of non-severe cases (42 *vs* 19 days, $p < 0.001$).

Laboratory findings of patients with COVID-19

Laboratory findings of patients with COVID-19 are shown in Table 2. The median levels of white blood count (WBC), lymphocyte count, aspartate aminotransferase (AST), total bilirubin, blood urea nitrogen (BUN), creatinine, creatine kinase (CK), D-dimer, procalcitonin, and C-reactive protein were $5.8 (4.3-7.6) \times 10^9/L$, $1.3 (0.7-1.6) \times 10^9/L$, 24 (18-36) U/L, 10.2 (8.0-14.0) $\mu\text{mol/L}$, 4.5 (3.8-5.6) mmol/L , 70 (57-81) $\mu\text{mol/L}$, 126 (88-241) U/L, 0.46 (0.26-1.08) ng/mL , 0.08 (0.03-0.11) ng/mL , and 3.4 (0.5-40.8) mg/L , respectively. The mean levels of platelet, alanine aminotransferase, and lactate dehydrogenase (LDH) were $207 \pm 78 \times 10^9/L$, 29 ± 17 U/L, and 295 ± 140 U/L, respectively. Compared with non-severe cases, severe cases had significantly lower lymphocyte (0.7 *vs* $1.6 \times 10^9/L$, $p < 0.001$) and platelet counts (181 *vs* $227 \times 10^9/L$, $p = 0.014$); but significantly higher levels of AST (41 *vs* 21 U/L, $p < 0.001$), BUN (5.2 *vs* 4.2 mmol/L , $p = 0.010$), CK (209 *vs* 104 U/L, $p < 0.001$), LDH (405 *vs* 208 U/L, $p < 0.001$), D-dimer (1.17 *vs* 0.27 ng/mL , $p < 0.001$), procalcitonin (0.12 *vs* 0.04 ng/mL , $p < 0.001$), and CRP (39.9 *vs* 0.5 mg/L , $p < 0.001$)

Table 2
Laboratory findings of patients with COVID-19

	All (n = 70)	Severe (n = 31)	Non-severe (n = 39)	P value
WBC (10 ⁹ /L)	5.8 (4.3–7.6)	4.9 (3.5–7.9)	5.8 (4.8–7.3)	0.291
Lymphocyte (10 ⁹ /L)	1.3 (0.7–1.6)	0.7 (0.5–0.9)	1.6 (1.3–1.9)	< 0.001
Platelet (10 ⁹ /L)	207 ± 78	181 ± 71	227 ± 79	0.014
ALT (U/L)	29 ± 17	32 ± 18	26 ± 16	0.181
AST (U/L)	24 (18–36)	44 (24–52)	21 (17–24)	< 0.001
TBIL (umol/L)	10.2 (8.0–14.0)	10.3 (8.6–14.2)	10.0 (6.2–14.0)	0.304
BUN (mmol/L)	4.5 (3.8–5.6)	5.2 (4.1–9.3)	4.2 (3.7–4.8)	0.010
Creatinine (umol/L)	70 (57–81)	80 (56–98)	69 (59–74)	0.085
CK (U/L)	126 (88–241)	209 (113–365)	104 (66–140)	< 0.001
LDH (U/L)	295 ± 140	405 ± 138	208 ± 55	< 0.001
D-dimer (ng/mL)	0.46 (0.26–1.08)	1.17 (0.56–1.85)	0.27 (0.21–0.45)	< 0.001
PCT (ng/mL)	0.08 (0.03–0.11)	0.12 (0.05–0.53)	0.04 (0.02–0.10)	< 0.001
CRP (mg/L)	3.4 (0.5–40.8)	39.9 (21.7–82.9)	0.5 (0.5–1.3)	< 0.001
WBC, white blood count; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; BUN, blood urea nitrogen; CK, creatine kinase; LDH, lactate dehydrogenase; PCT, procalcitonin; CRP, C-reactive protein; The p values indicate differences between severe group and non-severe group. $p < 0.05$ was considered statistically significant.				

Dynamic changes of cytokine profiles in patients with COVID-19

In this study, we combined the longitudinal cytokines data of severe group and non-severe group, and plotted their fluctuation patterns against the time point after admission (Fig. 1). Fluctuations in the serum levels of cytokines in the non-severe cases were minor. In contrast, the severe group showed more significant fluctuations in the serum levels of cytokines. Severe cases had markedly higher levels of IL-6, IL-8, and IL-10 than non-severe cases from baseline to 3 weeks after admission ($p < 0.001$) (Table 3). No significant differences were observed in the levels of IL-1 β , IL-2, IL-4, IL-5, IL-12P70, IL-17, TNF- α , IFN- α , and IFN- γ between the two groups during the follow-up ($p > 0.05$) (Fig. 1).

Table 3
Comparison in the levels of cytokine profiles between severe and non-severe group

		Severe (n = 31)	Non-severe (n = 39)	P value
IL-6 (pg/ml)	Baseline	38.88 (21.52–77.68)	0 (0–0)	< 0.001
	1 week	76.69 (45.77–214.80)	0 (0–0)	< 0.001
	2 week	64.42 (4.02–135.70)	0 (0–0)	< 0.001
	3 week	90.27 (20.20–298.71)	0 (0–0)	< 0.001
IL-8 (pg/ml)	Baseline	7.72 (2.78–23.79)	0.93 (0.34–2.41)	< 0.001
	1 week	9.55 (1.89–33.90)	0.54 (0.29–1.85)	< 0.001
	2 week	9.04 (3.17–25.68)	0.07 (0.02–1.84)	< 0.001
	3 week	9.50 (3.60–16.87)	0.07 (0.01–0.93)	< 0.001
IL-10 (pg/ml)	Baseline	1.44 (0.78–2.47)	0.28 (0.15–0.42)	< 0.001
	1 week	2.02 (0.56–3.13)	0.19 (0.13–0.62)	< 0.001
	2 week	1.24 (0.61–2.85)	0.13 (0.09–0.26)	< 0.001
	3 week	1.33 (0.81–1.66)	0.10 (0.05–0.12)	< 0.001
The p values indicate differences between severe group and non-severe group. $p < 0.05$ was considered statistically significant.				

Dynamic changes of T lymphocyte subsets in patients with COVID-19

In this study, we analyzed the dynamic changes of T lymphocyte subsets in severe and non-severe COVID-19 (Fig. 2). The absolute numbers of CD3+, CD4+, CD8+, and CD45 + T cells were markedly lower in severe cases compared with that in non-severe cases from baseline to 3 weeks after admission ($p < 0.001$) (Table 4). The decrease of T lymphocyte subsets reached its peak from day 1 to 3 after admission, and gradually increased from day 4 to 21 in the non-severe group; however, reached its peak from day 4 to 7 after admission, and sustained at a low levels in the severe group (Fig. 2).

Table 4
Comparison in the levels of lymphocyte subsets between severe and non-severe group

		Severe (n = 31)	Non-severe (n = 39)	P value
CD3 (cells/ul)	Baseline	346 (157–609)	1164 (894–1361)	< 0.001
	1 week	261 (197–598)	1433 (1183–1702)	< 0.001
	2 week	595 (231–950)	1483 (1327–1691)	< 0.001
	3 week	697 (389–939)	1772 (1436–1913)	< 0.001
CD4 (cells/ul)	Baseline	174 (98–407)	593 (453–744)	< 0.001
	1 week	173 (118–445)	697 (609–923)	< 0.001
	2 week	424 (180–601)	826 (706–934)	< 0.001
	3 week	439 (270–592)	1045 (862–1637)	< 0.001
CD8 (cells/ul)	Baseline	116 (56–207)	420 (326–543)	< 0.001
	1 week	109 (47–177)	539 (433–699)	< 0.001
	2 week	164 (81–236)	579 (448–765)	< 0.001
	3 week	248 (111–359)	612 (450–720)	< 0.001
CD45 (cells/ul)	Baseline	623 (408–986)	1630 (1300–1925)	< 0.001
	1 week	499 (372–1023)	1946 (1551–2204)	< 0.001
	2 week	887 (512–1409)	2060 (1875–2394)	< 0.001
	3 week	1167 (477–1369)	2468 (1898–2651)	< 0.001
The p values indicate differences between severe group and non-severe group. $p < 0.05$ was considered statistically significant.				

Discussion

Both clinical and epidemiological features of patients with COVID-19 have been reported [7, 12]. However, only a few study reported the immunological indicators of patients with COVID-19. In this study, we evaluated the immunological characteristics of COVID-19. Serum cytokines increased in the majority of severe cases with COVID-19, suggesting cytokine storms might be associated with the disease progression of COVID-19. Especially, the levels of IL-6, IL-8, and IL-10 were markedly higher in severe COVID-19, compared with non-severe COVID-19, suggesting the serum cytokines could be used as predictors for the prediction of COVID-19 progression. Additionally, we found that a laboratory feature of COVID-19 was lymphocytopenia, particularly in severe cases (initial test result after admission, $0.7 (0.5–0.9) \times 10^9/L$). Detailed analysis of T lymphocytes subtypes revealed that CD3+, CD4+, CD8+, and CD45 +

T cells were all significantly affected. More importantly, compared with non-severe cases, severe cases had markedly lower levels of T lymphocyte subtypes, suggesting that the decrease of CD3+, CD4+, CD8+, and CD45 + T cell counts might be correlated with the disease severity of COVID-19.

Previous studies also reported the correlation between immunological markers and disease severity of COVID-19. Chen et al reported that the SARS-CoV-2 infection may affect T lymphocytes, particularly CD4 + and CD8 + T cells [8]. Wan et al explored the relationships between lymphocyte subsets, cytokines and disease evolution in patients with COVID-19, and found that higher survival rates occurred in those with IL-6 within normal values, and CD4 + T, CD8 + T, IL-6, and IL-10 can be used as indicators for disease progression of COVID-19 [13]. Diao et al reported that the number of CD4 + and CD8 + T cells was dramatically reduced in COVID-19 patients, especially in patients requiring ICU care [14]. However, these studies included a small number of patients, and statistical non-significance may not rule out differences between groups. In addition, these studies only reported baseline data. Therefore, we showed the dynamics of cytokines and lymphocyte subsets from baseline to 3 weeks after admission.

Patients with COVID-19 admitted to the ICU have higher expression levels of cytokines, which may indicate patients at risk to develop ARDS and eventually death [7]. This circumstance is called “cytokine storm” [15]. The degree of cytokine storm determines the degree of COVID-19 progression. The more severe the cytokine storm, the more severe the ARDS, which is related to higher mortality. In this study, we found that the degree of increase in serum IL-6, IL-8, and IL-10 is significant, but the fluctuations in TNF- α , IL-1 β , IL-2, IL-4, IL-5, IL-12P70, IL-17, IFN- α , and IFN- γ were minor. The serum levels of IL-6, IL-8 and IL-10 are positively correlated with the severity of COVID-19. The results were consistent with a review, which reported that IL-6 contributes to host defense against infections and tissue injuries, and IL-6 blockade may constitute a novel therapeutic strategy for cytokine storm [16].

Lymphocytes and the subsets of CD4 + T cells and CD8 + T cells play an important role in the maintenance of immune system function. In 2004, Li et al had reported that a rapid decrease of T cell subsets is a unique characteristic in patients with SARS during acute infection, and a rapid and dramatic restoration of T cell subsets was seen in recovering patients [17]. Wang et al reported that lymphopenia occurred in 70.3% patients with COVID-19, but any alteration in the subsets was still unknown [18]. Wang et al reported that total lymphocytes, CD4 + T cells, and CD8 + T cells decreased in COVID-19 patients, and severe cases had a lower level than mild cases. [19]. In this study, we found that, CD3+, CD4+, CD8+, and CD45 + T cells decreased in patients with COVID-19, and severe cases had a lower level than non-severe cases. We also found the difference in the dynamics of lymphocyte subsets between severe and non-severe COVID-19. The decrease of T lymphocyte subsets reached its peak from day 1 to 3 after admission, and gradually increased from day 4 to 21 in the non-severe group; however, reached its peak from day 4 to 7 after admission, and sustained at a low levels in the severe group.

This study has some limitations. First, this is a retrospective study. The lymphocyte test kit focused on T cell subsets. We could not provide the dynamics of B cells and NK cells. However, previous study has

showed that for B cells and NK cells, no obvious changes were observed among mild and severe cases ($p = 0.47$) [20]. Second, the data regarding the viral load of SARS-CoV-2 are not available for patients with COVID-19 in this study. Further studies are needed to investigate the correlation between the viral load kinetics and the dynamics of cytokines.

Conclusion

In conclusion, SARS-CoV-2 infection induced cytokine storm and lymphopenia, particularly a decrease in CD3+, CD4+, CD8+, and CD45 + T cell counts, as well as an increase in the levels of IL-6, IL-8, and IL-10. The decrease of T lymphocyte subsets reached its peak from day 1 to 3 after admission, and gradually increased from day 4 to 21 in the non-severe group; however, reached its peak from day 4 to 7 after admission, and sustained at a low levels in the severe group. This study suggests a strong link between inflammatory cytokines storm and the pathogenesis of SARS-CoV-2 infection, and enhances a deeper understanding of T lymphocyte subnets and their association with the disease severity of patients with COVID-19.

Abbreviations

COVID-19

2019 novel coronavirus disease

SARS-CoV-2

severe acute respiratory syndrome coronavirus 2

RT-PCR

real-time polymerase-chain-reaction

IQR

interquartile ranges

WBC

white blood count

AST

aspartate aminotransferase

BUN

blood urea nitrogen

CK

creatinine kinase

LDH

lactate dehydrogenase

ICU

intensive-care unit

Declarations

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Authorship Statement:

- **Author contributions:** Study concept and design: Liang Chen. Data collection: Qiang Li, Wei Xu, Weixia Li, and Chenglu Huang. Analysis and interpretation of data: Qiang Li, Wei Xu, Weixia Li, and Chenglu Huang. Drafting of the manuscript: Qiang Li. Critical revision of the manuscript: Liang Chen.
- All authors approved the final version of the manuscript.

Consent for publication

All authors read and approved the manuscript.

Conflict of interest

None

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Role of the Sponsor

The funding organizations are public institutions and had no role in the design and conduct of the study; collection, management, and analysis of the data; or preparation, review, and approval of the manuscript.

Availability of data and materials

We declared that materials described in the manuscript, including all relevant raw data, will be freely available to any scientist wishing to use them for non-commercial purposes, without breaching participant confidentiality. The supporting data can be accessed from Liang Chen (corresponding author), E-mail: chenliang@shphc.org.cn

Ethical approval and Informed consent

The study was approved by the ethics committee of Shanghai Public Health Clinical Center. The verbal informed consents were obtained from all participants.

Declarations

This manuscript had contained Ethics approval and consent to participate, Consent for publication, Availability of data and materials, Competing interests, Funding, Authors' contributions, and Acknowledgements.

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Figures

Figure 1

Kinetic analysis of cytokines levels in patients with COVID-19.

Figure 2

Kinetic analysis of cell counts of lymphocyte subsets in patients with COVID-19.