

ORIGINAL ARTICLE

Cytokines and Other Laboratory Parameters of Hospitalized COVID-19 Patients that Predict Intensive Care Unit Admission

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SUMMARY

Background: This study aimed to investigate the roles of cytokines and other laboratory parameters in determining the need for intensive care in COVID-19 patients.

Methods: This is a retrospective observational study. Demographic, clinical, and laboratory parameters of the patients were evaluated. Thirteen cytokines were measured along with baseline laboratory tests at admission and at 48-hour intervals: IL-1 β , IFN- α , IFN- β , TNF- α , MCP-1, IL-6, IL -8, IL-10, IL-2p70, IL-17A, IL-18, IL-23, and IL-33.

Results: COVID-19 was confirmed by PCR in 116 hospitalized patients. The mean age was 55.3 ± 16.4 years. Seventy-four (63.8%) of the patients were male and 42 (36.2%) were female. Twenty-two (18.9%) patients (16 male, 6 female) were transferred to the intensive care unit. A significant increase in white blood cell (WBC), neutrophil (Neu) and lymphocyte (Lym) counts, Neu/Lym ratio (NLR), lactate dehydrogenase (LDH), INR (international normalized ratio), activated prothrombin time (aPTT), D-dimer (D-D), troponin (Trop), Pro-BNP (BNP), procalcitonin (PCT), ferritin (Fer), and alanine aminotransferase (ALT) values were observed in those requiring intensive care. A significant decrease was found in albumin (Alb) levels and Lym counts. Alb levels appeared to be protective against admission to intensive care. Except for IFN- α , IL-23, and IL-33, the baseline values of other cytokines were above the threshold values. MCP-1 and IL-6 were higher in patients requiring intensive care.

Conclusions: High NLR and LDH and low Alb levels, especially with an increase in MCP-1 and IL-6, were found to be the best predictors of a serious COVID-19 infection.

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Supplementary Data

Table S1. Clinical features of all patients on admission and treatment.

Symptoms	No. (%)
Asymptomatic cases	15 (13%)
Symptoms onset duration before admission	mean 4.3 days
Fever	41 (35%)
Dry cough	39 (33.6%)
Shortness of breath	37 (31.8%)
Malaise-fatigue	21 (18%)
Diffuse pain and myalgia	14 (12%)
Headache	12 (10.3%)
Nausea and vomiting	10 (8.6%)
Diarrhea	7 (6%)
Loss of smell and taste	7 (6%)
Chest pain and feeling of chest pressure	5 (4.3%)
Loss of appetite	4 (3.4%)
Sore throat	4 (3.4%)
Stroke	3 (2.6%)
Chills	3 (2.6%)
Abdominal pain	1 (0.8%)
Confusion	1 (0.8%)
Nasal congestion	1 (0.8%)
Comorbid conditions	
Hypertension	30 (27%)
Diabetes	29 (26%)
Chronic lung disease	11 (9.9%)
Coronary artery disease	10 (8.6%)
Neurological disease	7 (6.3%)
Malignancy	7 (6.3%)
Chronic heart failure	6 (5.4%)
Digestive system disease	5 (4.5%)
Kidney failure	5 (4.5%)
Thyroid dysfunction	5 (4.5%)
Rheumatological disease	3 (2.7%)
Cerebrovascular disease	2 (1.7%)
Renal transplant	1 (0.9%)
HIV	1 (0.9%)
Treatment	
Favipiravir	92 (79.3%)
Enoxaparin	72 (62%)
Corticosteroid	39 (33.6%)
Hydroxychloroquine	24 (20.6%)
Colchicum	24 (20.6%)
Tocilizumab	23 (19.8%)
Ascorbic acid	17 (14.6%)
Azithromycin	8 (6.8%)

Table S1. Clinical features of all patients on admission and treatment (continued).

Symptoms	No. (%)
Oseltamivir	7 (6%)
Lopinavir/ritonavir (200/50mg)	5 (4.3%)
Convalescent plasma	3 (2.5%)
Remdesivir	1 (0.8%)
Other antibiotics	28 (24.1%)

Table S2. Laboratory findings of all patients on admission and at 48-hour intervals.

	Basal n = 115 mean ± SD	1st 48 hours n = 74 mean ± SD	2nd 48 hours n = 49 mean ± SD	3rd 48 hours n = 27 mean ± SD	4th 48 hours n = 8 mean ± SD
Hematological parameters					
WBCcount μ/L (3,600 - 11,000)	7,381 ± 6,427	7,653 ± 5,102	6,743 ± 3,900	7,150 ± 2,916	6,310 ± 2,167
Neutrophil μ/L (1,500 - 6,600)	5,051 ± 3,124	5,665 ± 4,191	4,914 ± 3,812	5,032 ± 2,660	4,520 ± 2,086
Lymphocyte μ/L (1,500 - 3,500)	1,364 ± 1,036	1,420 ± 1,490	1,258 ± 586	1,340 ± 540	1,223 ± 863
Platelet 10 ³ μ/L (150 - 450)	244 ± 103	285 ± 123	288 ± 117	276 ± 108	317 ± 106
RBC 10 ⁶ /mm ³ (4.3 - 5.7)	4.43 ± 0.6	4.40 ± 0.6	4.43 ± 0.6	4.35 ± 0.6	4.47 ± 0.6
Hemoglobin g/dL (13 - 18)	12.8 ± 2.2	12.5 ± 1.9	12.7 ± 2	12.3 ± 2	12.4 ± 2.1
Hematocrit % (38 - 52)	38.2 ± 5.7	37.3 ± 5.1	37.6 ± 5.1	36.5 ± 5.1	36.8 ± 5.2
N/L ratio	5.3 ± 5.4	5.5 ± 5.1	4.8 ± 4.3	4.5 ± 3.7	5.8 ± 6.6
Blood biochemical tests					
Albumin g/L (35 - 50)	3.4 ± 0.6	3.4 ± 0.5	3.4 ± 0.6	3.3 ± 0.6	3.4 ± 0.4
CRP mg/dL (0 - 0.5)	4.8 ± 6	3.7 ± 4.6	2.7 ± 3.8	2.8 ± 3.3	3.3 ± 5.8
ALT μ/L (5 - 40)	45.7 ± 45.5	61.2 ± 66.5	82 ± 86.4	78.4 ± 78.7	83.2 ± 69
AST μ/L (5 - 40)	35 ± 33.2	42 ± 41.6	47 ± 47	36 ± 21	39 ± 43
LDH μ/L (200 - 450)	432 ± 246	479 ± 315	460 ± 259	473 ± 261	457 ± 341
Creatinine mg/dL (0.6 - 1.4)	1.1 ± 0.5	1.1 ± 0.6	1.2 ± 0.6	1.2 ± 0.7	1.1 ± 0.2
Ferritin ng/mL (22 - 275)	595 ± 913	566 ± 554	506 ± 418	393 ± 402	417 ± 574
Coagulation tests					
PT (11.5 - 15.5)/second	14.4 ± 2.3	14.7 ± 3.4	16.2 ± 7.5	15 ± 2.6	14.5 ± 2
APTT (23.6 - 34.8)/second	27.7 ± 10.5	27 ± 7.6	26.1 ± 3.7	26 ± 4.3	27.2 ± 4.3
INR (0.8 - 1.2)	1.1 ± 0.2	1.1 ± 0.3	1.3 ± 0.8	1.1 ± 0.2	1.1 ± 0.2
Fibrinogen mg/dL (200 - 400)	503.9 ± 162.5	516.6 ± 156.6	486.5 ± 163	451.1 ± 189.7	434 ± 189.6

Table S2. Laboratory findings of all patients on admission and at 48-hour intervals (continued).

	Basal n = 115 mean ± SD	1st 48 hours n = 74 mean ± SD	2nd 48 hours n = 49 mean ± SD	3rd 48 hours n = 27 mean ± SD	4th 48 hours n = 8 mean ± SD
D-dimers ng/mL (0 - 500)	1,022.7 ± 1,553.6	1,154.6 ± 2,567.4	1,339.5 ± 2,748.3	1,084.9 ± 1,278.8	1,252.3 ± 1,014.9
Electrolytes					
Na mmol/L (135 - 145)	138.6 ± 4.1	139 ± 3.9	139 ± 4.3	138.2 ± 4.1	138.1 ± 2
K mmol/L (3.5 - 5.3)	4.1 ± 0.5	4.1 ± 0.5	4.2 ± 0.5	4.3 ± 0.6	4.1 ± 0.2
Ca mg/dL (8.5 - 10.5)	8.6 ± 0.7	8.6 ± 0.6	8.7 ± 0.8	8.6 ± 0.8	8.4 ± 0.5
The others					
Procalcitonin ng/mL (0 - 0.05)	0.15 ± 0.38	0.1 ± 0.2	0.1 ± 0.1	0.4 ± 1.5	0.1 ± 0.1
Troponin ng/L (0 - 30)	33.5 ± 241.4	22.9 ± 103.3	22 ± 68.5	21.5 ± 58.7	22.8 ± 48.7
Pro-PNB pg/mL (0 - 160)	43.2 ± 54.2	56.8 ± 66.7	102.6 ± 206.2	47.6 ± 36.4	82 ± 69.6

WBC - White blood cell, RBC - Red blood cell, N/L - Neutrophil/Lymphocyte, CRP - C reactive protein, ALT - Alanin aminotransferase, AST - Aspartat aminotransferase, LDH - Lactic dehydrogenase, PT - Protrombin time, APTT - Activated partial tromboplastin time, INR - International normalizing ratio, pro-BNP - pro B type natriuretic peptide.

Table S3. Comparisons of the laboratory findings on admission between the ICU and non-ICU patients with COVID-19.

		Mean ± SD	95%CI for mean		Minimum	Maximum	p-value
Hematological parameters							
WBC count μ/L (3,600 - 11,000)	ICU (n: 22)	8,811 ± 4,172	6,961.49	10,661.24	3,550	18,520	0.013
	non-ICU (n:93)	7,043 ± 6,827	5,636.64	8,448.73	1,940	65,000	
Neutrophil μ/L (1,500 - 6,600)	ICU (n:22)	7,486 ± 3,682	5,853.34	9,118.48	2,480	16,050	< 0.001
	non-ICU (n:93)	4,475 ± 2,693	3,920.64	5,029.9	860	13,910	
Lymphocyte μ/L (1,500 - 3,500)	ICU (n:22)	967 ± 578	710.89	1,223.66	330	2,540	0.003
	non-ICU (n:93)	1,458 ± 1,099	1,231.87	1,684.47	300	9,740	
Neutrophil/ Lymphocyte Ratio	ICU (n:22)	9.7 ± 7.9	6.25	13.24	2.57	41.15	< 0.001
	non-ICU (n:93)	4.3 ± 4.1	3.41	5.09	0.36	22.8	
RBC 10⁶/mm³ (4.3 - 5.7)	ICU (n:22)	4.1 ± 0.6	3.9	4.8	2.8	5.7	0.45
	non-ICU (n:93)	4.3 ± 0.6	3.7	4.6	3.1	5.8	
Hemoglobin g/dL (13 - 18)	ICU (n:22)	11.7 ± 2	9.7	14.4	7.9	15.2	0.26
	non-ICU (n:93)	12.8 ± 2.2	9.4	14.6	7.1	16.7	
Hematocrit (38 - 53)	ICU (n:22)	35.6 ± 5.3	30.2	43.7	25.1	46.9	0.39
	non-ICU (n:93)	38.2 ± 5.7	32.5	39.4	25.7	48.5	
Platelet μ/L (150 - 450)	ICU (n:22)	244,864 ± 122,792	190,420.78	299,306.49	54,000	500,000	0.567
	non-ICU (n:93)	243,731 ± 98,272	223,492.25	263,970.12	56,000	594,000	

Table S3. Comparisons of the laboratory findings on admission between the ICU and non-ICU patients with COVID-19 (continued).

		Mean \pm SD	95%CI for mean		Minimum	Maximum	p-value
Blood Biochemical Tests							
CRP mg/dL (0 - 0.5)	ICU (n:21)	4.8 \pm 6.4	1.91	7.76	0.2	21.9	0.58
	non-ICU (n:93)	4.8 \pm 5.9	3.58	6.003	0.1	23.3	
Albumin g/L (35 - 50)	ICU (n:22)	2.9 \pm 0.5	2.63	3.076	1.9	3.7	< 0.001
	non-ICU (n:93)	3.6 \pm 0.6	3.47	3.72	1.7	4.8	
AST μ /L (5 - 40)	ICU (n:22)	49 \pm 49	27.01	70.17	9	202	0.075
	non-ICU (n:93)	32 \pm 28	25.84	37.30	7	171	
ALT μ /L (5 - 40)	ICU (n:22)	66 \pm 50	43.97	88.31	23	228	0.0007
	non-ICU (n:93)	41 \pm 43	31.91	49.71	8	253	
Creatinine mg/dL (0.6 - 1.4)	ICU (n:22)	1.3 \pm 0.6	0.996	1.50	0.69	3.26	0.068
	non-ICU (n:93)	1.1 \pm 0.5	0.97	1.16	0.42	4.06	
LDH μ /L (200 - 450)	ICU (n:22)	663 \pm 365	501.39	825.34	146	1,692	< 0.001
	non-ICU (n:92)	376 \pm 168	341.45	410.97	131	885	
Ferritin ng/mL (22 - 275)	ICU (n: 21)	1,011 \pm 848	624.61	1,396.67	86.46	3,207	< 0.001
	non-ICU (n:88)	442 \pm 549	325.38	557.86	1	2,878.1	
Coagulation Tests							
Fibrinogen mg/dL (200 - 400)	ICU (n:19)	530 \pm 159.4	453.13	606.77	206	785	0.3
	non-ICU (n:83)	497.9 \pm 163.6	462.14	533.60	144	950	
D-dimers ng/mL (0 - 500)	ICU (n:22)	1,855 \pm 2,483	754.14	2,956.23	110	8,400	0.014
	non-ICU (n:84)	805 \pm 1,123	560.93	1,048.37	106	7,230	
INR (0.8 - 1.2)	ICU (n:20)	1.2 \pm 0.2	1.12	1.28	0.98	1.6	0.002
	non-ICU (n:80)	1.1 \pm 0.1	1.05	1.1	0.85	1.88	
PT (11.5 - 15.5)/second	ICU (n:20)	15.6 \pm 1.8	14.73	16.44	13.3	19.8	0.002
	non-ICU (n:81)	14.2 \pm 2.3	13.65	14.65	1.22	25.3	
APTT (23.6 - 34.8)/second	ICU (n:16)	26.1 \pm 6	22.86	29.29	18.2	40.3	0.213
	non-ICU (n:64)	28.1 \pm 11.5	25.27	30.99	12.5	111.8	
Electrolytes							
Na mmol/L (135 - 145)	ICU (n:22)	138.8 \pm 5.1	136.51	141.04	131	151	0.72
	non-ICU (n:93)	138.6 \pm 3.9	137.76	139.36	125	147	
K mm/L (3.5 - 5.3)	ICU (n:22)	3.9 \pm 0.6	3.5	4.4	2.8	5.0	0.13
	non-ICU (n:93)	4.1 \pm 0.5	3.7	4.6	3.2	5.1	
Ca mg/dL (8.5 - 10.5)	ICU (n:22)	8.5 \pm 0.8	43,313	31,260	7.1	9.7	0.32
	non-ICU (n:89)	8.7 \pm 0.7	19,572	8.81	7.1	9.9	

Table S3. Comparisons of the laboratory findings on admission between the ICU and non-ICU patients with COVID-19 (continued).

		Mean \pm SD	95%CI for mean		Minimum	Maximum	p-value
The Others							
Troponin ng/L (0 - 30)	ICU (n:22)	134.6 \pm 536.8	-103.4	372.53	0.6	2,531	0.004
	non-ICU (n:91)	8.3 \pm 15.3	5.05	11.45	0	127.2	
Pro-BNP pg/mL (0 - 160)	ICU (n:15)	75.8 \pm 73.8	34.9	116.60	10.3	281.1	0.004
	non-ICU (n:56)	34.5 \pm 44.6	22.53	46.42	10	292.5	
Procalcitonin ng/mL (0 - 0.05)	ICU (n:22)	0.4 \pm 0.7	0.08	0.744	0.03	2.76	< 0.001
	non-ICU (n:79)	0.08 \pm 0.09	0.06	0.098	0.01	0.5	