

Laboratory parameters in patients with COVID-19 on first emergency admission is different in non-survivors: albumin and lactate dehydrogenase as risk factors

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ABSTRACT

Prompt identification of the clinical status and severity of COVID-19 can be a challenge in the emergency department (ED), as the clinical severity of the disease is variable, real-time reverse-transcription PCR (RT-PCR) results may not be immediately available, and imaging findings appear approximately 10 days after the onset of symptoms. There is currently no set of simple, readily available and fast battery of tests that can be used in the ED as prognostic factors. The purpose was to study laboratory test results in patients with COVID-19 at hospital emergency admission and to evaluate the results in non-survivors and their potential prognostic value. A profile of laboratory markers was agreed with the ED providers based on the International Federation of Clinical Chemistry and Laboratory Medicine recommendation of its usefulness, which was made in 218 patients with COVID-19. Non-survivors were significantly older, and the percentage of patients with pathological values of creatinine, albumin, lactate dehydrogenase (LDH), C reactive protein, prothrombin time, D-dimer, and arterial blood gas, PaO₂/FIO₂ and satO₂/FIO₂ indices were significantly higher among the patients with COVID-19 who died than those who survived. Patients who died also presented higher neutrophil counts. Among all studied tests, albumin and LDH were independent prognostic factors for death. The results of the study show pathology in nine laboratory markers in patients with COVID-19 admitted in the ED, valuable findings to take into consideration for its prompt identification when there is no immediate availability of RT-PCR results.

Prompt identification of the clinical status and severity of COVID-19 can be a challenge in the emergency department (ED), as the clinical severity of the disease is variable¹; real-time reverse-transcription PCR (RT-PCR) results may not be immediately available; and imaging findings appear approximately 10 days after the onset of symptoms.² There is currently no set of simple, readily available and fast battery of tests that can be used in the ED as COVID-19 risk factors.^{3–5}

Our purpose was to study laboratory test results in patients with COVID-19 at hospital emergency admission and their potential prognostic value. We hypothesised that there could be significant

differences in stat laboratory tests between survivors (finally did not die) and non-survivors (finally died).

A retrospective cohort to study COVID-19 cases was conducted. Data were retrospectively collected from 12 March to 20 May 2020. The clinical laboratory is located in a 370-bed suburban university community hospital that serves the population of the health department (234 551 inhabitants). The stat laboratory is independent but located in the main laboratory and receives samples from inpatients and patients in the ED. Laboratory requests are generated online, and the reports are sent electronically from the laboratory information system (LIS) (iGestLab) to the patient's electronic medical record. The samples were delivered from the ED to the laboratory by pneumatic tube or hand delivery immediately after collection. ED care providers can automatically consult the report via the intranet.

Blood specimens obtained from 218 patients admitted in the ED, who ultimately were diagnosed with COVID-19, were received for laboratory testing. COVID-19 diagnoses were confirmed by positive RT-PCR assay using Cobas 6800 (Roche Diagnostics, Barcelona, Spain), in nasopharyngeal or oropharyngeal swab specimens that were sent to a reference laboratory, an RT-PCR centralised and specialised laboratory in our health department, and the results were obtained within 24–48 hours. A profile of laboratory markers was agreed with the ED providers based on the International Federation of Clinical Chemistry and Laboratory Medicine recommendations.^{6–8}

Biochemistry tests were measured using Dimension RxL Max (Siemens Healthcare Diagnostics, Barcelona Spain), haematology tests by means of XT4000 (Sysmex Corporation, Barcelona, Spain), arterial blood gases (ABGs) using ABL⁸⁰⁰ (Radiometer, Madrid, Spain) and coagulation test by ACLTOP300 (Werfen, Barcelona, Spain). All assays had successfully passed daily internal quality control and monthly external quality controls. All ABG analyses were performed in the laboratory by trained personnel. No sample was analysed using point of care analyser.

Initial laboratory results and survival status were collected from LIS and patient medical records. We defined two groups, survivors and non-survivors.



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Descriptive statistics were presented as median and IQR, and percentages for continuous data and categorical data. The differences in laboratory values between groups were assessed using Mann-Whitney U test. A two-sided $p \leq 0.05$ rule was used as the criterion for rejecting the null hypothesis of no difference. A binary multiple logistic regression was performed to evaluate the relevant risk factors. Bonferroni correction was applied owing to multiple testing. Statistical analyses were conducted by means of Statistical Package for the Social Sciences V.22.

A summary of the results is provided in table 1. Twelve laboratory markers presented altered values in more than 50% of the patients, with C reactive protein (CRP), which was above the reference range in 85.2%, being the most frequently altered. Lactate dehydrogenase (LDH) was elevated in 81.2%, and neutrophil:lymphocyte ratio was above the values specified for COVID-19³ in 72.5% of patients, with COVID-19 at initial emergency admission. ABG, PaO₂:FIO₂ and satO₂:FIO₂ ratios

were decreased in 72.7% and 89.6%, respectively, and serum albumin in 71.5% of the cohort.

Non-survivors were significantly older and were more likely to present with elevated values of creatinine, albumin, LDH, CRP, prothrombin time and D-dimer than those who survived ($p < 0.05$) (table 1). Patients who died also presented higher neutrophil counts and decreased ABG PaO₂:FIO₂ and satO₂:FIO₂ indices.

Among all studied tests, albumin (OR 0.407, 95% CI 0.202 to 0.819) and LDH (OR 1.003, 95% CI 1.001 to 1.005) were independent risk factors for death (R^2 0.25, R^2_{albumin} 0.11 and R^2_{LDH} 0.09).

In our study, 100% of patients with COVID-19 who eventually died presented with elevated LDH and 93.1% presented with low albumin at admission, both markers being independent risk factors for death (figure 1).

Table 1 Demographic and laboratory data of survivors and non-survivors of COVID-19

	All patients			Survivors			Non-survivors		
	Median	IQR	% Path values	Median	IQR	% Path values	Median	IQR	% Path values
Age (years)*	65	22.25	–	62.5	21	–	79	12.5	–
Biochemistry									
Glucose (mmol/L)	5.88	1.74	45	5.88	1.54	42.6	6.83	3.9	60
Creatinine (µmol/L)*	88.42	35.37	31.7	79.58	35.37	28.2	97.26	35.37	53.3
Sodium (mmol/L)	138	5	7.8	138	5	7.4	138	4.8	10
Potassium (mmol/L)	3.8	0.7	8.7	3.8	0.7	7.4	4	0.8	16.7
Albumin (g/L)*	31	7	71.5	31	7	67.7	27	9	93.1
ALT (U/L)	31	29.5	62.4	30	30	63.5	38	33.5	55.2
LDH (U/L)*	300	168.5	81.2	294	149	78.1	407	156	100
CRP (mg/L)*	56	113	85.2	45	104	83.9	85	141	93.3
Haematology									
White blood cells (10 ⁹ /L)	6.9	4.3	14.2	6.8	4.3	14.9	8.4	4	10
N:L ratio	4.2	4.5	72.5	4.1	3.7	70.2	7.2	11.5	86.7
Neutrophils (10 ⁹ /L)*	5	3.8	23.4	4.7	3.5	21.3	7	4.8	36.7
Lymphocytes (10 ⁹ /L)	1.1	0.8	67	1.1	0.8	65.4	0.9	1	76.7
Monocytes (10 ⁹ /L)	0.5	0.4	15.1	0.5	0.4	16.5	0.4	0.3	6.7
Eosinophils (10 ⁹ /L)	0.1	0.7	4.6	0.1	0.7	4.8	0	0.2	3.3
Basophils (10 ⁹ /L)	0.1	0.1	0	0	0.1	0	0	0	0
Red blood cells (10 ⁶ /L)	4.6	0.7	22.9	4.6	0.7	21.8	4.6	0.9	30
Haemoglobin (g/L)	139	78	28.4	140	21	27.1	136	23	36.7
Haematocrit	0.4	0.05	39	0.4	0.06	35.6	0.4	0.06	60
Platelets (10 ⁹ /L)	191	106	40.8	191	109.3	20.2	185	104.3	20
Arterial blood gas									
pH	7.4	0.1	36.7	7.4	0.1	41.3	7.4	0.1	39.7
PCO ₂ (mm Hg)	34.5	8.2	53.6	34.8	8.5	53.9	33.3	6.8	51.7
PO ₂ (mm Hg)	80.3	35.7	66.3	80.7	39.5	65.3	70.8	25.7	72.4
PO ₂ :FIO ₂ ratio*	378.5	171.3	72.7	384	176	75.9	333	194	53.6
satO ₂ :FIO ₂ ratio*	456.7	30.4	89.6	457.9	23.8	90.2	437.1	128.9	85.7
Coagulation									
PT (s)*	13	2	69.8	13	2	66.5	14	7	90
aPTT (s)	30.9	5	14.5	30.9	4.5	12	30.6	5.9	30
D-dimer (ng/mL)*	636	1040	60.4	566	772	56.4	1107	1049.8	85.7

Glucose (3.89–6.11 mmol/L); creatinine (men: 61.89–106.1 µmol/L, women: 44.21–79.58 µmol/L); sodium (135–145 mmol/L); potassium (3.5–4.5 mmol/L); albumin (34–52 g/L); ALT (0–33 U/L); LDH (135–214 U/L); CRP (<5 mg/L); white blood cells (3.5–12.0×10⁹ cells/L); neutrophils (1.5–7.5×10⁹ cells/L); lymphocytes (1.3–4.0×10⁹ cells/L); monocytes (0.2–1.0×10⁹ cells/L); eosinophils (0.0–0.2×10⁹ cells/L); basophils (0.0–0.5×10⁹ cells/L); red blood cells (4.3–5.6×10⁶ cells/L); haemoglobin (men 135–175 g/L, women 120–155 g/L); haematocrit (men 41%–53%, women 36%–46%); platelets (140–450 10⁹/L); pH (7.32–7.42); PCO₂ (38.0–52.0 mm Hg); PO₂ (24.0–48.0 mm Hg); PT (9.4–12.5 s); aPTT (24–37 s); D-dimer (0–500 ng/mL).

*When comparing survivors with non-survivors $p < 0.05$.

ALT, alanine aminotransferase; aPTT, activated partial thromboplastin time; CRP, C reactive protein; L, lymphocyte; LDH, lactate dehydrogenase; N, neutrophil; PT, prothrombin time.

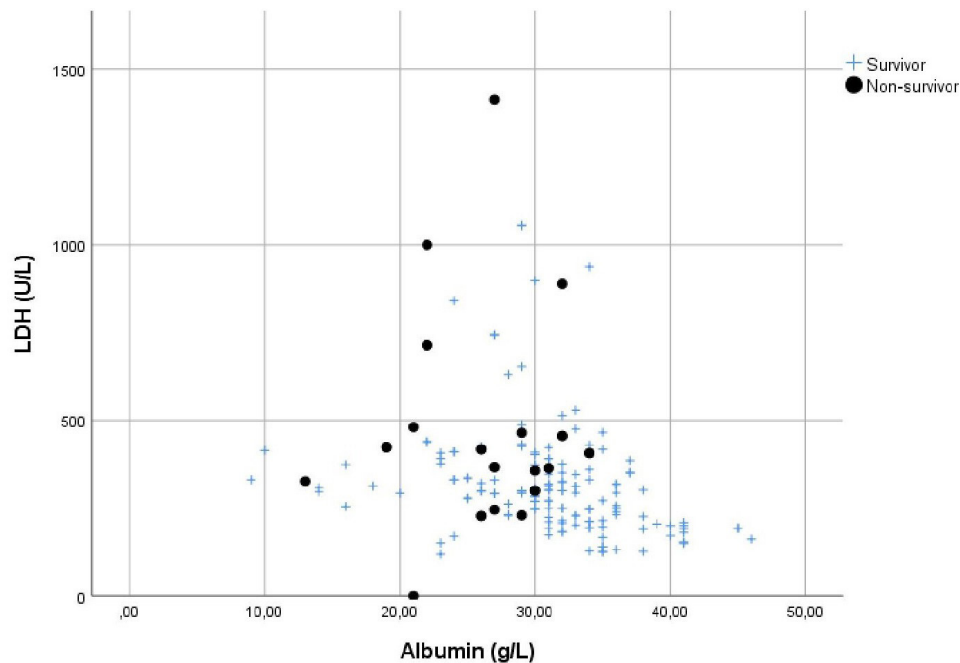


Figure 1 Distribution of LDH (U/L) and albumin (mg/dL) values in survivors and non-survivors. LDH, Lactate dehydrogenase.

The results and percentage of altered markers, of a battery of laboratory markers, can be used for a prompt preidentification of patients with COVID-19, when there is no immediate availability of RT-PCR result. Serum albumin, an outcome predictor in hospital emergency medical admissions,⁹ was more frequently decreased in patients with COVID-19 who did not survive.

The study had certain limitations. Ferritin and other laboratory markers as cytokines were not measured as these were not included in the stat laboratory menu. Time from admission to death or other clinical parameters not described in the study were not collected.

In conclusion, albumin and LDH were independent risk factors for death in patients with COVID-19 at hospital emergency admission. Measurement of both laboratory markers in such patients appears to be very relevant for patient assessment and prognosis. Further studies might be required to confirm these findings.

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