Dicle Tıp Dergisi / Dicle Med J (2022) 49 (1) : 85-91

www.diclemedj.org

Original Article / Özgün Araştırma

Which COVID-19 Patients Die in Intensive Care Unit (ICU) in Turkey

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Received: 29.12.2021; Revised: 15.02.2022; Accepted: 16.02.2022

Abstract

Objective: The World Health Organization labelled the COVID-19 outbreak a pandemic on March 11, 2020, the first day COVID-19 cases were diagnosed in Turkey. Since then, people's main concerns have been whether their lives or the lives of their relatives would be at risk if they became infected. The objective of this study was to determine the risk factors that increase mortality in COVID-19 patients treated in ICUs and to facilitate the appropriate precautions.

Methods: In this study, patients who were diagnosed with COVID-19 [positive on a polymerase chain reaction (PCR) test] and monitored in the Pandemic Hospital at Diyarbakır Dicle University between 15 March 15 and 15 May, 2020, were evaluated for risk factors for mortality.

Results: A total of 50 ICU patients were included in the study. Of them, 52% were males, and the mean age was 63.8±17.6 years. A comparison of deceased and surviving patients showed that being female, older than 62, and a smoker and having diabetes mellitus, hypertension, and/or coronary artery disease significantly increased mortality. An investigation of the findings from the patients' lung tomography examinations revealed that relatively prominent pulmonary involvement and localization did not affect mortality.

Conclusions: Because patients who are advanced in age, female and smokers and have comorbidities are in the high-risk group, measurements related to treating the COVID-19 disease should be improved. Laboratory parameters are useful for the evaluation of mortality and morbidity, while mechanical ventilation increased mortality.

Keywords: COVID-19, Turkey, ICU, hospital mortality, ventilatory support

DOI: 10.5798/dicletip.1086229

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Hangi COVID-19 Hastaları Yoğun Bakımda Ölüyor

Öz

Giriş: Dünya Sağlık Örgütü tarafından COVID-19 hastalığı pandemi olarak ilan edildiği 11 Mart 2020 tarihinde Türkiye'de de ilk vakalar görülmeye başlandı. O tarihten beri insanlarda paniğe neden olan düşüncelerin başında hastalığa yakalanmasıyla beraber kendi ve yakınlarının hayatının tehlikeye girip girmeyeceği oldu. Bu çalışmanın amacı COVID-19 hastalığına bağlı yoğun bakımda takip edilen hastalarda mortaliteyi arttıran risk faktörlerin tespit edilip bu yönde önlem alınmasını sağlamaktır

Yöntemler: Bu çalışmada, Diyarbakır Dicle Üniversitesi Pandemi Hastanesine 15 Mart 2020 ve 15 Mayıs 2020 tarihleri arasında COVID-19 Yoğun bakımlarında yatan ve polymerase chain reaction (PCR) ile COVID-19 tanısı konan yoğun bakım olguları değerlendirildi.

Sonuçlar: Çalışmaya alınan 50 yoğun bakım hastasının %54'ü erkekti. Hastaların yaş ortalaması 63.8 ± 17.6 yıl olarak hesaplandı. Ölen hastalarda sağ kalanlara göre kadın cinsiyet, 62 yaş üzeri hastalar, sigara kullanımı, diyabetes mellitus, hipertansiyon ve koroner arter hastalığının varlığının mortaliteyi istatistiksel olarak arttırdığı bulundu. Tomografi bulguları karşılaştırıldığında, akciğer tutulumun fazla olması ile mortalite arasında doğru orantı olmadığı bulundu.

Tartışma: İleri yaş, kadın cinsiyet, sigara kullanımı ve komorbid hastalıkları olanlar yüksek risk grubunda olduğundan dolayı COVID-19 hastalığından korunmak için önlemleri arttırmak gerekiyor. Akciğer tomografi bulguları tanısal olarak anlamlı olsa da hastalığın sürveyansında anlamlı olmayabilir. Laboratuvar bulguları mortalite ve morbidite üzerinde etkili parametreler olup, olup mekanik ventilatöre bağlananlarda mortalite oranı yüksek olarak rapor edildi.

Anahtar kelimeler: COVID-19, Türkiye, Yoğun Bakım, Mortalite, Solunum Desteği

INTRODUCTION

The COVID-19 outbreak, which started in December 2019 in China as an endemic, has grown into a continuing worldwide pandemic, resulting in millions of cases and almost 600,000 deaths. The virus is called SARS-Cov-2 and the disease caused by this virus COVID-19. The World Health Organization labelled the COVID-19 outbreaks a pandemic on 11 March, 2020, the first day COVID-19 cases were diagnosed in Turkey. At the present time, about 200,000 cases have been diagnosed with COVID-19 in Turkey, 5,000 of them resulting in death. The treatment and care of such patients have been carried out according to the guidelines published by the Turkish Ministry of Health, the recommendations and algorithms of which have been updated at certain intervals. The Dicle University Pandemic Hospital, where this study was conducted, is located in Diyarbakir (population 2 million).

The determination of the demographic characteristics and the related risk groups following the analysis of the factors affecting mortality will improve decisions related to the treatment and monitoring of COVID-19 patients and will thus contribute to the control of the pandemic. The objective of this study is to determine the factors related to mortality through a comparison of deceased and surviving COVID-19 patients treated in ICUs in Turkey, particularly in our region of the country.

METHODS

In this study, we investigated patients who were diagnosed as positive for COVID-19 with the PCR test and treated in the ICU in the Pandemic Hospital at Dicle University in Diyarbakir between 15 March, and 15 May, 2020. Information about the patients' age, gender, comorbidities, duration of hospitalization, COVID-19-related lung tomography findings, hemogram parameters (white blood cell (WBC), neutrophil, lymphocyte, and platelet counts, haemoglobin level, neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte ratios (PLR),

biochemical parameters, and ventilatory support [mechanical ventilation, non-invasive mechanical ventilation (NIMV), high-flow oxygen (HFNO)] were retrospectively accessed in the hospital records.

Since the first COVID-19 case was admitted on 15 March, 2020, a total of 618 patients have been diagnosed with COVID-19 in our hospital. Of those 618 patients, 205 received outpatient treatment, 413 patients were hospitalized, and 56 were referred to the ICU. In this study, we included 50 ICU patients between the ages of 18 and 95 years from both genders with at least one positive PCR test. Four patients younger than 18, two patients with missing clinical and laboratory records were not included in the study.

Laboratory and Radiographic Examinations

The samples, which were obtained from the patients with a nasal and oropharyngeal combined swap, were analysed with the real-time polymerase chain reaction (RT-PCR) test for SARS-Cov-2 RNA within 6-8 hours. The virus was confirmed by the laboratory. Hemogram (WBC, NLR, PLR, lymphocyte, and neutrophil counts) and laboratory parameters (ferritin, albumin, procalcitonin, C-reactive protein (CRP), and D-dimer) were measured while the patients were referred to the ICU. The tomographic images were obtained without using a contrast agent while the patients were in the supine position and were holding their breath following inspiration. The hospital reserved a tomography device for COVID-19 patients, and high resolution computed tomography of the lungs was used. The technical parameters included a 64-section scanner with 1 mm collimation at 5mm intervals. A radiologist appointed to evaluate the tomographic images of COVID-19 patients prepared the reports.

Statistical Analysis

The statistical analysis of the study data was done with the IBM SPSS v21.0 for Windows software package. The quantitative variables were given in mean±standard deviation (SD). Qualitative variables in numbers and percentages (%). All data were controlled for normal distribution. Two groups which had a normal distribution were compared with an independent t-test. The comparison of the paired groups with non-normal distribution was done with the Mann-Whitney U test. A one-way analysis of variance was used for the comparison of groups with normal distribution and multiple choices and the Kruskal-Wallis H test for the comparison of groups with non-normal distribution and multiple choices. For the variables that may affect mortality, we used a logistic regression analysis. The qualitative variables were compared with a chi-square (?2) test. The hypotheses were considered in two-way, and a p-value smaller than 0.05 was considered as statistically significant.

Ethics committee approval was received from the Ethics Committee of Dicle University (Ethics Committee No:231/04.06.2020). The Republic of Turkey Ministry of Health also approved this scientific research work (E-2020-05-11T12_25_43).

RESULTS

Twenty-six of the included 50 ICU patients were males (52%) and 24 were females (48%). The mean age of the patients was 63.8±17.6 years. Eighteen of the patients died. The mortality rates of ICU patients were 36%. Five of the deceased patients were males (27.8%) and 13 were females (72.2%), and their mean age was 73.2±11.4 years. Twenty-one of the surviving patients were male (65%) and 11 were female (35%), with a mean age of 58.5±18.4 years. A comparison of the deceased and surviving patients showed that being female and of advanced age significantly increased mortality

(p=0.018 and p=0.001, respectively). The comparison of the deceased and surviving patients also displayed that smoking (p=0.004), diabetes mellitus (p=0.007), hypertension (p=0.042), and coronary artery disease (p=0.049) statistically increased mortality. Although the hospitalization time was longer among deceased patients compared to surviving patients, the difference was not statistically significant (p=0.521). The ages, genders, smoking, drug use, hospitalization time, and comorbidities of the deceased and surviving patients are given in Table 1.

Table I: Patients' demographic and clinical characteristics

	Surviving n % 32 64	Deceased n % 18 36	p Value
Gender			
Male	21 65.6	5 27.7	0.018
Female	11 34.4	13 72.3	
Smoking	3 9.3	9 50	0.004
Drug Use			
Chemotherapy	1 3.1	2 11.1	0.291
Steroids	1 3.1	0 0	1.000
Comorbidity Diseases			
Diabetes Mellitus	4 12.5	9 50	0.007
Hypertension	13 40.5	13 72.2	0.042
Chronic Hepatic Disease	1 3.1	1 5.5	1.000
Chronic Renal Disease	4 12.5	4 22.2	0.436
Heart Failure	2 6.2	5 27.7	0.083
Cardiovascular Disease	1 3.1	4 22.2	0.049
Chronic Respiratory Disease	5 15.5	7 38.8	0.089
Age	58.5 18.4	73.2 11.4	0.001
Hospitalization time (day)	7.28 5.67	8.61 7.56	0.521

In our study, we also compared the lung tomography findings of the deceased and surviving patients and found that the survival rate was significantly higher in the group with bilateral lung involvement and the group with ground-glass opacities (GGO) concomitant with consolidation (p=0.041 and p=0.001, respectively). The tomography findings for the deceased and surviving patients are summarized in Table 2.

Table II: Distribution of radiological findings

Parameters	Surviving n % 32 64	Deceased n % 18 36	p Value
Ground-glass opacities (GGO)	12 37.5	10 55.5	0.249
GGO and interlobular septal thickening	13 40.5	3 16.6	0.117
GGO and consolidation	23 71.8	4 22.2	0.001
GGO and diffuse infiltration	15 46.8	8 44.4	1.000
Unilateral lung involvement	9 28.1.5	2 11.1	0.098
Bilateral lung involvement	28 87.5	11 61.1	0.041

In our study, the comparison of the laboratory parameters of the deceased and surviving patients showed that the platelet (p=0.006), white blood cell (p=0.048), and neutrophil counts (p=0.033), and NLR (p=0.010) and PLR (p=0.033) were significantly higher in the deceased group compared to the surviving group. On the other hand, the haemoglobin (p=0.003), albumin (p=0.021), and D-dimer (p=0.048) levels were significantly lower in the deceased group compared to the surviving group. The laboratory findings for the surviving and deceased patients are listed in Table 3.

Table III: Distribution of Laboratory findings

Laboratory Parameters	Normal Range	Surviving	Deceased	p Value
Haemoglobin (g/dL)	12.9-14.2	13.4 ± 2.5	10.7 ± 3.0	0.003
WBC (K/μL)	3.7-10.1	8950 ± 4397	13562 ± 8730	0.048
Lymphocyte count (10^3/μL)	1.09-2.99	1514 ± 779	1204 ± 588	0.120
Neutrophil count (10^3/μL)	1.63-6.96	6461 ± 4143	10460 ± 6821	0.033
Platelet count (10^3/μL)	155–360	201.3 ± 87.4	283.9 ± 99.1	0.006
NLR	1.49-2.32	5.2 ± 3.2	11.3 ± 8.7	0.001
PLR	142-120.4	182.9 ± 141.8	305.1 ± 204.0	0.033
Albumin (g/L)	3.5-5.2	3.3 ± 0.5	2.8 ± 0.7	0.021
D-Dimer (mg/L)	0.08-0.58	10.5 ± 25.1	1.3 ± 1.0	0.048
Ferritin (ng/mL)	10-291	535.9 ± 385.8	857.6 ± 638.3	0.063
CRP (mg/L)	0-0.5	11.3 ± 8.8	12.8 ± 10.9	0.634
Procalcitonin (ng/mL)	0-0.12	0.9 ± 3.7	0.6 ± 1.8	0.765

White blood cell (WBC), C-reactive protein (CRP), neutrophil-to-lymphocyte (NLR) and platelet-to-lymphocyte ratios (PLR) ;The comparison of the surviving and deceased patients for the respiratory support showed that HFNO along with prone positioning favoured a positive outcome, while mechanical ventilation significantly increased mortality (p<0.001). The respiratory support for deceased and surviving patients is shown in Table 4.

Table IV: Distribution of respiratory support

Respiratory Support Type	Surviving n % 32 64	Deceased n % 18 36	p Value
HFNO and Prone Position	25 78.1	0 0	< 0.001
NIMV	5 15.6	7 38.8	0.089
Mechanical Ventilation	5 15.6	18 100	< 0.001

Non-invasive mechanical ventilation (NIMV), high-flow oxygen (HFNO).

DISCUSSION

Although our study had a single-centre design, we believe that it could reflect the characteristics of the populations in both the Middle East and Turkey due to the location of our city, which being in southeast Turkey close to countries such as Syria, Iraq, and Iran, represents many sociocultural groups.

In studies conducted in two different regions in the USA[1,2], the ICU mortality rate in the Seattle region[1] was 50%, while Washington State2 was 52.4%. Another study in Georgia[3] reported that 48.7% of patients hospitalized in the ICU died. In our study, the case mortality rates in ICU patients were 36%. The reason why our intensive care mortality rate is lower than the examples is that we diagnose the patients early and find experienced and volunteer healthcare professionals in ICU. We believe that the early preparation of pandemic plans, development of diagnosis and treatment protocols immediately with the first cases, recommendations of the scientific committee of MoH, and devoted efforts of the hospital's healthcare professionals enabled this success.

In a Chinese study[4] conducted in Wuhan that investigated deceased COVID-19 patients, the authors determined that 72.9% of the deceased patients were male and that their mean age was over 65. A study conducted in Tehran (Iran)5 found that mortality was mainly associated with age (over 65) and gender (male). The mean age of deceased patients in this study was approximately 70 years, which is consistent with other studies. Although the majority of patients referred to the ICU were male, unlike in other studies, the mortality rate was higher among females (72.3%). A detailed analysis of the cases according to gender revealed that the mortality rate was higher among females as a result of their being older and having higher rates of comorbidities.

Studies conducted in different countries[5-7] have reported that comorbidities had a negative impact on mortality in almost all deceased ICU patients. In another Chinese study[6], in which the risk factors in adult COVID-19 patients were investigated, the authors found that smoking, diabetes mellitus, hypertension, and coronary artery disease statistically increased mortality, which was also consistent with our study.

While the characteristic pulmonary finding in the tomographic examination was the ground-glass opacities (GGO) seen in a typical COVID-19 patient, the condition may occur concomitantly with consolidation, septal thickening, and diffuse infiltration. Depending on the patient, these findings can be observed in isolation or in groups. In some patients[7,8], GGO may develop in one lobe and be seen as a unilateral lung involvement, but bilateral involvement is also common. A study conducted in China[7] reported that the mortality rate was higher in patients with diabetes mellitus and chronic lung disorder when bilateral lung involvement along with parahilar and median involvement were

observed in tomographic examinations. However, in another study[8], the authors reported that patients with diffuse pulmonary involvement had fewer symptoms at the time of application. The same study suggested that the mortality rate was higher in patients with the involvement of the lower pulmonary regions along with peripheral involvement compared to patients with bilateral involvement. However, they also determined that the mortality rate was lower in patients with findings of consolidation. Similarly, we determined that the mortality rate was lower in patients with bilateral involvement and consolidation. Although GGO were observed in different localizations in the lungs in each patient, we believe they can be used for diagnosis due to their similar appearance. Since the different findings observed in these studies showed that the lung findings in the tomographic images alone are not much help in the prediction of mortality, they should be used in conjunction with clinical and laboratory parameters.

Along with the abovementioned imaging findings, laboratory and haematological tests proved instructive in the diagnosis and surveillance of patients. As a result, several countries included these parameters in their guidelines and used them for clinical follow-up[9,10]. In one study[11], the authors reported a decrease in WBC and platelet counts and NLR and PLR values as patients recovered from the disease. In another study[12], it was reported that CRP and D-dimer values were slightly higher in deceased patients. In this study, the laboratory findings of deceased and surviving patients were compared, and the WBC, platelet, and neutrophil counts and NLR and PLR values were found to be higher in deceased patients than in surviving patients. On the other hand, the haemoglobin, albumin, and D-dimer levels were lower in deceased patients compared to surviving patients. In light of these results, we believe that these parameters can be important for the prevention of mortality during the follow-up of COVID-19 patients.

In addition to the rapid global spread of the virus, one of the most horrifying features of the outbreak was its high mortality rate in ICU patients. While some patients in need of respiratory support received mechanical ventilation, we observed that patients supported with non-invasive respiratory support or HFNO had better outcomes. In a study conducted in the US[13], the authors emphasized that patients referred to an ICU will most probably need mechanical ventilation and that countries should be prepared for most patients remaining connected to mechanical ventilation for a lengthy period of time. In a study conducted in New York[14], the mortality rate among patients who were connected to mechanical ventilation was 88.1%. Similar results were found by a Chinese study that determined almost all COVID-19 patients connected to mechanical ventilation passed away. In our study, the mortality rate among patients who were connected to mechanical ventilation was 80%, which we consider a significantly high rate. In another Chinese study[15], the investigators reported that 29% of ICU patients without mechanical ventilation support died. In our study, none of the patients who received HFNO in the prone position died, while approximately 60% of the patients who received non-invasive mechanical ventilation died.

In conclusion, elderly COVID-19 patients with comorbidities should be closely monitored in ICUs with the help of haematological and biochemical blood parameters to decrease death rates. Their lungs and oxygen saturation should be monitored, and oxygen support should be provided to prevent the need for mechanical ventilation. An HFNO device should be ready to use for each patient, and patients should be placed in the prone position.

Ethics committee approval: Ethics committee approval was received from the Ethics Committee of Dicle University (Ethics Committee No:231/04.06.2020). The Republic of Turkey Ministry of Health also approved this scientific research work (E-2020-05-11T12_25_43).

Conflict of Interest: The authors declare that they have no conflict of interest pertaining to the study.

Financial Support: The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for- profit sectors.

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