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Original Article

Retrospective study of fatal and recovered COVID-19 cases in the intensive care unit of Manavgat State Hospital

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ABSTRACT

Objectives: In this study we aimed to describe the clinical features, treatment, and outcomes of patients with COVID-19 admitted to the intensive care unit.

Patients and methods: In this retrospective, observational study, we enrolled 116 patients (69 males, 47 females; mean age: 66.9±13.6 years; range, 23 to 93 years) with COVID-19 confirmed by PCR tests who were admitted to Manavgat State Hospital. Demographic data, symptoms, laboratory findings, comorbidities, treatment, and outcomes were collected between August 1, 2020, and January 1, 2021. Data were compared between patients who died and those who survived.

Results: A total of 62 patients died, with a 53.4% mortality rate, while 54 recovered. The demographic analysis indicated that mortality for patients in the older age group (i.e., ≥60 years) was higher than those in the younger age group (84%, 68.5%). In addition, seven laboratory parameters were statistically associated with mortality: neutrophil ($p<0.001$), C-reactive protein ($p<0.001$), urea ($p<0.001$), lactate dehydrogenase ($p<0.001$), ferritin ($p<0.001$), D-dimer ($p<0.001$), and Troponin-I ($p<0.001$). Sixty-three patients (55%) required mechanical ventilation, and only one patient (2%) survived after mechanical ventilation. The median time from intensive care unit admission to death was 11.5 days (interquartile range 7.0-17). At 28 days and 60 days, 57 (49%) and four (3.5%) patients died, respectively. On the 72nd day, one (0.9%) patient died.

Conclusion: Neutrophil, C-reactive protein, urea, lactate dehydrogenase, ferritin, D-dimer, and Troponin-I counts were found to be predictive of death in these patients. Further studies are needed to aid efficient recognition and management of severe COVID-19 patients in our population.

Keywords: COVID-19, CRP, intensive care units, Manavgat, non-survivors, survivors.

Since the epidemic of novel coronavirus disease 2019 (COVID-19) struck Wuhan China in late December 2019, it has spread all over the world, resulting in more than 85 million confirmed cases and more than 1.8 million deaths, according to data on January 4, 2021.[1,2] The current study's aims are to analyze clinical and laboratory abnormalities in COVID-19 patients in the intensive care units (ICUs) in order to determine which predictors can distinguish between those who are at higher risk of developing death.

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Several meta-analyses have been conducted to identify any significant risk factors associated with severe COVID-19 and mortality. The first meta-analysis study consisted of 49 published studies conducted by Figliozzi et al.[3] revealed that advanced age, male sex, cardiovascular disease, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, acute organ injury, increased levels of C-reactive protein (CRP) and D-dimer, and lymphocytopenia are associated with the highest odds of mortality.

Factors affecting morbidity and mortality in patients with COVID-19 have been studied and analyzed by several research teams from different countries.[4-6] The presence of comorbidities such as hypertension, obesity, chronic pulmonary disease, diabetes mellitus, chronic kidney disease, malignancies, and old age were factors correlated with severe COVID-19.[4]

PATIENTS AND METHODS

In this study, we evaluated retrospectively the patients who were hospitalized in the Anesthesiology ICU at Manavgat State Hospital with the diagnosis of COVID-19 infection confirmed by a real-time polymerase chain reaction (RT-PCR) test in a nasopharyngeal or tracheal swab sample between August 1, 2020, and January 1, 2021. A total of 116 patients (69 males, 47 females; mean age: 66.9±13.6 years; range, 23 to 93 years) aged 18 and over who were diagnosed with COVID-19 were included in the study. The majority 89 (77%) of the patients (mean age: 67.0±11.8 years; range, 60 to 93) were older than 59 years. Clinical data were collected after reviewing the patients' electronic medical records, nursing records, clinical findings, laboratory findings, and outcome information including demographic information, chronic comorbidities, vital signs, symptoms, and laboratory tests. The patients were divided into three groups: all patients (n=116), 54 (46.5%) were survivors, and 62 (53.45%) were non-survivors in the current study.

Statistical analysis

All statistical analyses were conducted using SPSS for Windows version 10 software (SPSS Inc., Chicago, USA). Categorical variables were expressed as frequencies and percentages (%). Continuous variables were expressed as mean ± standard deviation, median and interquartile range (IQR). The Kolmogorov-Smirnov test was used to assess the normality assumption for the continuous variables. Differences between independent groups for continuous variables were evaluated by Student's t-test and Mann-Whitney U test accordingly. The differences in proportions between the groups were compared using chi-square or Fisher exact tests as appropriate. All *p*-values of less than 0.05 were considered to indicate statistical significance.

RESULTS

All patients' SARSCoV-2 RT-PCR test was positive. Considering that the age, sex, and comorbidities had been reported to be the common death risk factors of COVID-19, enrolled survivors and non-survivors were statistically summarized in Table 1. Also, non-survivors tended to have higher temperatures on admission, as shown in Table 2, and shorter time of hospital stay 11.5 (interquartile range 7.0-17) and 14.0 (interquartile range 6.0-19.0), (p=0.493) in non-survivors than survivors, as shown in Table 1.

All patients, and the vast majority of those who died, had type A blood. A total of 83 (71.5%) patients had at least one disease-causing comorbidity. The most common accompanying disease was hypertension. A total of 23 (20%) patients had diabetes and 43 (37%) had arterial hypertension, while 33 (28.5%) had no comorbid disease. In the death group, 22 (35.5%) patients had no comorbidity, while 40 patients (64.5%) had at least one comorbidity. At 28 days and 60 days, 57 (49%) and 4 (3.5%) patients died in the ICU, respectively. On the 72nd day, one patient (0.9%) died. It was found that 92% of the patients died within the first 28 days. The median ICU length of stay for all patients was 12.0 days (interquartile range 7.0-18.0), with survivors staying 14.0 days (interquartile range 6.0-19.0) and non-survivors staying 11.5 days (interquartile range 7.0-17). The main characteristics, comorbidities, and blood groups of COVID-19 patients are presented in Table 1.

Sixty-three (55%) of the patients received invasive respiratory support, and one of them survived. The mean fever of all patients admitted to the ICU was 37.0 (interquartile range 36.6-37.8), which was higher in non-survivor patients than in survivors but not statistically significant, as shown in Table 2.

The main laboratory parameters of the 116 patients are presented in Table 2, which indicates that neutrophil, CRP, urea, lactate dehydrogenase (LDH), ferritin, D-dimer, and Troponin-I counts were statistically significantly higher (p<0.001) in non-survivor patients compared to those in the survivor group and were associated with mortality.

Treatment of COVID-19 patients in the ICU during admission is summarized in Table 3. There was no statistically significant difference in the medical treatments used by non-survivors and survivors. All non-survivors received antibiotic treatment. Ninety-eight (84.5%) patients

Table 1. Baseline characteristics and comorbidities of COVID-19 ICU patients

	All patients (n=116)					Non-survivors (n=62)					Survivors (n=54)					
Variables	n	%	Mean±SD	Median	IQR	n	%	Mean±SD	Median	IQR	n	%	Mean±SD	Median	IQR	*p*
General characteristics																
Age (year)			66.9±13.6	67.0	60.0-76.0			70.1±11.9	70.0	61.8-79.3			63.2±14.6	64.5	57.0-74.0	0.006
≥60	89	77				52	84				37	68.5				0.051
Sex																0.453
Male	69	60				39	63				30	55.5				
Female	47	40				23	37				24	44.5				
Blood group																0.003
0	18	15.7				14	22.6				4	7.4				
AB	7	6.0				5	8.1				2	3.6				
A	34	29				22	35.5				12	22.2				
B	14	12.1				8	12.9				6	11.1				
Comorbidities																
Diabetes	23	20				8	13				15	28				0.050
Chronic cardiac disease	25	22				11	18				14	26				0.306
Hypertension	43	37				18	30				25	46				0.063
Asthma	16	14				11	18				5	9				0.175
Chronic pulmonary disease	2	2				2	3.5				0	0				0.497
Chronic kidney diseases	8	7				6	10				2	4				0.279
Neurological disorder	17	15				11	18				6	11				0.297
Malignancy	7	6				3	5				4	7.5				0.705
Others	13	11				5	8				8	15				0.263
Total number of comorbities																
No comorbidities	33	28.5				22	35.5				11	20.5				0.072
One comorbidity	36	31				14	22				22	40				0.035
Two comorbidities	21	18				12	19				9	16				0.708
Three or more comorbidities	26	22				14	22				12	22				0.963
Hospital stays			15.1±13.1	12.0	7.0-18.0			13.9±11.0	11.5	7.0-17			16.5±15.1	14.0	6.0-19.0	0.493

ICU: Intensive care unit; SD: Standard deviation; IQR: Interquartile range.

Table 2. Basic laboratory parameters of COVID-19 patients in the intensive care unit during admission

	All patients (n=116)			Non-survivors (n=62)			Survivors (n=54)			
Variables Laboratory findings at admission	Mean±SD	Median	IQR	Mean±SD	Median	IQR	Mean±SD	Median	IQR	*p*
Body temperature	37.1±0.7	37.0	36.6-37.8	37.4±0.7	37.2	37.0-38	36.8±0.5	36.8	36.4-37.1	0.003
Hemoglobin	11.1±2.1	10.9	9.4-12.5	10.7±2.2	10.6	9.0-11.7	11.5±2.0	11.7	9.6-12.9	0.059
WBC	12292.8±7724.4	10770	7270-15740	14506.4±9156.4	12835	8240-19570	9703.4±4447.7	8920	6505-12300	0.001
Neutrophil	10456.7±7423.3	8990	5430-13840	12729.6±8782.3	10925	6895-17835	7797.7±4118.6	7150	5050-10055	<0.001
Lymphocyte	922.0±708.4	690	400-1380	763.2±751	585	290-887.5	1107.6±611.1	1020	585-1605	0.009
PLT	217600±110799.4	200000	128000-294000	186064.5±111802.2	173000	100750-247250	254490.6±98376.4	229000	177500-325000	0.001
CRP	77.5±80.0	53.3	9.8-133.2	119.0±80.5	114.9	55.4-162.2	28.9±44.4	10.2	0.8-34.6	<0.001
Ferritin	916.1±613.5	754.6	336.6-1650.0	1213.8±548.6	1650	611.4-1650	567.9±492.8	433.5	194.3-881.0	<0.001
Fibrinogen	512.0±272.8	476.0	304.5-678.0	589.1±316.1	541	370-803	429.0±186.7	412.0	278.5-534.0	0.003
D-dimer	1550.2±2908.2	699.0	356.0-1512.0	2262.6±3674.8	1129	629.0-2483.8	716.7±1177.6	445	213.0-665.5	<0.001
Troponin- I	205.3±518.8	24.3	5.0-142.9	361.9±668.6	107.4	23.1-414.7	22.1±46.8	5.2	2.5-19.2	<0.001
INR	2.2±9.0	1.2	1.1-1.4	1.4±0.4	1.3	1.1-1.5	3.1±13.3	1.1	1.0-1.3	0.007
AST	82.7±153.4	30.0	19.0-58.0	121.9±183.7	52.5	30.0-137.5	36.8±89.7	22.0	16.5-28.5	0.003
ALT	241.1±1753.0	44.0	26.0-75.0	392.5±2383.7	53	22.8-112.3	63.9±110.4	37.0	26.0-58.0	0.319
LDH	443.2±257.8	382.0	247.0-664.0	580.4±264.2	622.3	454.5-665	282.7±123.0	250.0	210.5-309	<0.001
Urea	44.7±34.1	35.0	18.0-61.8	63.5±34.6	54.3	37.1-86	22.8±15.5	18.3	11.9-28.6	<0.001
Creatine	1.6±1.9	0.9	0.7-2.1	2±1.5	1.5	0.8-2.9	1.2±2.2	0.7	0.6-1.0	0.034

SD: Standard deviation; IQR: Interquartile range; WBC: White blood cell; PLT: Platelet; CRP: C-reactive protein; INR: International normalized ratio; AST: Aspartate aminotransferasez ALT: Alanin aminotransferase; LDH: Lactate dehydrogenase

Table 3. Treatment of COVID-19 patients in the intensive care unit during admission

	All patients (n=116)		Non-survivors (n=62)		Survivors (n=54)		
Variables treatment	n	%	n	%	n	%	*p*
Invasive mechanical ventilation	63	55	62	100	1	2	0.001
Steroid	70	60.5	41	66	29	54	0.172
Favipavir	98	84.5	51	82.3	47	87.1	0.478
Plaquenil	21	18.5	15	24.1	6	11.1	0.068
Azitromycıne	12	10	5	8	7	13	0.388
Respiratory quinolone	92	79.3	50	80	42	78	0.704
Piperacillin tazobactam	49	42	29	47	20	37	0.290
Cephalosporin	10	8	7	11	3	5.5	0.272
Carbapenem	17	15	6	10	11	20	0.104
Glycopeptide	9	8	4	6.5	5	9	0.573
Fluconazole	6	5	1	2	5	9	0.096
Colistin	1	1	1	1.6	0	0	0.999

received favipiravir, 21 (18.5%) patients received hydroxychloroquine, 70 (60.3%) patients received steroids as methylprednisolone and 114 (98.3%) patients received antimicrobials, while only 2 (1.7%) patients received no antimicrobials, as shown in Table 3.

DISCUSSION

Our study examined several basic, clinical, laboratory, and management characteristics and outcomes of critically ill COVID-19 patients admitted and followed up to hospital discharge or death. In our study, 62 patients (53.45%) were in the death group and 54 (46,55%) patients were in the recovered group among the severely ill 116 patients at admission. In Deng et al.'s study,[7] the death group had a rate of 48.45% and the recovered group had a rate of 51.55%.

Previous studies showed that 2019-nCoV mainly infects middle-aged and elderly people.[7-9] The median age of the deceased patients was 70.0 (interquartile range 61.8-79.3) in our study which is in line with a study conducted by Deng et al.[7] It was 61.5±13.4 years in the Ussaid et al.'s study,[9] with a male predominance (61.7%), in Wuhan, China Chen et al.[10]

According to a previous study that enrolled 199 patients, the median age of SARS non-survivors was 52 (range 25 to 78) years, and age (per 1-year increase) is a risk factor for death.[11]

The death group had more male patients (63.0% and 55.5%, p>0,453) than the recovered group, but the difference was not statistically significant. In their study, Deng et al.[7] found statistically significantly more male patients in the death group (67.0% and 44.0%, ×2=12.024, p<0.001).

Several previous studies have reported mortality among critically ill COVID-19 patients. A multi-center study conducted in several African countries found a 54.7% mortality rate 30 days after ICU admission.[12] Akbudak[13] found a mortality rate of 55.6% after 28 days and 66.7% after 60 days following ICU admission. We found a 28-day mortality rate of 49% and a 60-day mortality rate of 3.5%. On the 72nd day, one (0.9%) patient died. It was found that 92% of the patients died within the first 28 days.

Two comorbidities, particularly cardiovascular diseases and chronic pulmonary diseases, were found to be important predictors of in-hospital mortality in critically ill patients.[14] In the study by Deng et al.,[7] hypertension, lung disease, and heart disease were underlying diseases in

more patients in the death group, and more patients in the death group had more than one comorbidity. Ussaid et al.[9] found the most commonly observed comorbidity among the patients who had died was diabetes followed by hypertension. In our study, more patients in the death group had underlying diseases, especially hypertension, asthma, heart disease, and neurological disorder, and more patients (n=40 patients 64.5%) in the death group had more than one comorbidity.

According to a recent meta-analysis, blood type A may be more susceptible to COVID-19 infection, whereas blood type O may be less susceptible.[15] Both Latz et al.[16] and Zhao et al.[17] found blood type O had the lowest frequency of disease positivity. Alacam and Sari's[18] study included 427 patients with COVID-19, with the ABO blood group distribution being 47.1% A, 29.5% O, 15.9% B, and 7.5% AB. A meta-analysis of Spanish and Italian cohorts after adjusting for age and sex found that odds of having severe COVID-19 disease (defined by respiratory failure) were higher in A/AB groups than in B/O groups.[19] In our study, the majority of the patients who were hospitalized (n=34, 29%) and died (n=22, 35.5%) in the ICU were likely blood type A, but blood type AB was likely less (n=7, 6.0%). In their study, Zietz et al.[20] estimated that Rh-negative blood type had a protective effect against infection, intubation, and death. Ray et al.[21] found a lower risk of severe COVID-19 illness or death with type O blood group versus all others, as well as Rh-negative versus Rh-positive. In our study, 67 (90.5%) of 74 patients with Rh-positive blood types and 7 (9.5%) with Rh-negative blood types were likely ($p<0.001$).

Our study found increased WBC count on the day of admission into intensive care unit in the death group, suggesting that comorbid bacterial or fungal infection may have occurred in these deceased patients ($p=0.001$), as shown in Table 2. Previous studies have found that during SARS-CoV infection in humans, blood lymphocyte counts, in particular, were decreased.[7,22,23] Similar to previous studies, our study found that patients in the death group had a lower lymphocyte count, but the difference was not statistically significant ($p=0.009$). The death group had higher levels of CRP, ferritin, D-Dimer, troponin-I, LDH, and urea levels than the recovered group ($p<0,001$), as shown in Table 2. Significantly elevated cardiac troponin I (mean: 107.4 interquartile range 23.1-414.7) and LDH in the deceased patients, indicating severe cardiac insult, which is consistent with previous studies.[24]

C-reactive protein was considered to be a significant predictor of disease severity in SARS in studies similar to ours.[7,25] In their retrospective study, Ussaid et al.[9] showed increased CRP, ferritin, D-Dimer, troponin- I, and LDH levels in 47 death cases.

The study of Latz et al.[16] consist of 7,648 patients, of whom 123 (9.5%) were admitted to the ICU, and 108 (8.4%) were intubated. In our study, 63 (55%) patients were intubated, as shown in Table 3.

All the patients in intensive care were empirically given corticosteroids, anti-fungal drugs, or antibiotics without solid evidence.

The limitation of our study was that the initial conditions for the two groups were different. Therefore, these results do not provide conclusive data on the effects of different treatments. There was no statistically significant difference between the medical treatments used by the deceased and the surviving groups. It should be noted that the administration of multiple antibiotics had no effect on the disease course or outcome. Treatment of COVID-19 patients in the ICU during their admission is summarized in Table 3.

In conclusion, we studied the clinical records of 62 patients who died from the 2019-nCoV infection and 54 patients who recovered. Patients in the death group exhibited characteristics of advanced age, increased WBC count, elevated CRP, ferritin, D-Dimer, troponin-I, LDH, and urea levels, and were all intubated. We hope that our study will contribute to a better understanding of this disease.

Ethics Committee Approval: This study was approved by the medical ethics committee of Çanakkale 18 Mart University, Faculty of Medicine 113 (07/12.11.2020). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: Informed consent was waived because of the retrospective design of the study, and the researchers analyzed the anonymized data.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Collected the data and corresponding writer: I.D.A.; Collected the data: M.Ç.; Performed statistical analysis: D.S.

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