

Supplementary material

Follow-up of interleukin 6 and other blood markers during the hospitalization of COVID-19 patients: a single-center study

Supplementary Table S1. Clinical characteristics of COVID-19 patients (N=31)

Characteristic	Mild-moderate (n=17)	Severe-critical (n=14)	% of mild-moderate/ % of severe-critical patients	<i>p</i> -value
Age, years				
Median	60	67		0.2412
Interquartile range	43.5 - 73.5	61.8 - 77.5		
<66	6	7	35 / 50	
≥ 66	11	7	65 / 50	
Sex				
Female	10	5	59 / 43	0,3750
Male	7	8	41 / 57	
Oxygen saturation, %				
Median	97.0	89.5		<0.0001
Interquartile range	94.5 - 98.0	78.3 - 94.6		
Triage, level				
2	0	9	0 / 64	0.0071
3	15	3	88 / 21	
4	2	1	12 / 7	
5	0	1	0 / 7	
Glycaemia, mg/dL				
Median	110.0	117.5		0,1635
Interquartile range	97.8 – 131.5	107.5 – 197.0		
Blood systolic, mmHg				
Median	134	135		0,7355
Interquartile range	122 – 155	117 – 147		
Blood diastolic, mmHg				
Median	82	79		0,7518
Interquartile range	71 – 88	75 – 89		

Supplementary Table S2. Blood markers at hospital admission of mild-moderate and severe-critical patients (N=31) and discharge of severe-critical patients (N=14). HD: markers at hospital discharge.

Levels of markers in peripheral blood	Mean (\pm SD)	Median [IQR]	p-value
IL-6 (pg/mL)			
Mild-moderate	17.3 (16.8)	9.9 [4.6-33-3]	< 0.0001
Severe-critical	79.7 (64.3)	56.9 [32.6-18.4]	
Severe-critical HD	13.0 (15.7)	7.0 [4.1 – 14.5]	0.0002
PCT (ng/mL)			
Mild-moderate	0.04 (0.04)	0.02 [<0.01-0.06]	0.0077
Severe-critical	0.52 (0.83)	0.10 [0.05 – 1.05]	
Severe-critical HD	0.14 (0.18)	0.04 [< 0.01- 0.35]	0.0137
D-dimer (ng/FEU/mL)			
Mild-moderate	1491 (2045)	689 [435 – 1368]	0.0090
Severe-critical	3919 (4285)	2155 [1193 - 9788]	
Severe-critical HD	3858 (6745)	1680 [800 – 3626]	0.3396
CRP (mg/L)			
Mild-moderate	32.1 (37.8)	21.3 [12.8 – 34.8]	0.0006
Severe-critical	180 (139.2)	139 [42.1 – 263]	
Severe-critical HD	38.1 (40.2)	24.2 [15.0 – 52.0]	0.0034
Cortisol (ug/dL)			
Mild-moderate	16.2 (7.7)	13.5 [12.2 – 20.7]	0.2365
Severe-critical	19.7 (8.7)	17.8 [14.3 – 23.8]	
Severe-critical HD	7.9 (8.0)	4.0 [0.9 – 14.8]	0.0012
DHEA-S (ug/dL)			
Mild-moderate	133 (69.9)	124.3 [75.0 – 189]	0.0394
Severe-critical	88.7 (39.2)	85.8 [55.6 – 126]	
Severe-critical HD	25.8 (23.7)	21.8 [6.5 – 31.2]	0.0001
25-OH Vitamin D (ng/mL)			
Mild-moderate	22.3 \pm 12.4	19.9 [12.4 – 29.3]	0.4347
Severe-critical	19.3 \pm 8.5	19.7 [11.2 – 24.8]	
Severe-critical HD	18.5 \pm 10.7	15.6 [9.0 – 26.0]	0.1677
Positive neutralizing IgGs (%)			
Mild-moderate	23.5		
Severe-critical	50		
Severe-critical HD	85.7		
Positive viremia (%)			
Mild-moderate	31.3		
Severe-critical	92.9		
Severe-critical HD	21.4		

Supplementary Table S3. Ground-glass opacity (GGO) percent on chest computed tomography of 14 severe-critical COVID-19 patients

Patient	Ground-glass opacity (%)
1	36.0
2	1.0
3	3.7
4	25.0
5	7.6
6	29.5
7	6.0
8	0.1
9	2.4
10	9.4
11	26.5
12	25.0
13	0.3
14	5.5

Supplementary Table S4. Cortisol/DHEA-S ratio in mild-moderate and severe-critical patients with COVID-19 on admission to the emergency room (N=31)

Levels of markers in peripheral blood	Mean (± SD)	Median [IQR]	p-value
Cortisol/DHEA-S ratio			
Mild-moderate	0.17 (0.14)	0.14 [0.08 – 0.19]	0.0494
Severe-critical	0.28 (0.26)	0.24 [0.13 – 0.30]	

Supplementary Table S5. Blood markers in ICU (n=9) and non-ICU (n=22) patients

Levels of markers in peripheral blood	Mean (\pm SD)	Median [IQR]	p-value
IL-6 (pg/mL)			
ICU	102 (70.1)	93.8 [37.9 - 165]	0.0011
Non-ICU	29.6 (31.9)	17.9 [6.0 - 44.5]	
PCT (ng/mL)			
ICU	0.72 (0.91)	0.40 [0.09 - 1.04]	0.0027
Non-ICU	0.11 (0.36)	0.02 [<0.01 - 0.06]	
D-dimer (ng/FEU/mL)			
ICU	4576 (4963)	2753 [1050 - 8990]	0.0330
Non-ICU	1774 (2222)	732 [448 - 2078]	
CRP (mg/L)			
ICU	181 (147)	146 [53.1 - 299]	0.0277
Non-ICU	70.5 (99.4)	28.9 [17.1 - 62.1]	
Cortisol (ug/dL)			
ICU	19.1 (10.2)	15.6 [11.6 - 25.5]	0.6503
Non-ICU	17.6 (7.4)	15.8 [12.7 - 22.7]	
DHEA-S (ug/dL)			
ICU	92.1 (41.4)	89.4 [55.1 - 131]	0.2173
Non-ICU	121 (66.9)	118 [62.6 - 177]	
25-OH Vitamin D (ng/mL)			
ICU	17.0 (7.5)	13.6 [10.8 - 21.8]	0.1978
Non-ICU	22.6 (11.6)	22.7 [13.0 - 29.2]	
Positive neutralizing IgGs (%)			
ICU	66.7		
Non-ICU	18.2		
Positive viremia (%)			
ICU	77.8		
Non-ICU	47.6		

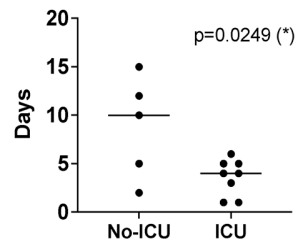
Supplementary Table S6. Association between initial levels of blood markers on admission to the emergency room and hospital stay length (N=14)

Blood marker	Pearson coefficient (r)	p-value
IL-6	0.36	0.232
PCT	0.24	0.431
DD	-0.13	0.709
Cortisol	0.56	0.046
DHEA-S	0.08	0.802

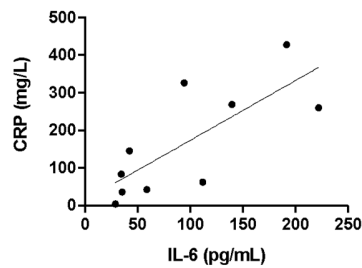
Supplementary Table S7. Association between the first positive (n=4) or negative (n=7) event and the levels of blood markers on the day of the event.

Blood Marker	Mean (± SD)	Median [IQR]	p-value
IL-6 (pg/mL)*			
Positive event	3.9 (3.1)	4.1 [0.9 – 6.6]	0.049
Negative event	86.1 (57.9)	77.0 [39.1 – 122]	
PCT (ng/mL)			
Positive event	0.33 (0.37)	0.27 [0.03 – 0.71]	0.648
Negative event	0.21 (0.25]	0.14 [0.04 – 0.33]	
D-dimer (ng/FEU/mL)			
Positive event	1618 (1784)	868 [508-3479]	0.331
Negative event	3086 (3598)	2255 [719 – 4383]	
CRP (mg/L)			
Positive event	66.7 (78.9)	40.8 [9.3 – 150]	0.979
Negative event	82.9 (59.4)	64.8 [48.2 – 127]	

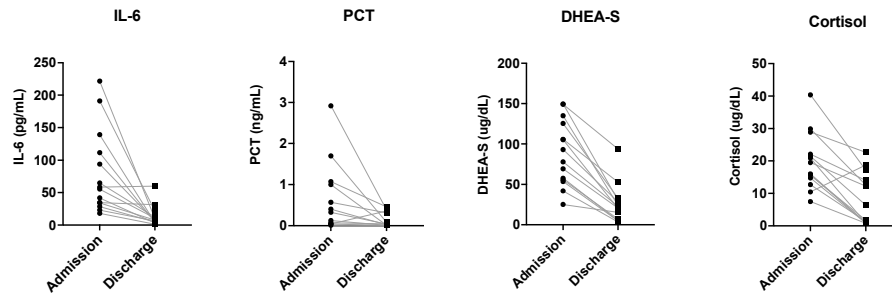
*Additionally, IL-6 showed a significant correlation with the second event (N=6).



Supplementary Figure S1. Days up to the exponential change in anti-SARS-CoV-2 neutralizing antibodies (IgG) during hospitalization of admitted to ICU and non-admitted to ICU severe-critical patients with COVID-19.



Supplementary Figure S2. Correlation between IL-6 and CRP levels in severe-critical patients with COVID-19. The figure shows a linear correlation between blood IL-6 and CRP at hospital admission of severe-critical COVID-19 patients, Pearson coefficient = 0.7595 ($p=0.0108$).



Supplementary Figure S3. Blood markers in hospital admission and discharge of severe-critical patients with COVID-19. Markers were measured when they were admitted to hospital care compared to levels at hospital discharge. p-values for IL-6, PCT, DHEA-S, and cortisol were 0.0002, 0.0137, 0.0001 and 0.0012 respectively (Wilcoxon test).