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Original Scientific Paper

FACTORS AFFECTING PROGNOSIS AND MORTALITY IN SEVERE COVID-19 PNEUMONIA PATIENTS

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SUMMARY – Fatality rate in coronavirus disease 2019 (COVID-19) cases has been reported to be 3.4% worldwide. The aim of this study was to evaluate the factors that determine prognosis and mortality in severe COVID-19 pneumonia patients. Eighty adult patients with severe COVID-19 pneumonia hospitalized and monitored at Izzet Baysal State Hospital (Bolu, Turkey) between August and November 2020 were included in this retrospective single-center study. Demographic and laboratory data, severity of radiological involvement, comorbidities, agents used in treatment, and clinical results were recorded, and data were grouped as survivors and non-survivors. The mean patient age was 67.8±12.6 years. There were 59 (73.8%) male patients. Comorbid diseases were present in 53 (66.3%) patients. There was no significant relationship between patient age, gender, smoking status or presence of comorbidity and mortality ($p>0.05$). The variables such as pulmonary involvement above 50%, intubation, or ferritin (>434.8 μg/L), troponin I (>14.05 ng/L) and procalcitonin (>0.125 ng/mL) as the sole variables of laboratory data were found to have significant relationship with increased mortality ($p<0.05$). Mortality was significantly higher in patients using steroid pulse therapy + tocilizumab, steroid pulse therapy + hydroxychloroquine, or solely steroid pulse therapy, while it was significantly lower in patients receiving azithromycin therapy and those in the plasma + steroid pulse therapy group. The severity of pulmonary involvement, intubation, and increase in inflammation markers such as ferritin, troponin and procalcitonin were found to be significantly associated with mortality ($p<0.05$). Treatment approaches with azithromycin and plasma + steroid pulse therapy were found to reduce mortality.

Key words: *COVID-19; Pneumonia; Prognosis; Mortality*

Introduction

The 2019 novel coronavirus (SARS-CoV-2) was first detected in Wuhan Province of China and has infected millions of people around the world so far, and the pandemic still continues. It has a wide spectrum from asymptomatic patients to respiratory failure. Fatality rate in coronavirus disease 2019 (COVID-19) cases has been reported to be 3.4% worldwide[1].

After initially infecting cells lining the nose, it progresses to the respiratory tract and alveoli containing surfactant-producing type II cells rich in angiotensin-converting enzyme (ACE) 2 receptors, leading to cytokine storm with excessive release of proinflammatory cytokines in some patients[2]. Inflammation is prominent in other conditions[3], as well as in COVID-19 infection. The SARS-Cov-2 infection may present with flu-like symptoms, nevertheless, nearly half or 3 of 4 subjects with positive polymerase chain reaction (PCR) results remain asymptomatic[4]. Having a frequency of 5% in COVID-19 pneumonia, increased inflammation or cytokine storm determines mortality. The aim of this study was to determine the

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factors predicting the prognosis in COVID-19 pneumonia, to follow the individuals at risk more closely, to determine the role of medication treatments in reducing mortality, and to contribute to the choice of appropriate treatment.

Materials and Methods

Patient selection

This retrospective and single-center study was carried out in patients hospitalized and monitored at Department of Chest Diseases, İzzet Baysal State Hospital. Eighty Rt-PCR (+) COVID-19 patients with severe pneumonia in line with WHO Interim Guidance[5] were included in this study. Ethical approval was obtained from the local Ethics Committee (no. 2020/319 as of January 19, 2021).

Patients under 18 years of age, pregnant and postpartum women were not included in the study. Patient disease history, demographic and laboratory data, severity of radiological involvement and medication treatments were recorded retrospectively. Favipiravir (1600 mg BID on day loading, 600 mg/day maintenance) and methylprednisolone 0.5-1 mg/kg/day were administered to all patients routinely. Besides official approval by the Hospital Ethics Committee, informed consent was obtained from all patients involved in the study.

Data collection

Patient comorbidities (grouped as cardiovascular disease, chronic lung disease, diabetes mellitus, cancer), laboratory data (complete blood count, biochemical parameters, coagulation parameters, procalcitonin), severity of radiological computer tomography (CT) involvement (above and below 50%), medication treatments (hydroxychloroquine, corticosteroid, convective plasma, tocilizumab, antibiotics) and presence of intubation were recorded.

Statistical analysis

The data obtained in this study were analyzed by use of SPSS 20. Descriptive statistics were expressed as frequency, mean, standard deviation, median, and minimum-maximum. In addition to Kolmogorov-Smirnov test, normal distribution was tested based on the coefficients of skewness and kurtosis as ±2. Parametric data were expressed as mean ± standard deviation and compared with the independent sample t test. On the other hand, nonparametric data were expressed as median (minimum-maximum) and compared with Mann-Whitney U test. The relationship between categorical variables was tested using the χ^2-test. The effect size was tested with Cohen d, and Cohen d: 0.10 showed small effect; d: 0.25 showed medium effect; d: 0.40 showed large effect (Cohen, 1988). The cut-off value was determined by the receiver operative characteristics (ROC) analysis for data used in mortality prediction. The level of statistical significance was set at $p<0.05$.

Results

The mean patient age was 67.8±12.6 years. There were 59 (73.8%) male patients. Comorbid diseases were present in 53 (66.3%) patients. Of the 80 patients, mortality was witnessed in 46.3% (37 patients), while the mortality rate was 96.9% in intubated patients ($p<0.05$). There was no significant relationship of age (65.34±13.94 in survivors and 70.70±10.41 in non-survivors) and non-smoking status (52.1% in survivors and 29.7% in non-survivors) with mortality ($p>0.05$). There were no smokers among study patients. Gender and presence of comorbidity were not statistically significant factors in mortality either ($p>0.05$). In the order of frequency, cardiovascular diseases (47%), coexistence of diabetes mellitus and cardiovascular diseases (24.5%), chronic pulmonary disease (9.4%), malignancy (7.5%), and coexistence of cardiovascular and chronic pulmonary diseases (3.8%) were identified as comorbidities in the patients reported to have comorbidities. On chest CT, 50% pulmonary involvement was detected in 44.1% of survivors and 55.9% of non-survivors ($p<0.05$) (Table 1).

Among laboratory data, only increased ferritin (Cohen large effect), troponin (Cohen medium effect) and procalcitonin (Cohen large effect) were significantly associated with mortality ($p<0.05$) (Table 2). The cut-off value for ferritin was identified as 434.8 μg/L (normal: 23.9-366.2 μg/L) while it was 14.05 ng/L (normal: 12.6-20.7 ng/L) for troponin and 0.125 ng/mL for procalcitonin ($p<0.05$) (Table 3). The results of ROC analysis showed that while the cut-off values for ferritin and procalcitonin were significantly related to mortality, the relationship between troponin and mortality was identified as $p>0.05$ (Fig. 1).

The major antibiotics used in the order of their frequency were azithromycin (58.8%), moxifloxacin (36.3%) and ceftriaxone (32.5%). A consideration of treatments showed that while mortality was significantly higher in patients administered steroid pulse therapy + tocilizumab, steroid pulse therapy + hydroxy-

Table 1. Demographics and baseline characteristics of patients with severe COVID-19 pneumonia

	n	Survivors (n=43)	Non-survivors (n=37)	χ^2 value	p-value
Gender: Female Male	 21 59	 12 (27.9%) 31 (72.1%)	 9 (24.3%) 28 (75.7%)	0.13	0.8
Smoking status: Non-smoker Ex-smoker	 33 47	 22 (51.2%) 21 (48.8%)	 11 (29.7%) 26 (70.3%)	3.77	0.07
Comorbidity: Present Not present	 53 27	 31 (72.1%) 12 (27.9%)	 22 (59.5%) 15 (40.5%)	1.42	0.25
CT involvement: CT below 50% CT above 50%	 21 59	 17 (39.5%) 26 (60.5%)	 4 (10.8%) 33 (89.2%)	8.48	<0.001*
Intubation: Yes No	 32 48	 1 (2.3%) 42 (97.7%)	 31 (83.8%) 6 (16.2%)	54.9	<0.001*

*p<0.05 statistically significant; CT = computed tomography

Table 2. Comparison of laboratory parameters according to mortality

	Survivors (n=43)	Non-survivors (n=37)	p-value	Cohen
	$\underline{X}$±ss**			
CRP (mg/L)	96.02±39.78	101.42±39.34	0.54	-
Ferritin (**µ**g/L)	453.41±410.69	668.75±431.74	0.025*	0.51
Lymphocytes (K/uL)	0.86±0.47	0.75±0.41	0.26	-
Platelets (K/**µ**L)	205.49±85.33	207.43±90.79	0.92	-
Median (min-max)***				
D-dimer (mg/L)	0.33 (0.14-12.10)	0.51 (0.08-7.70)	0.24	-
Troponin (ng/L)	8.80 (1.70-687.50)	17.40 (2.20-2327.00)	0.005*	0.27
Lymphocytes % (K/**µ**L)	11.30 (3.40-33.6)	9.90 (1.00-30.90)	0.15	-
LDH (U/L)	420 (183-1884)	440. (237-1375)	0.71	-
Procalcitonin (ng/mL)	0.08 (0.02-4.34)	0.23 (0.02-35.60)	0.008*	0.44
Prothrombin time (s)	14.80 (12.30-193.00)	15.80 (12.60-54.90)	0.15	-

*p<0.05 statistically significant; **independent sample t test; ***Mann-Whitney U test; CRP = C-reactive protein; LDH = lactate dehydrogenase

Table 3. Receiver operating characteristic (ROC) analysis *of laboratory parameters*

	AUC (95% CI)	Cut-off	p-value	Sensitivity (%)	Specificity (%)
CRP (mg/L)	0.536 (0.407-0.664)	-	0.59	-	-
Ferritin (µg/L)	0.659 (0.534-0.785)	434.8	0.014*	70.3	69.8
D-Dimer (mg/L)	0.577 (0.448-0.705)	-	0.24	-	-
Troponin (ng/L)	0.681 (0.564-0.799)	14.05	0.005*	64.9	65.1
Lymphocytes (K/µL)	0436 (0.309-0.563)	-	0.33	-	-
Lymphocytes % (K/µL)	0.407 (0.282-0.533)	-	0.15	-	-
LDH (U/L)	0.524 (0.395-0.653)	-	0.71	-	-
Procalcitonin (ng/mL)	0.673 (0.555-0.792)	0.125	0.008*	64.9	64.3
Platelets (K/uL)	0.497 (0.367-0.627)	-	0.96	-	-
Prothrombin time (s)	0.594 (0.467-0.720)	-	0.15	-	-
	Survivors (n=43)		Non-survivors (n=37)	χ^2 value	p-value
Ferritin (µg/L)	0-434.80 ≤434.81	30 (73.2%) 13 (33.3%)	11 (26.8%) 26 (66.7%)	12.76	<0.001*
Troponin (ng/L)	0-14.05 ≤14.06	21 (56.8%) 16 (64.0%)	16 (43.2%) 9 (36.0%)	0.32	0.61
Procalcitonin (ng/mL)	0-0.125 ≤0.126	27 (67.5%) 15 (38.5%)	13 (32.5%) 24 (61.5%)	6.69	0.01*

AUC = area under the ROC curve; 95% CI = 95% confidence interval; CRP = C-reactive protein; LDH = lactate dehydrogenase

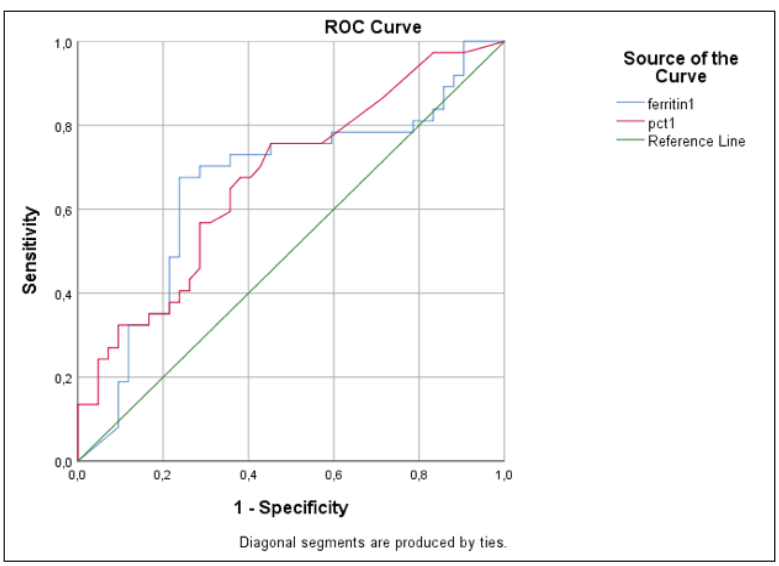

Fig. 1. ROC curve of the parameters significant in predicting mortality.

Table 4. Comparison of result parameters according to medication status (survivors/non-survivors)

	All patients	Survivors (n=43)	Non-survivors (n=37)	χ^2 value	p-value
HCQ user	36	21 (58.3%)	15 (41.7%)	0.55	0.50
HCQ non-user	44	22 (50.0%)	22 (50.0%)		
Pulse steroid user Pulse steroid non-user	28 52	7 (25.0%) 36 (69.2%)	21 (75.0%) 16 (30.8%)	14.32	<0.001*
Pulse + plasma Pulse + plasma Pulse non-user	11 17 52	1 (2.3%) 6 (14.0%) 36 (83.7%)	10 (27.0%) 11 (29.7%) 16 (43.2%)	16.17	<0.001*
Pulse + tocilizumab- Pulse + Tocilizumab + Pulse non-user	15 13 52	4 (26.7%) 3 (23.1%) 36 (69.2%)	11 (73.3%) 10 (76.9%) 16(30.8%)	14.36	<0.001*
HCQ + pulse- HCQ + pulse + HCQ non-user	23 13 44	17 (78.3%) 4 (30.8%) 22 (50.0%)	6 (21.7%) 9 (69.2%) 22 (50.0%)	6.78	0.03*
Azithromycin user Azithromycin non-user	47 33	30 (63.8%) 13 (39.4%)	17 (36.2%) 20 (60.6%)	4.66	0.04*

*p<0.05 statistically significant; HCQ = hydroxychloroquine; Pulse = steroid pulse therapy

chloroquine, or only steroid pulse therapy, it was significantly lower in patients administered azithromycin or convalescent plasma + steroid pulse therapy (Table 4).

Discussion

Fatality rate in COVID-19 cases has been reported to be 3.4% worldwide[1]. Xie *et al*. showed that dyspnea at admission and hypoxia despite oxygen support were strong independent predictors of mortality. While 99% of the patients with an oxygen saturation level of 90% and above survived with oxygen support administered during hospitalization, 69% of those with oxygen saturation of 90% or less died despite oxygen support[6]. In the present study, mortality rate was 46.3% (37 patients) in 80 patients with severe pneumonia, and this rate was 96.9% in intubated patients (p<0.05).

The Centers for Disease Control categorize advanced age, cancer, chronic obstructive pulmonary disease, chronic kidney disease, immune system suppression due to solid organ transplantation, obesity, severe heart disease, sickle-cell anemia and type 2 diabetes as the risk factors for severe disease and complications[7]. In this study, 53 (66.3%) patients had comorbid diseases. In the order of their frequency, cardiovascular diseases (47%), coexistence of diabetes mellitus and cardiovascular diseases (24.5%), chronic pulmonary disease (9.4%), malignancy (7.5%), and coexistence of cardiovascular and chronic pulmonary diseases (3.8%) were identified as the diseases in the patients reported to have comorbidities. However, the level of significance of the relationship between the presence of comorbidity and mortality was p>0.05.

To date, in 10624 patients requiring critical care in the UK, their median age was 60 (interquartile range (IQR), 51-68) and 70.2% of them were males[8]. In the present study, the mean age of patients was 67.83±12.64, and 73.8% of them were males, which is comparable to the study mentioned above. The mean age was 65.34±13.94 in survivors and 70.70±10.41 in non-survivors, yielding no statistical significance (p>0.05). Gender and mortality were not significantly related (p>0.05). However, Xie *et al*. report on a significant relationship between age, gender or comorbidity and mortality[6].

While the rate of non-smokers was higher in the survivor group (52.1%) than in the non-survivor group (29.7%), there was no significant difference between the two groups in terms of non-smoking status. It is

strange to note that there were no smokers among patients in this study. Lippi and Henry revealed that there was no relationship between active smoking and the severity of COVID-19[9]. The most frequently observed laboratory anomalies were increase in troponin and C-reactive protein (CRP) (>60%) and lactate dehydrogenase (LDH) (~50%-60%) with lymphopenia (83%); increased D-dimer level (43%-60%), increase in aspartate aminotransferase (AST) (~33%) and serum alanine aminotransferase (ALT) (~25%); prolonged prothrombin time (>5%) and moderate thrombocytopenia (~30%)[10,11]. Serum procalcitonin level was found to be normal in most of the patients[12]. The mean values of inflammation parameters obtained in our study are shown in Table 5. Among laboratory data, only the increase in ferritin (Cohen large effect), troponin (Cohen medium effect) and procalcitonin (Cohen large effect) was associated with mortality ($p<0.05$). The cut-off value was determined as 434.8 for ferritin, 14.05 for troponin, and 0.125 for procalcitonin ($p<0.05$). As a result of ROC analysis, cut-off values of ferritin and procalcitonin were significantly related to mortality while the cut-off value of troponin was found to be $p>0.05$ in relation to mortality. In a study conducted on 140 patients with COVID-19 pneumonia in Wuhan, leukopenia, increased CRP and D-dimer were associated with mortality[6]. In the study conducted by Guo *et al*., troponin increase was detected in 27.3% of hospitalized patients with a diagnosis of COVID-19. In these patients, increased in-hospital mortality was found compared to those with normal troponin values (59.6% and 8.9%, $p<0,001$)[13].

Favipiravir (1600 mg/day loading, 600 mg/day maintenance) and methylprednisolone 0.5-1 mg/kg/day were administered routinely to all patients. Favipiravir is a nucleotide analog and RNA polymerase inhibitor. While favipiravir is an antiviral agent developed against influenza[14], it is also expected to be effective against COVID-19[15]. This agent is included in the standard treatment in the COVID-19 Guide of the Ministry of Health in our country.

COVID-19 causes diffuse lung injury with dysregulation and excessive inflammation. Glucocorticoids also reduce the progression of lung damage to respiratory failure and death by modulating inflammation. In the study conducted by the RECOVERY Collaborative Group, it was found that the use of dexamethasone decreased 28-day mortality in the group of COVID-19 patients receiving mechanical ventilation or oxygen support[16]. Gao *et al*. showed that chloroquine reduced the severity of pneumonia, improved lung damage, and shortened recovery time[17]. In our study, there was no significant relationship between hydroxychloroquine use and mortality (the rate of mortality among those using hydroxychloroquine was 41.7%, while that rate was 50% among those not using hydroxychloroquine, $p>0.05$) (Table 4).

Having a frequency of 5% in COVID-19 pneumonia, cytokine storm (symptoms such as persistent fever despite treatment, persistently high or increasing CRP and ferritin levels, high D-dimer levels, cytopenia in the form of lymphopenia and thrombocytopenia, deterioration in liver function tests, hypofibrinogenemia or increased triglyceride values) determines mortality.

High dose corticosteroid, i.v. immunoglobulin, anakinra (IL-1 receptor antagonist) or tocilizumab (IL-6 receptor antagonist) are the agents used in cytokine storm[18]. In our study, tocilizumab was administered to patients with increased oxygen need or acute phase reactants manifested within 24 hours despite methylprednisolone 0.5-1 mg/kg/day treatment. However, if clinical deterioration persisted, pulse steroid (1 g/day methylprednisolone for 3 days, followed by 0.5-1 mg/day maintenance) was administered. It was stated in the November 7 guide[19] that anti-cytokine treatment should be considered in patients not responding to high-dose steroid therapy used for at least 3 days, therefore a group of patients were administered pulse steroid first. There were 10 patients who were administered tocilizumab but did not use pulse steroids, and because of their small number, no statistically significant results were obtained. In this study, it was found that pulse steroid alone and in combination with tocilizumab and hydroxychloroquine increased mortality. Monreal *et al*. also report that high-dose steroids were associated with higher mortality, increased need for mechanical ventilation and death as compared to low-dose steroids. The risk of developing severe acute respiratory distress syndrome (ARDS) in these two steroid groups was found to be similar. Interaction analysis showed that high dose steroid increased mortality only in elderly patients. It is recommended that 1-1.5 mg/kg day corticosteroids should not be exceeded in severe COVID-19 cases with ARDS, especially in elderly people. This approach supports the need to modulate rather than suppress immune responses in patients[20]. In a study with pulse steroids (3 days, 1000

mg methylprednisolone, followed by 8 mg dexamethasone for 3-5 days), decreased dyspnea, improved oxygen saturation and decreased CRP were observed; however, there was an increase in D-dimer[21]. In another retrospective study, no difference was observed in survival of two groups of patients, one group receiving pulse steroid and the other group receiving steroid at a dose of 1 mg/kg day[22].

Tocilizumab is a recombinant humanized monoclonal antibody targeting the IL-6 receptor and was found to reduce the risk of invasive mechanical ventilation and death in a multicenter retrospective study[23]. In another meta-analysis, tocilizumab was not found to have an additional benefit in treatment[24]. Tocilizumab reduced the use of invasive mechanical ventilation when used early in the presence of bilateral lung infiltration and hypoxemia during cytokine storm[25]. No statistically significant difference was found between a single dose of tocilizumab (8 mg/kg, maximum 800 mg, intravenous infusion) and placebo with regards to intubation or pre-intubation mortality[26]. Adding corticosteroids to tocilizumab treatment was demonstrated to have a beneficial effect on reducing mortality[27]. In our study, there was no patient taking only tocilizumab, and an increase in mortality was found in those who received pulse steroid in combination with tocilizumab ($p<0.05$).

In the study comparing early (before intubation or within one day after intubation) and late administration (one day after intubation) of tocilizumab in treatment, a significantly lower mortality was found in the patients given tocilizumab early (13.5% and 68.2%, $p<0.05$)[28]. However, the exact timing of the first dose of tocilizumab is controversial.

Convalescence plasma can be administered as an addition to supportive treatments, along with the use of antiviral agents in patients with COVID-19[29]. Convalescence plasma is passive immunotherapy through which the antibodies obtained from healed people are administered.

In a cohort study of COVID-19 patients, a decrease in symptoms and mortality besides a decrease in CRP and viral load, an increase in lymphocyte percentage, and radiological improvement were found in severely and critically ill patients receiving convalescence plasma[30]. In a randomized controlled study on patients with COVID-19 pneumonia, no significant difference was found between the convalescent plasma group and placebo receiving group in terms of clinical improvement, mortality, and side effects[31]. According to the guideline published in April 2020 in our country, it is recommended that patients with a diagnosis of COVID-19 be administered convalescence plasma preferably at 7-14 days after the onset of symptoms, and the patients in this study were administered convalescence plasma in this way[32]. In our study, the mortality rate was reduced through a combination of convalescence plasma and pulse steroid ($p<0.05$).

The single-center and retrospective design were limitations of the present study. Another limitation could be a relatively small study cohort. However, the results of our study are important for providing useful data on COVID-19 infection.

In conclusion, having a frequency of 5% in COVID-19 pneumonia, cytokine storm determines mortality. In this study, it was determined that the increase in ferritin, troponin and procalcitonin, which are among the poor prognostic factors in COVID-19 pneumonia, was associated with mortality. Furthermore, the present study showed that among treatment strategies, the use of pulse steroid + tocilizumab, pulse steroid + hydroxychloroquine and pulse steroid alone increased mortality, whereas azithromycin treatment and combined use of plasma + pulse steroid reduced mortality. However, studies involving larger numbers of cases and control groups are needed. The factors predicting the prognosis in COVID-19 pneumonia should be determined and the individuals at risk should be followed more closely, and more effective treatments should be preferred in order to reduce mortality.

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Sažetak

ČIMBENICI KOJI UTJEČU NA PROGNOZU I SMRTNOST BOLESNIKA S TEŠKOM PNEUMONIJOM UZROKOVANOM INFEKCIJOM COVID-19

E. Afşin i *M. E. Demirkol*

Stopa smrtnosti bolesnika s bolešću koronavirus 2019. (COVID-19) iznosi 3,4% širom svijeta. Cilj ovoga istraživanja bio je procijeniti čimbenike koji određuju prognozu i smrtnost bolesnika s teškom pneumonijom uzrokovanom infekcijom COVID-19. U ovu retrospektivnu studiju provedenu u jednom centru bilo je uključeno 80 bolesnika s teškom COVID-19 pneumonijom koji su hospitalizirani i praćeni u Izzet Baysal State Hospital, Bolu, Turska, od kolovoza do studenoga 2020. godine. Bilježili smo demografske i laboratorijske podatke, težinu radiološke zahvaćenosti, supostojeće bolesti, lijekove primijenjene u liječenju i kliničke rezultate, a podaci su grupirani kao preživjeli i ne-preživjeli. Srednja dob bolesnika bila je 67,8±12,6 godina, bilo je 59 (73,8%) muških bolesnika, a subolesti su bile prisutne u 53 (66,3%) bolesnika. Utvrđen je značajan odnos bolesnikove dobi, spola, pušenja ili prisutnosti subolesti i smrtnosti ($p>0,05$). Značajan odnos s povećanom smrtnošću ($p<0,05$) utvrđen je za varijable kao što su zahvaćenost pluća iznad 50%, intubacija ili feritin (iznad 434,8 μg/L), troponin I (iznad 14,05 ng/L) i prokalcitonin (iznad 0,125 ng/mL) kao pojedinačne varijable iz laboratorijskih nalaza. Smrtnost je bila značajno viša među bolesnicima koji su uzimali pulsnu terapiju steroidom + tocilizumab, pulsnu terapiju steroidom + hidroksiklorokin ili samo pulsnu terapiju steroidom, dok je bila značajno niža među bolesnicima koji su primali azitromicin te u bolesnika iz skupine koja je primala plazmu + pulsnu terapiju steroidom. Težina zahvaćenosti pluća, intubacija i porast upalnih biljega poput feritina, troponina i prokalcitonina bila je značajno udružena sa smrtnošću ($p<0,05$). Utvrđeno je da pristup liječenju azitromicinom i plazmom + pulsnom terapijom steroidom snižavaju smrtnost.

Ključne riječi: *COVID-19; Pneumonija; Prognoza; Smrtnost*