

Patient Characteristics, Clinical Courses, Fatality Rates, Predictors of Severe Diseases, and Deaths in Intensive Care Unit: A Retrospective Cohort of COVID-19 Patients in Lebanon

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Abstract

Background: The novel coronavirus 2019 (COVID-19) pandemic is straining Intensive Care Units' (ICU) capacities worldwide. It was demonstrated that the ICU mortality rate from Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is higher than from other viral pneumonia.

Aim: The goal of this research is to determine ICU COVID-19 patient characteristics, clinical courses, fatality rates, as well as risk factors for severe diseases and mortality in Lebanon, a country known to suffer from a deficiency in ICU capacity as well as a high COVID-19 infection rate.

Methods: We conducted a retrospective monocentric cohort study that enrolled COVID-19 patients admitted to the ICU at Baabda Governmental Hospital, between January 1, 2021, and March 31, 2021. Demographics, clinical, radiological, laboratory characteristics, treatments, and medical and infectious complications were gathered and compared between survivor and non-survivor groups, as well as between mild/moderate and severe/septic groups. Parameters were then entered in a multivariate regression analysis to identify predictors of death and disease severity.

Results: A total of 191 patients were included in our study. The fatality rate reached 35.6% in our population with a median ICU length of stay of 8 days. Non-survivors were more likely older ($p < 0.001$), active smokers ($p = 0.008$), and in severe or septic stage at admission ($p < 0.001$). Elevated levels of neutrophils ($p = 0.013$), ferritin ($p = 0.002$), lactate dehydrogenase ($p < 0.001$), and C-reactive protein ($p = 0.008$) were more frequently encountered in non-survivors. The latter were more commonly intubated ($p < 0.001$) and suffered from complications such as ventilator-associated pneumonia, sepsis, cytokine storm, myocardial infarction, and pulmonary embolism ($p < 0.001$). Multivariate analysis showed that older age, intubation, and severe/septic stage at admission were associated with an increased risk of death.

Conclusion: Older COVID-19 patients who were intubated, and those who were in severe or septic stages at ICU admission, had an increased risk of death. COVID-19 ICU fatality rate was 35.6%.

Keywords: COVID-19, SARS-CoV-2, Intensive Care, Fatality, Mortality, Lebanon

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Introduction

The first case of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2) infection was reported in Wuhan, China, in December 2019; nevertheless, the novel coronavirus 2019 (COVID-19) pandemic continues to be a major global health issue. Healthcare systems, particularly Intensive Care Units (ICU), are still facing unprecedented stress and challenges worldwide [1]. Notably, a study revealed that the rate of coronavirus-infected individuals admitted to the ICU exceeded 30% [2]. Besides, current literature reports that ICU mortality from SARS-CoV-2 ranged between 35.5% and 41.6%, which is higher than the estimated ICU fatality rate from other viral pneumonia [3,4]. These elevated death rates could be attributed to the severity of the virus itself or the shortage of healthcare resources. In a country like Lebanon, which has a relatively high infection rate (~535,000 people) [5], and a deficiency in ICU capacity [6], the high ICU fatality poses a real challenge to the healthcare system. Therefore, it is of great importance to identify the clinical phenotype of patients with a higher risk of death in an ICU setting, to be able to detect early deterioration and to properly allocate critical care resources. Studies have proved that older age, male gender, underlying chronic conditions, active smoking, obesity, decreased SpO₂/FiO₂ ratio, high endothelial biomarkers, and medical complications are predictors of death in ICU settings [7–10]. However, in Lebanon, there is insufficient data regarding the clinical features and risk factors related to the mortality of patients infected with COVID-19 and admitted to the ICU. Hence, in this study, our aim is to describe ICU patient characteristics and clinical course, estimate their fatality rates, and identify predictors of serious illness and death in Lebanese COVID-19 ICU patients.

Methods

Study design and population

This was a retrospective monocentric study of COVID-19 adult (above 18 years old)

patients admitted to the ICU in Baabda Governmental Hospital between the 1st of January 2021 and the 31st of March 2021, amid a surge in COVID-19 cases in Lebanon. Enrolled individuals were identified from the hospital electronic database, and separated into two groups (survivor/non-survivor) according to their ICU outcome (alive/dead) at the end of March 2021. Patients with incomplete data and those who were still in the ICU during the time of data collection were excluded from the study.

Data collection

We extracted from electronic medical files the following data: age, gender, smoking history, preexisting chronic conditions, and blood groups. Furthermore, we gathered the following variables recorded within the first 24 hours of ICU admission: symptoms, vital signs (blood pressure, heart rate, oxygen saturation, and temperature), radiological findings, electrocardiogram (ECG) abnormalities, laboratory results (complete blood count with differential (CBCD), electrolytes, blood urea nitrogen (BUN), creatinine, prothrombin time (PT), partial thromboplastin time (PTT), calcium, magnesium, liver function tests, gamma-glutamyl transferase (GGT), amylase, lipase, CO₂ level, blood glucose, HbA1C, creatine phosphokinase (CPK), troponin, ferritin, D-Dimer, C-reactive protein (CRP), interleukin-6 (IL6), and lactate dehydrogenase (LDH)). We also collected data regarding the classification of the stage of disease at the time of admission to the hospital, using the guidelines of the Lebanese Society of Infectious Diseases and Clinical Microbiology (LSIDCM) [11]. In addition, treatments and interventions used, disease course (improvement, progression, or no changes), polymerase chain reaction (PCR) results (changed to negative/ still positive) during ICU stay, need for intubation, and medical and infectious complications were utilized as data in our study.

Ethics

Owing to the retrospective aspect of the study, a waiver was granted as informed

consent; instead, an access letter to patients' medical records was received. This study was conducted according to the principles of the Declaration of Helsinki (7th revision).

Statistical analysis

Categorical variables were represented as frequencies or percentages with 95% Confidence Intervals (CI) and Odds Ratio (OR). As for continuous variables, they were reported as median with ranges. We calculated: the ICU mortality rate, length of stay in the ICU, and duration from COVID-19 diagnosis to death. In addition, we compared survivor and non-survivor groups using the Mann-Whitney U test for continuous variables. As for categorical tests, Chi-squared and Fisher's Exact tests were performed. This was done as the data was non-parametric according to the Shapiro-Wilk test of normality. Furthermore, to identify predictors of ICU mortality, a multivariate logistic regression model was computed. We also explored factors related to severe diseases by comparing mild/moderate and severe/septic groups using Chi-squared and Fisher's Exact tests. Data analysis was performed by Statistical Package for the Social Sciences (SPSS) Version 22, and p -value <0.005 is the statistical significance criteria.

Results

1. Demographic characteristics and fatality rate in the ICU setting

Over a period of 90 days, 191 COVID-19 infected patients were admitted to Baabda Governmental Hospital's ICU. Only 123 (64.4%) survivors were discharged from the critical care unit by the 31st of March 2021. The fatality rate in our population reached 35.6% with a median period of 11 days (range: 0-41 days) from diagnosis to death. Patients' demographics, comorbidities, and blood groups are summarized in Table 1. The median age of patients admitted to the ICU was 69 years (range: 22-98 years), and the majority of patients were males (67.5%). Deceased patients were older ($p<0.001$); however, there was no significant gender

difference among survivors compared to non-survivors (Figure 1A and B).

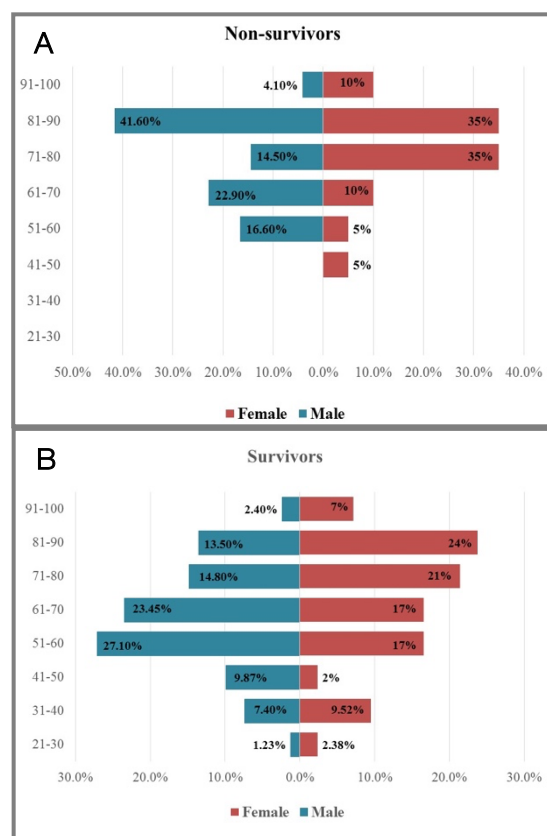


Figure 1: A: Distribution of non-survivors according to age groups and gender. B: Distribution of survivors according to age groups and gender.

Furthermore, 23% of patients were active smokers, with deceased individuals being more frequent smokers ($p=0.008$). Hypertension was the most common underlying chronic condition (62.8%), followed by dyslipidemia (43.5%) and diabetes (40.3%). In addition, non-survivors were more likely to have a history of coronary artery disease, peripheral artery disease, dyslipidemia, heart failure, Alzheimer's disease, benign prostatic hyperplasia, and chronic obstructive pulmonary disease (COPD) ($p<0.05$). The most prevalent blood group in ICU patients was A positive (44.0%) and there were no significant differences in blood groups between deceased and alive individuals.

2. Clinical, radiological, and laboratory characteristics in patients with COVID-19 on admission to ICU

Clinical, radiological, and laboratory characteristics of patients admitted to ICU are represented in Table 2. Cough (87.4%) and fever (83.8%) were the most frequent symptoms at admission. Compared to survivors, non-survivors were more likely to experience fever, dyspnea, chest pain, and septic shock ($p < 0.05$). Moreover, 67% of ICU patients presented to the hospital in severe conditions. Besides, severe and septic stages at admission were frequently reported among non-survivors, whereas mild to moderate stages were more likely seen in survivors ($p < 0.001$).

No statistically significant difference was detected between both groups in regards to abnormal radiological findings; However, abnormal ECGs were more commonly seen in deceased patients ($p < 0.001$).

As for vital signs at admission, the median blood pressure in our population was 130 over 70 mmHg. Half of the patients had a temperature of 37°C, oxygen saturation of 92%, and a heart rate of 85 beats per minute. Among all these signs, only the heart rate was significantly higher in non-survivors, but with the absence of clinical significance ($p < 0.001$).

Regarding laboratory findings, non-survivors presented at admission with statistically higher white blood cells (WBC) ($p = 0.006$), creatinine ($p < 0.001$), aspartate aminotransferase (AST) ($p < 0.001$), and troponin ($p < 0.001$) but without reaching any clinical significance. Furthermore, deceased patients had statistically lower calcium ($p = 0.036$), magnesium ($p = 0.004$), albumin ($p < 0.001$), and monocyte ($p = 0.044$) levels without achieving clinical significance. Levels of neutrophils ($p = 0.013$), blood urea nitrogen (BUN) ($p < 0.001$), ferritin ($p = 0.002$), direct bilirubin ($p = 0.047$), LDH ($p < 0.001$), CRP ($p = 0.008$), and prolonged PT ($p = 0.008$) were significantly higher among non-survivors.

3. Main interventions and treatments

Treatment and interventions provided in the ICU are shown in Table 3. Among all drugs administered for the treatment of COVID-19, levofloxacin usage stood out (85.3%) and

corticosteroids were frequently administered with other drugs (68.8%). We did not notice any statistical difference after comparing treatments of survivors to that of non-survivors, except for the increased usage of Piperacillin-Tazobactam ($p < 0.001$), Meropenem ($p = 0.011$), Teicoplanin ($p < 0.001$), and Tigecycline ($p = 0.005$) in non-survivors. Out of 191 ICU patients, 32 patients were intubated (16.8%) and intubation was more common among deceased patients ($p < 0.001$).

4. ICU complications and outcomes

ICU complications and outcomes are reported in Table 3. The most common complication in COVID-19 ICU patients was cytokine storm (43, 22.5%) while the least common was deep vein thrombosis (1, 0.5%). In addition, more likely encountered adverse events among non-survivors were: ventilator-associated pneumonia (VAP), sepsis, cytokine storm, myocardial infarction, and pulmonary embolism ($p < 0.001$).

During their ICU stay, the majority (63.4%) of the patients experienced an improvement in their condition. Progression ($p < 0.001$) and no changes ($p = 0.004$) in disease status were more likely observed among non-survivors. In contrast, condition improvement was more frequently encountered in survivors ($p < 0.001$). Among 191 patients, the polymerase chain reaction (PCR) test changed to negative in 56 (29.3%) patients, during a median period of 12 days (range, 0-27 days). A change to negative in a PCR test was more likely reported in survived individuals ($p < 0.001$). The median length of stay (LOS) in the ICU and also in the hospital was 8 days (range, 0-37 days) for both survivors and non-survivors, with an increased LOS in the hospital ($p = 0.025$) and the ICU ($p = 0.005$) in survivors.

5. Mortality Predictors of COVID-19 patients in ICU settings

Multivariable regression analysis identified older age, intubation, and severe or septic stage at admission as predictors of death in COVID-19 ICU patients ($p < 0.001$) as shown

in Table 4.

6. Parameters affecting the severity of COVID-19 disease in patients admitted to the ICU.

Since severe and septic stages at admission were clinical predictors of mortality in the ICU setting, we evaluated parameters influencing disease severity in our population. Comorbidities such as diabetes ($p=0.050$), hypertension ($p=0.003$), and dyslipidemia ($p=0.006$) were more likely seen in severe or septic patients. O negative blood group was frequently encountered in mild and moderate COVID-19 patients ($p=0.044$) while O positive was more common in severe or septic patients ($p=0.002$) (Table 5). However, none of these factors was shown to be a predictor of severe disease in multivariate analysis.

Discussion

Previous reports showed that SARS-CoV-2 is a mild disease in the majority of cases, but it can be severe and deadly in a small proportion of individuals, who might require ICU admission [12]. The widespread outbreak of COVID-19 worldwide strained ICUs' capacities, particularly in Lebanon, which is a country that lacks sufficient critical care resources. Herein, we conducted a monocentric retrospective cohort study that included 191 COVID-19 ICU patients in Baabda Governmental Hospital over a period of 90 days (from January 1, 2021, to March 31, 2021). This study revealed two important findings. First, the mortality rate in ICU COVID-19 patients was 35.6%. Second, older age, intubation, and severe/septic stages at admission were associated with an increased risk of death. ICU fatality rate in our study was in line with recently published meta-analyses [4]; however, this proportion might not be very reflective of the mortality rate in critically ill patients, as a study reported a 6% in-hospital death rate after ICU discharge [13]. In addition, the mortality rate varies between studies [7–9,14–18] as a result of different population sizes, length of follow-up, and availability of ICU beds. This percentage is also dependent on the country and stage of

the outbreak.

Our data showed that older age was a risk factor for ICU admission and mortality [7,9,14]. Indeed, advanced age is characterized by multiple comorbid conditions, and frailty, and is coupled with an aged immune system, which might increase the risk of COVID-19 poor outcome and death. Similar to our findings, the most prevalent blood group among Lebanese COVID-19 patients was A positive, [19] with no association existing among blood group, COVID-19 severity, and death inside or outside of the ICU [9,19]. Furthermore, smoking was positively associated with ICU mortality as demonstrated by Alharthy et al. [9]. As for underlying chronic conditions, hypertension, dyslipidemia, and diabetes were the leading comorbidities in ICU settings [8,16]. In addition, dyslipidemia and COPD were more prevalent in deceased ICU patients, results which were also observed in a study done in Lombardy, Italy [17]. Other chronic comorbidities such as hypertension, diabetes, and chronic kidney diseases were also associated with decreased survival in ICU [15,17,18]. Pre-existing chronic diseases such as hypertension, diabetes, and dyslipidemia were also correlated with disease severity as demonstrated in our results [18].

Regarding laboratory findings, elevated levels of LDH, CRP, and ferritin were associated with a higher risk of ICU mortality. As of matter of fact, current literature underlines the role of these factors in predicting mortality and worsening of COVID-19 conditions [20–22]. Other biomarkers such as D-dimer, procalcitonin, and fibrinogen were also reported as predictors of mortality in critically ill patients [9,23–25].

In contrast to our findings, COVID-19 active treatments were not found as determinative factors for ICU death [8,26]. On the other hand, we found that active treatment for COVID-19 with Piperacillin-Tazobactam, Meropenem, and Teicoplanin was more prevalent among non-survivors. Thus, inappropriate use of antibiotics, particularly

broad-spectrum ones, should be avoided. In addition, we recorded lower rates of intubation in our population (16.7%) compared to 88% in Lombardy [16] and 80% in France, Belgium, and Switzerland [27]. Our study identified intubation as an independent risk factor for ICU mortality. This is consistent with the meta-analysis done by Chang et al. who also revealed a 43% mortality rate among intubated patients [18]. This could be explained by the fact that invasive mechanical ventilation itself carries many adverse events [28]. Conversely, a study done in central Florida proved that intubation was not necessarily associated with poor COVID-19 outcomes when applied according to guidelines [29].

Severe and septic stages at hospital admission were recognized as predictors of death in ICU settings. This is similar to a study done by Ayed et al, where moderate to severe Acute Respiratory Disease Syndrome (ARDS) was a predictor of death in critically ill individuals [26]. Another study proved that each 5 –point increase in Acute Physiologic Assessment and Chronic Health Evaluation (APACHE) II score was correlated with a 51% increased risk of death in ICU [7]. These findings could be attributed to the fact that severe COVID-19 disease is characterized by hyperinflammatory and hypercoagulability states, resulting in an increased risk of complications, hence an elevated probability of death [30].

Limitations

This study presents several limitations. Firstly, this is a retrospective observational research conducted in a single center over a short period of time. Secondly, a small number of patients were enrolled in the study. Both of these limitations could affect the generalization of our results to a wider population. The effect of Body Mass Index (BMI), PO₂/FIO₂, and procalcitonin on mortality risk was not assessed due to a lack of data in electronic medical records.

Perspectives and Recommendations

To our knowledge, this is the first study in Lebanon that assesses clinical

characteristics, disease course, and mortality risk factors of patients infected with COVID-19, in ICU settings. Our findings will allow accurate identification of critically ill patients with COVID-19, guide the effective use of ICU capacity, and help prioritization the patients with the greatest clinical needs. In addition, these mortality predictors should be taken into consideration while planning public health interventions (awareness and vaccinations), to protect the most vulnerable from contracting the virus. Due to previously mentioned limitations, larger prospective and multicentric studies are needed to provide more accurate and representative results.

Conclusion

SARS-CoV-2 is exhausting the ICUs in Lebanon and throughout the world physically, materially, and emotionally. In this cohort, the fatality rate reached 35.6%, and older age, intubation, and severe/septic stage at admission were significant predictors of mortality in ICU settings. These findings will help in risk assessment, management of patients, and proper allocation of critical care resources. They will also assist public health interventions to be more targeted toward vulnerable populations.

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Appendix

Table 1. Demographic characteristics, medical history and blood group of patients admitted to ICU with COVID-19.

Data are expressed as median with range or frequency with percentage. Total counts are presented for each cell. Comparison between survivors and non-survivors have been performed by a non-parametric Mann-Whitney U test for continuous variable or by the Chi-square and Fisher's Exact tests for categorical variables. For abbreviations: CKD: Chronic Kidney Disease; COPD: Chronic Obstructive Pulmonary Diseases; OR: Odds ratio NS: Non-Survivors; S: Survivors; CI: Confidence Interval.

		Total (N = 191)	NS (N = 68)	S (N = 123)	P-value	OR	95% CI	
							Lower	Upper
Demographics								
Gender	Male	129	48	81	0.503	1.244	0.655	2.363
		67.5%	70.6%	65.9%				
	Female	62	20	42				
		32.5%	29.4%	34.1%				
Age	Median	69.00	79.00	63.00	<0.001	----	----	----
	(Min - Max)	(22-98)	(49-94)	(22-98)				
Medical History								
Active Smoking	No	147	45	102	0.008	0.403	0.203	0.801
		77.0%	66.2%	82.9%				
	Yes	44	23	21				
		23.0%	33.8%	17.1%				
Diabetes	No	114	36	78	0.158	0.649	0.356	1.184
		59.7%	52.9%	63.4%				
	Yes	77	32	45				
		40.3%	47.1%	36.6%				
Hypertension	No	71	20	51	0.099	0.588	0.312	1.108
		37.2%	29.4%	41.5%				
	Yes	120	48	72				
		62.8%	70.6%	58.5%				
Dyslipidemia	No	108	32	76	0.049	0.550	0.302	1.001
		56.5%	47.1%	61.8%				
	Yes	83	36	47				

		43.5%	52.9%	38.2%				
Coronary Artery Disease	No	133	37	96	0.001	0.336	0.177	0.637
		69.6%	54.4%	78.0%				
	Yes	58	31	27				
		30.4%	45.6%	22.0%				
Heart Failure	No	148	43	105	<0.001	0.295	0.146	0.595
		77.5%	63.2%	85.4%				
	Yes	43	25	18				
		22.5%	36.8%	14.6%				
Peripheral Artery Disease	No	165	54	111	0.037	0.417	0.181	0.963
		86.4%	79.4%	90.2%				
	Yes	26	14	12				
		13.6%	20.6%	9.8%				
Hypothyroidism	No	183	64	119	0.458	0.538	0.130	2.222
		95.8%	94.1%	96.7%				
	Yes	8	4	4				
		4.2%	5.9%	3.3%				
Hyperthyroidism	No	188	67	121	0.934	1.107	0.099	12.441
		98.4%	98.5%	98.4%				
	Yes	3	1	2				
		1.6%	1.5%	1.6%				
Alzheimer	No	153	46	107	0.001	0.313	0.151	0.649
		80.1%	67.6%	87.0%				
	Yes	38	22	16				
		19.9%	32.4%	13.0%				
Benign Prostatic Hyperplasia	No	163	53	110	0.032	0.418	0.185	0.940
		85.3%	77.9%	89.4%				
	Yes	28	15	13				
		14.7%	22.1%	10.6%				
Cancer	No	172	58	114	0.102	0.458	0.176	1.189
		90.1%	85.3%	92.7%				
	Yes	19	10	9				
		9.9%	14.7%	7.3%				
CKD	No	176	60	116	0.135	0.453	0.157	1.308
		92.1%	88.2%	94.3%				
	Yes	15	8	7				

		7.9%	11.8%	5.7%				
COPD	No	167	52	115	0.001	0.226	0.091	0.562
		87.4%	76.5%	93.5%				
	Yes	24	16	8				
		12.6%	23.5%	6.5%				
Blood Group								
A (Positive)	No	79	33	46	0.338	1.401	0.702	2.793
		56.0%	61.1%	52.9%				
	Yes	62	21	41				
		44.0%	38.9%	47.1%				
A (Negative)	No	136	52	84	0.636	0.929	0.150	5.744
		96.5%	96.3%	96.6%				
	Yes	5	2	3				
		3.5%	3.7%	3.4%				
B (Positive)	No	127	48	79	0.712	0.810	0.265	2.477
		90.1%	88.9%	90.8%				
	Yes	14	6	8				
		9.9%	11.1%	9.2%				
B (Negative)	No	139	54	85	0.524	0.612	0.536	0.698
		98.6%	100.0%	97.7%				
	Yes	2	0	2				
		1.4%	0.0%	2.3%				
AB (Positive)	No	130	49	81	0.611	0.726	0.210	2.505
		92.2%	90.7%	93.1%				
	Yes	11	5	6				
		7.8%	9.3%	6.9%				
AB (Negative)	No	140	53	87	0.383	----	----	----
		99.3%	98.1%	100.0%				
	Yes	1	1	0				
		0.7%	1.9%	0.0%				
O (Positive)	No	100	36	64	0.381	0.719	0.343	1.506
		70.9%	66.7%	73.6%				
	Yes	41	18	23				
		29.1%	33.3%	26.4%				
O (Negative)	No	137	53	84	0.579	1.893	0.192	18.676
		97.2%	98.1%	96.6%				

	Yes	4	1	3				
		2.8%	1.9%	3.4%				

Table 2. Clinical, radiological and laboratory characteristics of patients admitted to ICU with COVID-19.

Data are expressed as median with range or frequency with percentage. Total counts are presented for each cell. Comparison between survivors and non-survivors have been performed by a non-parametric Mann-Whitney U test for continuous variable or by the Chi-square test for categorical variables. For abbreviations: NS: Non Survivors; S: Survivors; CI: Confidence Interval; ALT: Alanine Transaminase; AST: Aspartate Aminotransferase; BUN: Blood Urea Nitrogen; CPK: Creatine Phosphokinase; CRP: C - Reactive Protein; DBP: Diastolic Blood Pressure; GGT: Gamma-Glutamyl Transferase; HBA1C: Hemoglobin A1C; IL6: Interleukin-6; INR: International Normalized Ratio; LDH: Lactate Dehydrogenase; MCH: Mean Corpuscular Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; MCV: Mean Corpuscular Volume; OR: Odds Ratio; PT: Prothrombin Time; PTT: Partial Thromboplastin Time; RBC: Red Blood Cell; RDW: Red Cell Distribution Width; SBP: Systolic Blood Pressure; WBC: White Blood Cell.

		Total (N = 191)	NS (N = 68)	S (N = 123)	P-value	OR	95% CI	
							Lower	Upper
Symptoms								
Fever	No	31	17	14	0.015	2.595	1.188	5.671
		16.2%	25.0%	11.4%				
	Yes	160	51	109				
		83.8%	75.0%	88.6%				
Cough	No	24	12	12	0.115	1.982	0.837	4.695
		12.6%	17.6%	9.8%				
	Yes	167	56	111				
		87.4%	82.4%	90.2%				
Sore throat	No	109	37	72	0.581	0.845	0.465	1.536
		57.1%	54.4%	58.5%				
	Yes	82	31	51				
		42.9%	45.6%	41.5%				
Malaise	No	43	16	27	0.803	1.094	0.541	2.213
		22.5%	23.5%	22.0%				
	Yes	148	52	96				
		77.5%	76.5%	78.0%				
Headache	No	103	34	69	0.418	0.783	0.432	1.417
		53.9%	50.0%	56.1%				
	Yes	88	34	54				
		46.1%	50.0%	43.9%				
Muscle	No	82	30	52	0.806	1.078	0.593	1.959

pain		42.9%	44.1%	42.3%				
	Yes	109	38	71				
		57.1%	55.9%	57.7%				
Nausea	No	124	39	85	0.103	0.601	0.325	1.111
		64.9%	57.4%	69.1%				
	Yes	67	29	38				
		35.1%	42.6%	30.9%				
Vomiting	No	137	47	90	0.551	0.821	0.428	1.573
		71.7%	69.1%	73.2%				
	Yes	54	21	33				
		28.3%	30.9%	26.8%				
Diarrhea	No	133	48	85	0.831	1.073	0.562	2.049
		69.6%	70.6%	69.1%				
	Yes	58	20	38				
		30.4%	29.4%	30.9%				
Dyspnea	No	63	13	50	0.002	0.345	0.171	0.697
		33.0%	19.1%	40.7%				
	Yes	128	55	73				
		67.0%	80.9%	59.3%				
Chest Pain	No	149	42	107	<0.001	0.242	0.118	0.495
		78.0%	61.8%	87.0%				
	Yes	42	26	16				
		22.0%	38.2%	13.0%				
Septic Shock	No	183	62	121	0.017	0.171	0.033	0.871
		95.8%	91.2%	98.4%				
	Yes	8	6	2				
		4.2%	8.8%	1.6%				
Staging								
Staging at admission	Mild	7	0	7	<0.001	----	----	----
		3.7%	0.0%	5.7%				
	Moderate	47	1	46				
		24.6%	1.5%	37.4%				
	Severe	128	60	68				
		67.0%	88.2%	55.3%				
	Sepsis	9	7	2				

		4.7%	10.3%	1.6%				
Radiology								
Pleural effusion	No	177	62	115	0.556	0.719	0.239	2.165
		92.7%	91.2%	93.5%				
	Yes	14	6	8				
		7.3%	8.8%	6.5%				
ECG								
ECG Findings at admission	Abnormal	58	32	26	<0.001	3.316	1.743	6.311
		30.4%	47.1%	21.1%				
	Normal	133	36	97				
		69.6%	52.9%	78.9%				

Total (N = 191)		NS (N = 68)		S (N = 123)		P-value
Median	(Min - Max)	Median	(Min - Max)	Median	(Min - Max)	

Laboratory							
WBC (x10 ⁹ /L)	7.37	(0.99-37.22)	8.58	(0.99-37.22)	6.34	(1.86-19.25)	0.006
RBC (x10 ¹² /L)	4.59	(1.20-7.09)	4.46	(2.26-7.09)	4.64	(1.20-6.10)	0.150
Hemoglobin (g/dl)	12.85	(3.40-18.90)	12.60	(7.70-18.90)	13.00	(3.40-16.60)	0.394
Hematocrit (%)	39.20	(10.40-53.20)	38.90	(22.00-53.20)	39.40	(10.40-51.30)	0.569
MCV (fL)	86.15	(58.20-112.30)	87.40	(64.70-112.30)	85.60	(58.20-102.90)	0.131
MCH (pg)	28.50	(18.30-99.70)	28.80	(21.50-99.70)	28.50	(18.30-34.10)	0.555
MCHC (g/dl)	32.80	(23.20-38.70)	32.70	(26.00-38.70)	32.90	(23.20-36.30)	0.223
RDW (%)	13.90	(11.00-20.10)	14.50	(11.00-19.90)	13.50	(12.00-20.10)	<0.001
Platelet count (x10 ⁹ /L)	220.00	(54.00-816.00)	204.00	(62.00-816.00)	220.00	(54.00-584.00)	0.908
MPV (fL)	10.60	(8.30-	10.60	(8.50-	10.60	(8.30-	0.265

		12.60)		12.30)		12.60)	
Neutrophil (%)	84.40	(26.30-98.00)	86.40	(26.30-98.00)	82.70	(50.40-96.50)	0.013
Lymphocyte (%)	10.70	(0.30-72.30)	9.50	(1.70-72.30)	11.50	(0.30-40.90)	0.016
Neutrophil / Lymphocyte	8.07	(0.36-281.33)	9.00	(0.36-56.94)	7.28	(1.27-281.33)	0.015
Monocyte (%)	4.25	(0.50-12.50)	3.30	(0.70-8.60)	4.60	(0.50-12.50)	0.044
Eosinophil (%)	0.00	(0.00-3.50)	0.00	(0.00-3.50)	0.00	(0.00-2.70)	0.934
Basophil (%)	0.10	(0.00-2.00)	0.10	(0.00-1.10)	0.10	(0.00-2.00)	0.423
INR	1.21	(0.94-6.00)	1.25	(1.00-5.56)	1.18	(0.94-6.00)	0.058
D-Dimer (ng/ml)	801.00	(100.00-20000.00)	1600.00	(100.00-16333.00)	576.00	(100.00-20000.00)	0.146
PT (seconds)	14.55	(11.60-80.00)	15.20	(12.30-46.70)	14.40	(11.60-80.00)	0.008
PTT (seconds)	30.70	(21.20-130.00)	30.30	(24.00-53.90)	30.70	(21.20-130.00)	0.148
Glucose (mg/dL)	125.50	(35.00-778.00)	129.50	(35.00-579.00)	125.50	(61.00-778.00)	0.955
BUN (mg/dL)	24.00	(7.00-175.00)	31.50	(9.00-175.00)	20.00	(7.00-140.00)	<0.001
Creatinine (mg/dL)	1.00	(0.26-12.81)	1.32	(0.61-12.81)	0.85	(0.26-5.25)	<0.001
BUN / Creatinine Ratio	22.00	(8.14-65.08)	24.72	(8.14-52.17)	20.82	(9.80-65.08)	0.029
Calcium serum (mg/dL)	8.10	(5.20-10.00)	8.10	(5.20-9.30)	8.25	(5.40-10.00)	0.036
Magnesium (mg/dL)	1.95	(1.37-3.01)	2.03	(1.39-3.01)	1.92	(1.37-2.80)	0.004
Sodium (mEq/L)	136.00	(124.00-155.00)	136.00	(124.00-155.00)	136.00	(124.00-153.00)	0.367
Potassium (mEq/L)	3.90	(2.68-6.37)	3.99	(2.88-6.37)	3.87	(2.68-5.75)	0.211

Chloride (mEq/L)	100.00	(79.00-121.00)	99.00	(79.00-121.00)	100.00	(83.00-118.00)	0.471
Carbone Dioxide (mEq/L)	24.00	(10.00-35.00)	24.00	(10.00-35.00)	25.00	(16.00-30.00)	0.173
Albumin (g/L)	31.00	(16.00-50.00)	29.00	(16.00-40.00)	31.50	(17.00-50.00)	<0.001
Ferritin (µg/L)	629.30	(8.00-2105.00)	899.05	(60.80-2105.00)	498.80	(8.00-2100.00)	0.002
Total Bilirubin (mg/dL)	0.78	(0.16-6.58)	0.77	(0.20-1.56)	0.78	(0.16-6.58)	0.798
Direct Bilirubin (mg/dL)	0.21	(0.06-4.34)	0.22	(0.07-0.86)	0.18	(0.06-4.34)	0.047
ALT (IU/L)	25.00	(3.00-876.00)	26.00	(10.00-114.00)	24.00	(3.00-876.00)	0.854
AST (IU/L)	40.00	(11.00-1429.00)	45.00	(13.00-250.00)	38.00	(11.00-1429.00)	<0.001
Alkaline Phosphatase (IU/L)	45.00	(23.00-268.00)	42.00	(23.00-268.00)	46.00	(24.00-188.00)	0.261
GGT (U/L)	29.50	(5.00-490.00)	31.00	(8.00-395.00)	29.00	(5.00-490.00)	0.788
Troponin (ng/ml)	0.02	(0.00-7.70)	0.04	(0.00-7.70)	0.02	(0.00-3.14)	<0.001
CPK (U/L)	115.00	(19.00-5521.00)	123.50	(19.00-5521.00)	110.00	(20.00-2610.00)	0.512
Amylase (U/L)	60.50	(23.00-407.00)	62.00	(30.00-407.00)	57.00	(23.00-246.00)	0.336
Lipase (U/L)	30.00	(8.00-670.00)	31.00	(12.00-670.00)	29.00	(8.00-354.00)	0.265
LDH (U/L)	279.50	(115.00-880.00)	358.50	(143.00-880.00)	255.50	(115.00-744.00)	<0.001
CRP (mg/dL)	125.78	(5.72-534.56)	144.93	(17.24-534.56)	113.87	(5.72-429.13)	0.008
IL6 (pg/ml)	44.28	(7.06-	44.28	(18.80-	47.17	(7.06-	0.916

		528.00)		140.00)		528.00)	
HBA1C (%)	7.10	(5.50-15.20)	7.20	(5.50-15.20)	7.10	(5.50-13.10)	0.721
Vital Signs							
SBP (mmHg)	13.0000	(7.00-18.00)	13.00	(7.00-18.00)	13.00	(7.00-18.00)	0.164
DBP (mmHg)	7.0000	(4.00-16.00)	7.00	(4.00-16.00)	7.00	(5.00-11.00)	0.115
Heart Rate (beats per minute)	85.0000	(50.00-136.00)	86.00	(50.00-124.00)	83.00	(60.00-136.00)	<0.00 1
Oxygen Saturation (in %)	92.0000	(45.00-99.00)	88.00	(45.00-97.00)	93.00	(45.00-99.00)	0.532
Temperature (°C)	37.0000	(36.00-40.00)	36.80	(36.00-39.00)	37.00	(36.00-40.00)	0.699

Table 3. Management, interventions, clinical course, complications and length of stay (LOS) of patients admitted to ICU with COVID-19.

Data are expressed as median with range or frequency with percentage. Total counts are presented for each cell. Comparison between survivors and non-survivors have been performed by a non-parametric Mann-Whitney U test for continuous variable or by the Chi-square and Fisher's Exact tests for categorical variables. For abbreviations: NS: Non Survivors; S: Survivors; CI: Confidence Interval; IVIG: Intravenous Immunoglobulin; LOS: Length of Stay; OR: Odds Ratio; PCR: Polymerase Chain Reaction; VAP: Ventilator Associated Pneumonia.

		Total (N = 191)	NS (N = 68)	S (N = 123)	P-value	OR	95% CI Lower Upper	
Treatment								
Pulse Steroid	No	159	53	106	0.144	0.567	0.263	1.222
		83.2%	77.9%	86.2%				
	Yes	32	15	17				
		16.8%	22.1%	13.8%				
Actemra	No	170	62	108	0.476	1.435	0.530	3.889
		89.0%	91.2%	87.8%				
	Yes	21	6	15				
		11.0%	8.8%	12.2%				
Remdisivir	No	148	52	96	0.803	0.914	0.452	1.849
		77.5%	76.5%	78.0%				
	Yes	43	16	27				
		22.5%	23.5%	22.0%				
Baricitinib	No	162	54	108	0.122	0.536	0.241	1.190
		84.8%	79.4%	87.8%				
	Yes	29	14	15				
		15.2%	20.6%	12.2%				
Pirfenidone	No	186	66	120	0.835	0.825	0.134	5.062
		97.4%	97.1%	97.6%				
	Yes	5	2	3				
		2.6%	2.9%	2.4%				
IVIG	No	188	67	121	0.934	1.107	0.099	12.441
		98.4%	98.5%	98.4%				
	Yes	3	1	2				
		1.6%	1.5%	1.6%				

Levofloxacin	No	28	7	21	0.205	0.557	0.224	1.388
		14.7%	10.3%	17.1%				
	Yes	163	61	102				
		85.3%	89.7%	82.9%				
Azithromycin	No	175	64	111	0.424	1.730	0.535	5.588
		91.6%	94.1%	90.2%				
	Yes	16	4	12				
		8.4%	5.9%	9.8%				
Piperacillin Tazobactam	No	133	36	97	<0.001	0.302	0.158	0.574
		69.6%	52.9%	78.9%				
	Yes	58	32	26				
		30.4%	47.1%	21.1%				
Meropenem	No	144	44	100	0.011	0.422	0.215	0.826
		75.4%	64.7%	81.3%				
	Yes	47	24	23				
		24.6%	35.3%	18.7%				
Teicoplanin	No	140	39	101	<0.001	0.293	0.150	0.570
		73.3%	57.4%	82.1%				
	Yes	51	29	22				
		26.7%	42.6%	17.9%				
Tigecycline	No	184	62	122	0.005	0.085	0.010	0.719
		96.3%	91.2%	99.2%				
	Yes	7	6	1				
		3.7%	8.8%	0.8%				
Colchicine	No	177	60	117	0.080	0.385	0.128	1.159
		92.7%	88.2%	95.1%				
	Yes	14	8	6				
		7.3%	11.8%	4.9%				
Ivermectine	No	184	64	120	0.249	0.400	0.087	1.842
		96.3%	94.1%	97.6%				
	Yes	7	4	3				
		3.7%	5.9%	2.4%				
Pulse Steroid	Only	10	5	5	0.467	1.750	0.385	7.951
		31.3%	38.5%	26.3%				
	Combination	22	8	14				
		68.8%	61.5%	73.7%				

Intubation								
Intubation	No	159	39	120	<0.001	0.034	0.010	0.116
		83.2%	57.4%	97.6%				
	Yes	32	29	3				
		16.8%	42.6%	2.4%				
Disease Status								
Improvement	No	70	66	4	<0.001	981.7	175.1	5503.6
		36.6%	97.1%	3.3%				
	Yes	121	2	119				
		63.4%	2.9%	96.7%				
Progression	No	130	9	121	<0.001	0.003	0.001	0.012
		68.1%	13.2%	98.4%				
	Yes	61	59	2				
		31.9%	86.8%	1.6%				
No Change	No	181	60	121	0.004	0.124	0.026	0.602
		94.8%	88.2%	98.4%				
	Yes	10	8	2				
		5.2%	11.8%	1.6%				
PCR								
Changed To Negative	No	135	61	74	<0.001	5.770	2.438	13.656
		70.7%	89.7%	60.2%				
	Yes	56	7	49				
		29.3%	10.3%	39.8%				
Time to change to be negative	Median	12.00	17.00	11.00	0.783	----	----	----
	(Min - Max)	(0-27)	(9-27)	(0-25)				
Complications								
VAP	No	181	59	122	<0.001	0.054	0.007	0.434
		94.8%	86.8%	99.2%				
	Yes	10	9	1				
		5.2%	13.2%	0.8%				
Sepsis	No	160	39	121	<0.001	0.022	0.005	0.097
		83.8%	57.4%	98.4%				
	Yes	31	29	2				
		16.2%	42.6%	1.6%				
Cytokine Storm	No	148	40	108	<0.001	0.198	0.096	0.409
		77.5%	58.8%	87.8%				

	Yes	43 22.5%	28 41.2%	15 12.2%				
Myocardial infarction	No	169 88.5%	50 73.5%	119 96.7%	<0.001	0.093	0.030	0.290
		Yes	22 11.5%	18 26.5%				
	No		176 92.1%	56 82.4%				
		Yes	15 7.9%	12 17.6%				
Deep vein thrombosis	No		190 99.5%	67 98.5%	123 100.0%	0.356	----	----
		Yes	1 0.5%	1 1.5%	0 0.0%			

Total (N = 191)		NS (N = 68)		S (N = 123)		P- value
Median	(Min - Max)	Median	(Min - Max)	Median	(Min - Max)	

LOS							
Length of Stay in the hospital	8.00	(1-37)	6.50	(1-37)	9.00	(1-23)	0.025
Length of Stay in the ICU	8.00	(1-37)	6.00	(1-37)	9.00	(1-23)	0.005

Table 4. Multivariate logistic regression analysis of mortality in patients admitted to ICU with COVID-19.

For abbreviations: B: Beta coefficient; DF: Degrees of Freedom; EXP (B): exponentiation of the B coefficient; SE: Standard Error; Sig: Significance Probability.

Multivariate logistic regression analysis of mortality in ICU patients						
Covariates	B	S.E.	Wald	DF	Sig.	Exp(B)
Age	0.073	0.018	17.171	1	<0.001	1.076
Intubation	3.308	0.699	22.423	1	<0.001	27.331
Staging at admission	2.530	0.638	15.719	1	<0.001	12.558
Constant	-13.613	2.504	29.557	1	<0.001	0.000

Table 5. Comparison between mild/ moderate and severe/ sepsis groups in ICU COVID-19 patients regarding medical history and blood groups.

Data are expressed as frequency with percentage. Total counts are presented for each cell. Comparison between mild/ moderate and severe/ sepsis groups have been performed by a non-parametric Chi-square and Fisher's Exact tests. For abbreviations: OR: Odds Ratio; CI: Confidence Interval.

		Staging at admission			P-value	OR	95% CI	
		Total (N=191)	Mild / Moderate (N= 54)	Severe / Sepsis (N=137)			Lower	Upper
Medical History								
Diabetes	No	114	38	76	0.050	1.906	0.971	3.741
		59.7%	70.4%	55.5%				
Yes	77	16	61					
		40.3%	29.6%	44.5%				
Hypertension	No	71	29	42	0.003	2.624	1.374	5.009
		37.2%	53.7%	30.7%				
Yes	120	25	95					
		62.8%	46.3%	69.3%				
Dyslipidemia	No	108	39	69	0.006	2.562	1.294	5.074
		56.5%	72.2%	50.4%				
Yes	83	15	68					
		43.5%	27.8%	49.6%				
Blood Group								
A (Positive)	No	79	17	62	0.416	0.726	0.335	1.574
		56.0%	50.0%	57.9%				
Yes	62	17	45					
		44.0%	50.0%	42.1%				
A (Negative)	No	136	33	103	0.827	1.282	0.138	11.872
		96.5%	97.1%	96.3%				
Yes	5	1	4					
		3.5%	2.9%	3.7%				
B (Positive)	No	127	31	96	0.805	1.184	0.310	4.519
		90.1%	91.2%	89.7%				
Yes	14	3	11					
		9.9%	8.8%	10.3%				
B (Negative)	No	139	33	106	0.425	0.311	0.019	5.116

		98.6%	97.1%	99.1%				
	Yes	2	1	1				
		1.4%	2.9%	0.9%				
AB (Positive)	No	130	29	101	0.085	0.345	0.098	1.211
		92.2%	85.3%	94.4%				
	Yes	11	5	6				
		7.8%	14.7%	5.6%				
AB (Negative)	No	140	34	106	0.759	0.757	0.689	0.832
		99.3%	100.0%	99.1%				
	Yes	1	0	1				
		0.7%	0.0%	0.9%				
O (Positive)	No	100	31	69	0.002	5.691	1.631	19.852
		70.9%	91.2%	64.5%				
	Yes	41	3	38				
		29.1%	8.8%	35.5%				
O (Negative)	No	137	31	106	0.044	0.097	0.010	0.971
		97.2%	91.2%	99.1%				
	Yes	4	3	1				
		2.8%	8.8%	0.9%				