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Hastaneye Yatan COVID-19 Pnömonili Hastalarda Açlık Kan Şekeri Düzeyinin Prognostik Rolü?

Prognostic Role of Fasting Blood Glucose Level in Hospitalized COVID-19 Pneumonia Patients

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ÖZ

Giriş: COVID-19, ciddi akut solunum yetmezliğine neden olan yeni bir enfeksiyondur. Coronavirüs enfeksiyonunda Diabetes Mellitus'un kötü prognoz ile ilişkili olduğu bilinmektedir. Açlık Kan Şekeri Düzeyi ile prognoz arasında bir ilişkinin varlığının gösterilmesi hastalığın seyrini etkileyebilir. Çalışmamızın amacı, COVID-19 pnömonisi ile hastaneye yatırılan hastalarda başvuru anında açlık kan glukoz düzeyi ile prognoz arasındaki ilişkiyi araştırmaktır.
Yöntem: Çalışmaya retrospektif olarak, kesin veya olası COVID-19 tanılı tüm hastalar alındı. Hastalara ait yaş, cinsiyet, sigara öyküsü, komorbiditeler, laboratuvar değerleri (D-dimer, ferritin,C-Reaktif Protein, Laktat Dehidrojenaz, lenfosit ve açlık kan glukoz düzeyi) seviyeleri kaydedildi. Radyolojik tutulum, steroid/pulse steroid ihtiyacı, yoğun bakım ihtiyacı ve mortalite ile ilgili veriler de kaydedildi.

Bulgular: Çalışma Grubunu toplam 574 hasta oluşturdu. Medyan yaş 60 (20-99); Hastaların 326'sı (%56,8) erkekti. Açlık kan glukoz düzeyi>159 mg/dL olan hastalarda pulse steroid ihtiyacı riski 3 kat; açlık kan glukoz düzeyi>138 mg/dL olan hastalarda yoğun bakım ihtiyacı riski 2 kat; ve açlık kan glukoz düzeyi>136 mg/dL olan hastalarda mortalite riski 2,5 kat daha yüksek bulundu. Ayrıca açlık kan glukoz düzeyi >136 mg/dL olan hastalarda kötü prognoz riski 2,5 kat daha fazla bulundu.

Sonuç: Açlık kan glukoz düzeyinin 136 mg/dL (7.6 mmol/L)'nin üzerinde olmasının, kötü prognoz riskini arttırdığı gösterildi.

Anahtar Kelimeler: COVID-19, açlık kan glukoz düzeyi, mortalite, kötü prognoz

ABSTRACT

Objective: COVID-19 is a new infection causing severe acute respiratory failure. It is known that Diabetes Mellitus is associated with poor prognosis in Coronavirus infection. Showing the presence of a relation between fasting blood glucose level and prognosis might affect the course of the disease. The aim of our study was to investigate the relation between fasting blood glucose level at admission and prognosis in patients hospitalized with COVID-19 pneumonia.

Method: For this retrospective study, we enrolled all patients diagnosed as confirmed or probable COVID-19. The age, gender, smoking history, and comorbidities of the patients, laboratory values (D-dimer, ferritin, C-Reactive Protein, Lactate Dehydrogenase, lymphocyte, fasting blood glucose level) were recorded. The data about radiological involvement, steroid/pulse steroid need, need for intensive care unit and mortality were also recorded.

Results: A total of 574 patients constituted the Study Group. The median age was 60 (20-99); and 326 (56.8%) of the patients were male. In patients with fasting blood glucose level>159 mg/dL, the risk of pulse steroid need is 3 times; in patients with fasting blood glucose level>138 mg/dL, the risk of need for intensive care unit is 2 times; and the risk of mortality in patients with fasting blood glucose level>136 mg/dL was found to be 2.5 times higher. Also, the risk of poor prognosis was found to be 2.5 times higher in patients with fasting blood glucose level>136 mg/dL.

Conclusion: It was shown that when fasting blood glucose level is>136 mg/dL (7.6 mmol/L), it increases the risk of poor prognosis.

Keywords: COVID-19, fasting blood glucose level, mortality, poor prognosis

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INTRODUCTION

COVID-19 pandemic is a new infection causing severe acute respiratory failure, spreading worldwide, and posing a global threat (1). The disease might be asymptomatic or might result in severe respiratory failure and even in mortality (2). It is known that Diabetes Mellitus (DM) is associated with poor prognosis in Coronavirus infection (3). However, no studies were conducted in our country investigating the relation between Fasting Blood Glucose Level (FBGL) and prognosis since the onset of the disease. Studies conducted in China suggested that FBGL and prognosis might be related (3-6). DM was detected in 16.2% of 1099 patients who were diagnosed with COVID-19 in a study conducted in China (7). The prevalence of DM was reported to be 13.5% in Turkey (8). With high rates of patients diagnosed with DM, it is obvious that the rate of undiagnosed DM patients will also be higher in a country with a high rate of obesity like Turkey. The main reasons why COVID-19 is more severe in patients with a diagnosis of DM are chronic hyperglycemia, chronic inflammation because of insulin resistance, the tendency to cellular binding (more viruses enter the cell more easily), impairment of T-cell functions, decreased viral clearance, hyperinflammation and cytokine storm (9). For this reason, even if there is no known DM diagnosis, showing the presence of a relation between FBGL and prognosis might affect the course of the disease. It is important to predict which COVID-19 patients must undergo more aggressive treatment according to FBGL examined at admission.

The purpose of our study was to investigate the relation between FBGL at admission and prognosis in patients hospitalized with COVID-19 pneumonia.

MATERIALS AND METHODS

Patient selection: For this retrospective, non-interventional,single-center cohort study, we enrolled all patients diagnosed as confirmed or probable COVID-19 who applied between June 01,2020-December 31,2020. The medical data of these patients were obtained from the Hospital Information Management System. All patients underwent a nasopharyngeal swab test for the SARS-CoV-2 virus using Real-Time Reverse-Transcriptase-Polymerase-Chain-Reaction (RT-PCR). A positive result according to the RT-PCR assay of nasal and pharyngeal swab specimens was accepted as a laboratory-confirmed patient. Patients with a history of contact in the last 14 days and symptoms such as cough, fever, shortness of breath and the cases whose thorax computed tomography (CT) were compatible with COVID-19 pneumonia were evaluated as probable cases although a negative RT-PCR result. The probable and definite diagnosis of COVID-19 and all treatment strategies were based on the Guidelines by the Scientific Committee of the Ministry of Health.

Inclusion criteria:

1) Patients diagnosed with COVID-19 with positive PCR test or with typical COVID-19 pneumonia detected in thorax CT even if PCR test was negative
2) Patients hospitalized with COVID-19 pneumonia
3) Patients whose fasting blood glucose levels were measured at admission
4) Having adequate clinical data in the Hospital Information Management System

Exclusion criteria:

1) Patients whose COVID-19 PCR test were negative and typical COVID-19 pneumonia was not detected in Thorax CT
2) Patients who were not hospitalized due to COVID-19 pneumonia
3) Patients whose fasting blood glucose levels were not measured at admission
4) Lack of adequate clinical data in the Hospital Information Management System

The age, gender, smoking history and comorbidities of the patients, laboratory values (D-dimer, ferritin, C-Reactive Protein (CRP), Lactate Dehydrogenase (LDH), lymphocyte, and FBGL) levels were recorded. The data about radiological involvement, steroid/pulse steroid need, need for intensive care unit and mortality were also recorded.

The patients were divided into two groups as those with FBGL≤110 mg/dL and >110 mg/dL, taking the limit value of FBGL as 110 mg/dL in line with the American Diabetes Association Guideline (10) to investigate the effect of 110 mg/dL limit value on prognosis in our patient group. FBGL unit is given as mg/dL and mmol/L (1 mg/dL=0.0555 mmol/L) in table-2 to make a comparison with the studies conducted outside our country (11). Also, the cut-off value of FBGL was determined in independent variables such as pulse steroid need, need for intensive care unit and mortality; and the effects of the cut-off value on the prognosis were evaluated. Finally, the pulse steroid need, need for intensive care unit and mortality were referred to as poor prognosis together and were analyzed separately.

This study was approved by both the Scientific Committee of our hospital (29.01.2021-139) and by the Ministry of Health COVID-19 Scientific Research Evaluation Committee.

Statistical analysis: The data obtained in the study were entered to the database created in SPSS (Statistical Package for Social Sciences) 18.0 Program (SPSS Inc. Chicago,IL,USA). Statistical Analyses were made with MedCalc and SPSS Program. The suitability of the continuous variables to normal distribution was examined. The comparison of the independent subgroups of the suitable variables was made with the Student T-test, and mean and standard deviation data were given. To compare the independent subgroups of the variables, the median (min, max) values were calculated for the variables that did not fit normal distribution by using the Mann-Whitney U-test. The optimal cut-off value was determined according to the Youden Index with the ROC Analysis of FBGL in the independent variables, such as pulse steroid need, need for intensive care unit and mortality. The Odds Ratio was given according to high and low FBGL levels and the survival was predicted according to the cut-off value with the Kaplan-Meier method. Cross-squares were formed according to the cut-off values for disease severity and their distributions were made with the Chi-Square Test Method. All of these comparisons were taken to the Logistic Regression Analysis, and the Odds Ratio was calculated with Multivariate Analysis. All comparison tests and Type 1 Error Coefficient were determined as Alpha 0.05 and were then tested with the double-tailed test.

RESULTS

A total of 1009 patients who were hospitalized in our hospital with the pre-diagnosis of COVID-19 were detected. When patients who were not found to have COVID-19, who did not have pneumonia radiologically and who did not have FBGL were excluded, the remaining 574 patients constituted the Study Group (Figure 1).

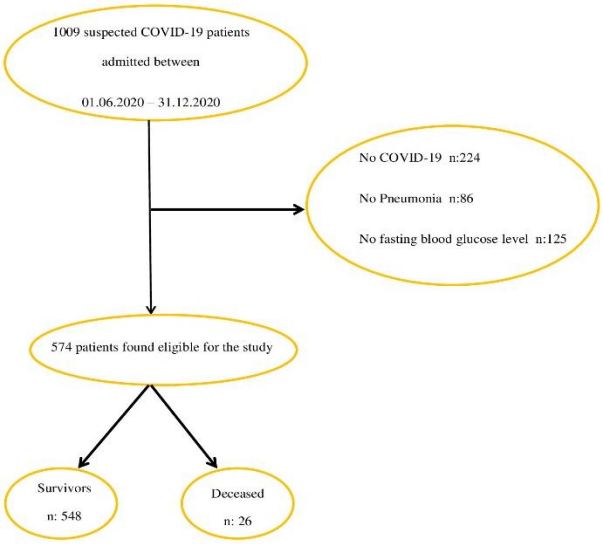


Figure 1. Flowchart of the study

In the study group, the median age was 60(20-99) and 326(56.8%) of the patients were male and 248(43.2%) were female. A total of 127 (48.1%) among the 264 patients who had smoking data were smokers (current or former) and 137 (51.9%) were never-smoker. Smoking data were not available for 310(54%) patients. The median FBGL of the patients was 115 mg/dL (63-368), and 321 patients (55.9%) had FBGL>110 mg/dL. A total of 528(94.6%) of the 558 patients who underwent thorax CT had typical tomography findings specific to COVID-19. The SARS-CoV-2 virus RT-PCR was positive in 428(74.6%) of the patients. At least one chronic disease was detected in 349(62.4%) of the 559 patients whose chronic disease data were available. The most common chronic diseases were hypertension (HT) with 194 patients (34.7%), DM with 141 patients (25.2%) and coronary artery disease (CAD) with 64 patients(11.4%). A total of 26(4.5%) patients died due to COVID-19 at the end of the hospitalization period. Demographic characteristics of the patients are given in Table 1.

The relation between the FBGL 110 mg/dL limit value, which was determined in line with the guidelines, and pulse steroid need was investigated. It was found that FBGL was>110 mg/dL in 10(71.4%) of the patients who needed pulse steroid (Table 1), and in 311(55.5%) of the patients who did not need pulse steroid (p=0.24). In the Study Group, the most appropriate cut-off value was found to be 159 mg/dL in the ROC Analysis of FBGL made according to the pulse steroid need (AUC: 0.640), (95% CI 0.599-0.679), (p=0.04) (Table 2).

Table 1. Demographic Characteristics of Patients

	n, (%)
The Number of The Patients	574
Median Age	60 (20-99)
Male / Female	326 (56.8) / 248 (43.2)
Smoking History (+/-)	127 (48.1) / 137 (51.9)
The Intensity of Smoking (package/year)	30 (0-100)
Median Fasting Blood Glucose Level (mg/dl)	115 (63-368)
Chronic Diseases	
Yes	349 (62.4)
No	210 (37.6)
Chronic Diseases	
Hypertansion	194 (34.7)
Diabetes Mellitus	141 (25.2)
Coronary Artery Disease	64 (11.4)
Chronic Obstructive Pulmonary Disease	50 (8.9)
Malignancy	36 (6.4)
Asthma	16 (2.9)
Heart failure	12 (2.1)
Other Laboratory Findings	
Median Lymphocyte (/µL)	1100 (100-13000)
Median C- Reactive Protein (mg/L)	53.1 (0.1-739)
Median Ferritin (ng/mL)	275 (9-2277)
Median D-Dimer (ng/mL)	962 (124-10000)
Median Lactate Dehydrogenase (U/L)	265 (115-1137)
Pulse Steroid Need	14 (2.4)
Need For Intensive Care Unit	47 (8.2)
Mortality	26 (4.5)
Poor Prognosis	68 (11.8)

Table 2. Sensivity and Specificity of Fasting Blood Glucose Cut-Off Levels For Pulse Steroid Need, Need For Intensive Care Unit, Mortality and Poor Prognosis

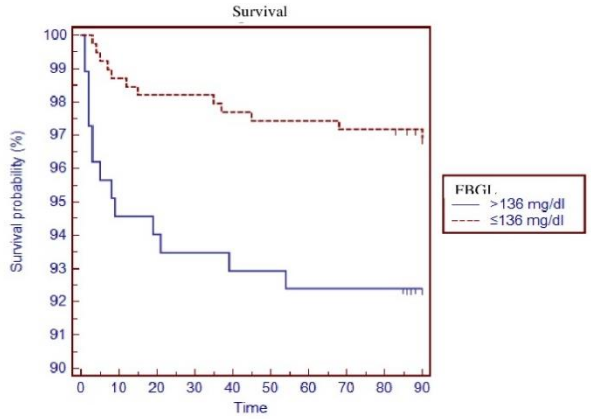
	Fasting Plasma Glucose Level				
	Cut-off	**5-AUC (95% CI)**	**Sensitivity (%)**	**Specificity (%)**	**P**
Pulse Steroid Need	159 mg/dL (8.8 mmol/L)	0.640 (0.599-0.679)	42.86	81.07	0.04*
Need For Intensive Care Unit	138 mg/dL (7.7 mmol/L)	0.572 (0.531-0.613)	46.81	70.21	0.09
Mortality	136 mg/dL (7.6 mmol/L)	0.572 (0.530-0.613)	53.85	68.98	0.27
Poor Prognosis	136 mg/dL (7.6 mmol/L)	0.608 (0.567-0.648)	51.47	70.55	0.004*

*p <0.05 was considered statistically significant

It was found that FBGL was > 159 mg/dL in 6(42.9%) of the patients who needed pulse steroid and in 106 (18.9%) of the patients who did not need pulse steroid and the difference between these results was at a statistically significant level (p=0.03).

The relation between FBGL 110 mg/dL cut-off value and the need for intensive care unit was also examined in the study. FBGL was found to be >110 mg/dL in 31(66.0%) of the patients who needed intensive care unit (Table 1), and in 290(55.0%) of the patients who did not need intensive care unit (p=0.15). In our study group, the most appropriate cut-off value was found to be 138 mg/dL in the ROC analysis of FBGL made according to the need for intensive care unit (AUC: 0.572), (95% CI 0.531-0.613), (p=0.09) (Table 2). FBGL was found to be >138 mg/dL in 22(46.8%) of the patients who needed intensive care unit, and in 158(29.8%) of the patients who did not need intensive care unit, and the difference between the results was at a statistically significant level (p=0.02).

The relation between FBGL 110 mg/dL cut-off value and mortality was examined, and it was found that FBGL was >110 mg/dL in 15(57.2%) of the patients who died (Table 1), and in 306(55.8%) of the patients who survived (p=0.85). In our Study Group, the most appropriate cut-off value was found to be 136 mg/dL in the ROC analysis of FBGL made according to mortality (AUC: 0.572), (95% CI 0.530-0.613), (p=0.3) (Table 2). FBGL was found to be> 136 mg/dL in 14(53.8%) of the patients who died, and in 170(31.0%) of the patients who survived, and the difference between the results was found to be at a statistically significant level (p=0.015). In Kaplan-Meier Survival Analysis, 14(7.6%) of the 184 patients with FBGL >136 mg/dL died at the end of the 90-day follow-up period, and 12 (3.1%) of the 390 patients with FBGL ≤136 mg/dL died, and the difference was at a statistically significant level (p=0.01) (Figure 2).



FBGL: Fasting plasma glucose level

Figure 2: Survival curves for Kaplan-Meier Survival Analysis for FBGL > 136 mg/dL at 90-day follow-up.

The relation between FBGL 110 mg/dL cut-off value and poor prognosis was also examined, and it was found that FBGL was >110 mg/dL in 47(69.1%) of the patients with poor prognosis (Table 1), and in 274(54.2%) of the patients without poor prognosis, and the difference was found to be at a statistically significant level (p=0.02). In our Study Group, in the ROC analysis of FBGL made according to the poor prognosis, the most appropriate cut-off value was found to be 136 mg/dL (AUC: 0.608), (95% CI 0.567-0.648), (p=0.004) (Table 2). It was found that FBGL was >136 mg/dL in 35(51.5%) of the patients with poor prognosis, and in 149(29.4%) of the patients without poor prognosis, and the difference between the results was found to be at a statistically significant level (p=0.000).

The cut-off values specific to our Study Group were determined for all the laboratory values, which might be associated with poor prognosis along with FBGL (Table 3).

It was found in the univariate analysis that age >64, male gender, presence of oxygen need at admission, FBGL>136 mg/dL, white blood cell count>8330/µL, neutrophil count>6500/µL, lymphocyte≤800/µL, monocyte≤200/µL, Hemoglobin (Hb)≤12 g/dL, CRP>74.2 mg/L, LDH>398 U/L, ferritin>746 ng/mL, and D-dimer>1571 ng/mL were found to be significantly associated with poor prognosis(p=0.000, p=0.000, p=0.000, p=0.000, p=0.001, p=0.000, p=0.000, p=0.02,p=0.000, p=0.000, p=0.000, p=0.000, p=0.000, respectively). The presence of chronic disease was not found to be associated with poor prognosis (p = 0.34) (Table 4).

Table 3. Sensivity and Specificity of Age and Other Laboratory Findings That Effect Poor Prognosis					
	Cut-off	**AUC (95% CI)**	**Sensitivity (%)**	**Specificity (%)**	**P**
Age	64	0.693 (0.653-0.730)	66.2	65.6	< 0.0001*
White Blood Cell	8330/µL	0.623 (0.582-0.663)	52.9	68.4	0.001*
Lymphocyte	800/µL	0.707 (0.668-0.744)	64.7	74.3	< 0.0001*
Monocyte	200/µL	0.534 (0.492-0.575)	20.6	89.9	0.399
Neutrophil	6500/µL	0.662 (0.622-0.701)	55.9	72.3	< 0.0001*
Hemoglobin	12 gr/dL	0.608 (0.566-0.648)	42.6	77.7	0.007*
Thrombocyte	210000/µL	0.565 (0.524-0.606)	45.6	67.0	0.08
C-Reactive Protein	74.2 mg/L	0.720 (0.682-0.757)	72.1	66.4	< 0.0001*
Ferritin	746 ng/mL	0.679 (0.639-0.717)	45.6	82.8	< 0.0001*
Lactate Dehydrogenase	398 U/L	0.634 (0.593-0.673)	38.2	85.0	0.0005*
D-dimer	1571 ng/mL	0.636 (0.596-0.676)	51.5	73.1	< 0.0001*

Table 4. Univariate Analysis of Age, Male Sex, Oxygen Need at Admission, Presence of Chronic Disease, FPGL and Other Laboratory Findings and Poor Prognosis		
	Univariate Analysis	
	Odds ratio (95% CI)	**P**
Age > 64	3.73 (2.18-6.37)	0.000*
Male Sex	3.32 (1.79-6.12)	0.000*
Oxygen Need at Admission	11.9 (4.27-33.22)	0.000*
Presence of Chronic Disease	1.29 (0.75-2.22)	0.34
FBGL > 136 mg/dl	2.54 (1.52-4.24)	0.000*
White Blood Cell > 8330/µL	2.43 (1.45-4.05)	0.000*
Neutrophil > 6500/µL	3.31 (1.97-5.55)	0.000*
Lymphocyte ≤ 800/µL	5.30 (3.10-9.06)	0.000*
Monocyte ≤ 200/µL	2.31 (1.20-4.45)	0.02*
Hemoglobin ≤ 12 gr/dL	2.58 (1.53-4.36)	0.000*
CRP > 74.2 mg/L	5.09 (2.90-8.93)	0.000*
Ferritin > 746 ng/mL	4.03 (2.37-6.85)	0.000*
LDH > 398 U/L	3.50 (2.02-6.05)	0.000*
D-dimer > 1517 ng/mL	2.88 (1.72-4.82)	0.000*

FBGL: Fasting Blood Glucose Level, CRP: C-Reactive Protein, LDH: Lactate DeHydrogenase
*p <0.05 was considered statistically significant

In the multivariate analysis made for the factors that were associated with poor prognosis,a statistically significant relation was detected between age >64, presence of oxygen need at admission, FBGL>136 mg/dl, lymphocyte≤800/µL, Hb≤12 gr/dL, CRP>74.2 mg/L, ferritin>746 ng/mL, and LDH>398 U/L and poor prognosis (p=0.001, p=0.01, p=0.015, p=0.004, p=0.04, p=0.015, p=0.004, p=0.04,respectively) (Table 5).

Table 5. Multivariate Analysis of Poor Prognosis

	Multivariate Analysis	
	Odds ratio (95% CI)	**P**
Age > 64	2.84 (1.53-5.29)	0.001*
Oxygen need at admission	4.18 (1.41-12.43)	0.01*
FBGL > 136 mg/dl	2.09 (1.15-3.78)	0.015*
Lymphocyte ≤ 800/µL	2.46 (1.34-4.50)	0.004*
Hemoglobin ≤ 12 gr/dL	1.93 (1.03-3.59)	0.04*
CRP > 74.2 mg/L	2.22 (1.17-4.19)	0.015*
Ferritin > 746 ng/mL	2.53 1.35-4.74)	0.004*
LDH > 398 U/L	1.95 (1.02-3.74)	0.04*

FBGL: Fasting Blood Glucose Level, CRP: C-Reactive Protein, LDH: Lactate Dehydrogenase, *p <0.05 was considered statistically significant

DISCUSSION

Our study is the first one conducted in TURKEY to investigate the relation between FBGL and poor prognosis in the COVID-19 patient group. Although there are similar studies in the literature, our study results are significant since the results differed in different patient populations. Also, since most of the studies in the literature were conducted in the first 3 months after the pandemic was declared, the inclusion of patients after the vaccination of elderly patients in our study, makes a difference in the literature. Obesity and FBGL cut-off values might also differ in each society. In our study group, in patients with FBGL>159 mg/dL, the risk of pulse steroid need is 3 times; in patients with FBGL>138 mg/dL, the risk of need for intensive care unit is 2 times; and the risk of mortality in patients with FBGL>136 mg/dL was found to be 2.5 times higher. Also, the risk of poor prognosis was found to be 2.5 times higher in patients with FBGL>136 mg/dL. Additionally, it was found that age >64, presence of oxygen need at admission, lymphocyte≤800/µL, Hb≤12 gr/dL, CRP>74,2 mg/L, ferritin>746 ng/mL, and LDH>398 U/L were associated with poor prognosis. Contrary to what is already known, the presence of chronic disease and elevated d-dimer levels were not found to be associated with poor prognosis.

In the study conducted by Sheng-ping et al., they evaluated 255 patients with COVID-19 diagnosis and compared the patient groups with and without intensive care unit need (2). The incidence of DM was found to be significantly higher in the group that needed intensive care unit (p = 0.04). FBGL was found to be higher in patients who needed intensive care unit at admission to the hospital than those who did not need intensive care unit (p <0.001). It was also shown that the presence of DM history, elevated FBGL, IL-6 and D-dimer levels were independent markers for poor prognosis (p=0.01, p<0.001, p=0.01, p=0.03, respectively) (2). The results of this patient group were similar to the results of our study in terms of the need for intensive care unit. However, the fact that there was a high number of patients in our study group and the need for pulse steroid and mortality were also evaluated is the most significant difference between the two studies. Also, D-dimer was not found to be associated with poor prognosis in our Study Group. We think that the reason that D-dimer was not associated with poor prognosis was the high number of patients presenting with pneumonia in our study, but the lower number of patients presenting with thrombosis.

Yan et al. conducted a study by including 258 COVID-19 patients and compared groups with and without DM (3). The mean age of the study group was 64, which is similar to our study. The clinical characteristics of the patients were also similar. As a result of the study, it was found that DM diagnosis (p=0.028) and high FBGL levels (p<0.001) were associated with poor prognosis in COVID-19 (3). However, subgroup analyses were not made for those who were diagnosed with DM in our Study Group.

Yuli et al. (4) evaluated the relation between FBGL and mortality in 941 COVID-19 patients that required hospitalization in their study. They identified a cut-off value of 7 mmol/L for FBGL. The leukocyte and CRP levels were found to be significantly elevated in patients with FBGL>7 mmol/L, and the lymphocyte and thrombocyte values were found to be significantly lower. Also, the rate of bilateral pneumonia was also detected to be high (p<0.001). Mortality was found to be significantly higher in the group with FBGL>7 mmol/L in patients without DM diagnosis (21.6% & 6.1%, p<0.001) (4). The 7.6 mmol/L FBGL cut-off value detected in our study group was higher than in this study. Although other results were similar, mortality rates were found to be lower in our patient group (7.6% & 3.1%).

Yun et al. (5) examined 151 patients who were diagnosed with COVID-19 in terms of mortality. The number of patients with male gender (p 0.0067) and chronic diseases such as hypertension (p=0.019) and Chronic Obstructive Pulmonary Disease (p=0.0015) was higher in the patient group that died (5). Again, FBGL was found to be higher in the group with mortality (5.86 & 5.03 mmol/L,p=0.0003). Unlike our study group, patients were divided into three groups according to FBGLs; Group 1(4.09-4.91 mmol/L), Group 2(4.91-5.38 mmol/L), and Group 3(5.38-6.09 mmol/L). When Group 1 and Group 3 were compared in terms of mortality, statistically significant differences were detected between the groups (22% & 1.92%, p<0.05) (5). Unlike the results reported in the literature and this study, the presence of the chronic disease did not affect the development of poor prognosis in our study group. It was found that the FBGLs of the patients were lower than the cut-off values of our study group. Only the patients in Group 3 had a similar FBGL value of 110 mg/dL (6.1 mmol/L), which was determined in line with the guidelines. The mortality rate in the group with FBGL>110 mg/dL in our study was found to be lower compared to this study (4.7%).

In the study that was conducted by Min et al. (6), the mortality rate was reported as 28.3% in the 106 patients who were diagnosed with COVID-19; and 24.5% of the patients required intensive care unit and invasive

mechanical ventilation. Although chronic lung disease and DM did not cause significant risks in terms of mortality in the patient group, it was found that age (> 72) (p=0.013), and FBGL (>168 mg/dL) (p=0.000) were significant risk factors (6). There was a DM diagnosis in 39.6% of the patient group. Elevated FBGL levels were found to be associated with mortality in the analysis made by excluding those who were diagnosed with DM (p=0.038). The cut-off value of FBGL was detected to be significantly higher in this study group than in most studies in the literature and our study. The fact that the rate of patients who were diagnosed with DM was 25.2% in our Study Group might explain the difference in FBGL.

A total of 35 studies and 14502 patients were analyzed in a meta-analysis that was published by Gilbert et al. (12). It was shown that there is an independent relation between FBGL and poor prognosis. It was determined that the risk of developing severe COVID-19 was higher within the range of 6.6-8.1 mmol/L and every 1 mmol/L increase in FBGL at admission increased the risk of developing severe disease at a rate of 33% (p<0.001) (12). A total of 12 studies and 9045 patients were analyzed in a meta-analysis that was published by Dewi et al. (13), and it was reported that the cut-off value of FBGL was within the range of 7-7.7 mmol/L in most of the studies, which is similar to our Study Group. When all studies were evaluated together, it was shown that hyperglycemia increased the poor prognosis risk at a rate of 4.72 times (13). In our Study Group, although the cut-off value of FBGL was similar to other studies, the lower poor prognosis risk increase (2.5 times) suggested that FBGL and other clinical and laboratory markers were also effective in determining the poor prognosis.

Our study had some limitations. FBGL measurements were taken from venous blood in some patients, and from capillary blood samples taken from the fingertip in some others. This is one of the most important limitations, which might have affected our results. Also, the lack of a separate analysis after those diagnosed with DM was excluded in our patient group was among the limitations.

As a conclusion, it was shown that when FBGL is >136 mg/dL (7.6 mmol/L), it increases the risk of poor prognosis. It was also found that advanced age, presence of oxygen need at admission, low lymphocyte and hemoglobin levels, elevated CRP, ferritin and LDH levels are associated with poor prognosis. Starting early steroid treatment in patients by identifying risk factors associated with poor prognosis at admission prevents the development of cytokine storm and deterioration of the disease.

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