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Türk Hijyen ve Deneysel Biyoloji Dergisi

The role of Diabetes mellitus in the progression and prognosis of COVID-19

COVID-19'un progresyonu ve prognozunda Diabetes mellitus'un rolü

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ABSTRACT

Objective: The COVID-19 pandemic, caused by SARS-CoV-2 of Coronaviruses types, is a highly infectious disease caused by SARS-CoV-2, which first appeared in China. The presence of comorbid diseases, especially diabetes, and advanced age are determinants of the mortality and morbidity of the disease. In this study, it was aimed to examine the possible role of Diabetes mellitus (DM) in the course of the novel coronavirus disease (COVID-19).

Methods: In this study, the data of 81 patients who applied to Ankara Polatlı Duatepe State Hospital between January 01 and May 05, 2021 and were confirmed to have COVID-19 and were hospitalized in the COVID-19 service for 5 to 20 days were analyzed. 39 female and 42 male patients were included in the study and the patients were divided into three groups. COVID-19 group (n=26; 10 female, 16 male), COVID-19+DM group (n=28; 13 female, 15 male), and COVID-19+hypertension (HT) group (n=27; 16 female, 11 male). Demographic, clinical, radiological and laboratory records of the patients were reviewed retrospectively.

Results: There was a statistically significant difference between the groups when they matched for age and gender (p<0.05). The mean age of the COVID-19+DM and

ÖZET

Amaç: Koronavirüs ailesinden SARS-CoV-2'nin neden olduğu COVID-19 pandemisi, ilk olarak Çin'de görülen ve bulaşıcılık özelliği yüksek bir hastalıktır. Hastalığın mortalite ve morbiditesinde diyabet başta olmak üzere komorbid hastalıkların varlığı ve ileri yaş belirleyici olmaktadır. Bu çalışmada Diabetes mellitus (DM)'un, yeni koronavirüs hastalığının (COVID-19) seyrindeki olası rolünün incelenmesi amaçlanmıştır.

Yöntem: Bu çalışmada, 01 Ocak-05 Mayıs 2021 tarihleri arasında Ankara Polatlı Duatepe Devlet Hastanesine başvuran ve COVID-19 olduğu doğrulanan ve COVID-19 servisinde 5 ila 20 gün yatan 81 hastanın verileri incelendi. Çalışmaya 39 kadın ve 42 erkek hasta dahil edildi ve hastalar üç gruba ayrıldı. COVID-19 grubu (n=26; 10 kadın, 16 erkek), COVID-19+DM grubu (n=28; 13 kadın, 15 erkek) ve COVID-19+hipertansiyon (HT) grubu (n=27; 16 kadın, 11 erkek). Hastaların demografik, klinik, radyolojik ve laboratuvar kayıtları geriye dönük olarak incelendi.

Bulgular: Gruplar arasında yaş ve cinsiyet açısından istatistiksel olarak anlamlı bir fark vardı (p<0.05). COVID-19+DM ve COVID-19+HT gruplarının yaş ortalaması COVID-19 grubuna göre yüksekti. COVID-19

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COVID-19+HT groups was higher than the COVID-19 group (p<0.05). COVID-19 group 55.96±15.545 years, COVID-19+DM 68.29±12.849 years, COVID-19+HT 71.48±11.416 years. Only 32 patients had positive PCR tests, and the rate was 39.5%. The number of patients with CT is 69, and the rate is 85.2%. The number of CT-positive patients is 56 and the positivity rate is 81%. The PCR test positivity rate is lower than the CT positivity rate. The serum fasting blood glucose (FBG) and C-reactive protein (CRP) levels were significantly higher in the COVID-19+DM group when compared to the COVID-19 group and COVID-19+HT group (p<0.05). The serum sodium (Na) and chlorine (Cl) levels were significantly lower in the COVID-19+DM group when compared to the COVID-19 group and COVID-19+HT group (p<0.05). The serum creatinine and phosphorus (P) levels were significantly higher in the COVID-19+DM group when compared to the COVID-19 group (p<0.05).The serum hemoglobin (HGB) and hematocrit (HCT) levels were considerably higher in the COVID-19 group compared to the COVID-19+DM group (p<0.05).

Conclusion: When all the data we obtained in our study are evaluated; we determined that the comorbidity effect of DM is important in the clinical course of patients infected with the SARS-CoV-2 virus. We think that SARS-CoV-2 pneumonia patients with diabetes may be more severe than those without diabetes in terms of organ damage, and inflammatory variables, and are more likely to evolve to a worse prognosis, regardless of whether the additional comorbidities were present or not.

Key Words: COVID-19, Diabetes mellitus, hypertension, CRP, fasting blood glucose

grubunun yaş ortalaması 55.96±15.545 yıl, COVID-19+DM grubunun yaş ortalaması 68.29±12.849 yıl, COVID-19+HT grubunun yaş ortalaması 71.48±11.416 yıl idi. 81 COVID-19 hastasının sadece 32'sinin PCR testi pozitifti ve oran %39.5 idi. BT'li hasta sayısı ise 69, oran %85.2'dir. BT pozitif hasta sayısı 56 ve pozitiflik oranı %81'dir. PCR testi pozitiflik oranı, BT pozitiflik oranından daha düşüktür. COVID-19+DM grubunda serum açlık kan şekeri ve C-reaktif protein (CRP) düzeyleri COVID-19 grubu ve COVID-19+HT grubuna göre anlamlı derecede yüksekti (p<0.05). COVID-19+DM grubunda serum sodyum (Na) ve klor (Cl) düzeyleri COVID-19 ve COVID-19+HT grubuna göre anlamlı derecede düşüktü (p<0.05). COVID-19+DM grubunda serum kreatinin ve fosfor (P) düzeyleri COVID-19 grubuna göre anlamlı derecede yüksekti (p<0.05). COVID-19+DM grubunda serum Serum hemoglobin (HGB) ve hematokrit (HCT) düzeyleri COVID-19+DM grubuna göre COVID-19 grubunda oldukça yüksekti (p<0.05).

Sonuç: Çalışmamızda elde ettiğimiz tüm veriler değerlendirildiğinde; SARS-CoV-2 virüsü ile enfekte hastaların klinik seyrinde DM'nin komorbidite etkisinin önemli olduğunu saptadık. Diyabeti olan SARS-CoV-2 pnömoni hastalarının, organ hasarı ve inflamatuar değişkenler açısından diyabeti olmayanlara göre daha şiddetli olabileceğini ve ek komorbiditelerin olup olmadığına bakılmaksızın daha kötü bir prognoza dönüşme olasılığının daha yüksek olduğunu düşünmekteyiz.

Anahtar Kelimeler: COVID-19, Diabetes mellitus, hipertansiyon, CRP, açlık kan şekeri

INTRODUCTION

On December 31, 2019, by WHO China Country Office; After reporting that there are many unknown cases of pneumonia in Wuhan city of Hubei province of China, WHO first announced that the cause of these complaints is a new type of coronavirus (2019-nCoV).

The WHO Director-General declared this outbreak as the "COVID-19 Pandemic" on March 11, 2020, and in the past two weeks, the number of cases outside China has increased by thirteen times, and the number of affected countries has tripled. After

the announcement, the epidemic spread to many countries, especially in the Asian region countries, and reached an international dimension affecting the whole world (1).

The virus is transmitted mainly through infected respiratory droplets and in close contact with the infected person. The incubation period can be as long as 2 weeks or even longer, and it is highly contagious (2). Found that the mean R0 of COVID-19 was approximately 2.68 (95% CI: 2.47-2.86). An increasing number of outbreaks of familial transmission stressed the possibility of person-to-person transmission (3). The most common manifestations of COVID-19 included fever, dry cough, dyspnea, myalgia, fatigue, hypo lymphoma, and radiographic evidence of pneumonia. Complications (eg, acute respiratory distress syndrome [ARDS], arrhythmia, shock acute cardiac injury, secondary infection, and acute kidney injury) and death may occur in severe cases (4). Diagnosis of infections in general; in the appropriate clinical material taken from the site of infection in the infected patient, it can be placed directly using microscopic indication, production, determination of antigens or nucleic acids, or indirectly by showing specific antibodies against the agent in the patient serum.

The diagnosis of COVID-19 was confirmed as a positive result for a nasopharyngeal swab and respiratory pathogen nucleic acid test with high-throughput sequencing or real-time reverse transcriptase-polymerase chain reaction (RT-PCR). For this method, sensitive and specific (sensitive and specific) results are obtained by using oligonucleotide probes marked with fluorescent dyes, which are unique detection systems. Chest CT imaging plays a critical role in the surveillance and diagnosis of COVID-19 viral pneumonia with higher sensitivity (5). Although the sensitivity of the PCR tests are high, taking the test result in 4-6 hours (reduced to 2-4 hours in the last kits), and rapid anticorrosion tests (immunoassay) have been produced due to the need for experienced personnel. Tests have been produced that can detect IgM and IgG antibodies produced against SARS-CoV-2 in 15 minutes. However, there is a 13% chance of giving false negatives in catching positive cases.

Notably, it is confirmed that 2019-nCoV uses the same cell entry receptor angiotensin-converting enzyme II (ACE2) as SARS-CoV (6). ACE2 is the surface receptor for SARS (SARS-CoV), straightforwardly interacting with the spike glycoprotein (S protein) (7). A new report proposes that the partiality among ACE2 and the receptor-restricting space (RBD) of SARS-CoV-2, is 10 to multiple times higher than that with the RBD of SARS-CoV, demonstrating that ACE2 may likewise be the receptor for SARS-CoV-2 (8). ACE2 was accounted for to be generally communicated in different organ frameworks including the cardiovascular framework, kidneys, lungs, and mind, which may clarify why some Coronavirus patients kicked the bucket of numerous organ disappointment (9).

Diabetes mellitus (DM) is one of the main sources of dreariness worldwide and is expected to rise considerably throughout the following many years (10). A few examinations have exhibited a higher defenselessness to some irresistible infections in diabetic individuals, similar to Staphylococcus aureus and Mycobacterium tuberculosis (11), presumably inferable from the dysregulated safe framework (12). It has been revealed that plasma glucose levels and diabetes are autonomous indicators for mortality and bleakness in patients with SARS (13). A review concentrated in Wuhan, China uncovered that of the 41 Coronavirus patients, 32% of them had fundamental sicknesses, and among which 20% was diabetes (14). Consequently, these diabetic patients may be at an expanded danger of Coronavirus and have a less fortunate visualization (15-17).

In this study, DM was examined as a risk factor affecting the progression of the new type of coronavirus disease (COVID-19). In this study, it was aimed to examine the possible role of Diabetes mellitus (DM) in the clinical course of patients infected with the COVID-19 virus.

MATERIAL and METHOD

This study is a retrospective cohort study conducted with patients who had COVID-19 and also had diabetes and comorbidities. All patients who applied to Ankara Polatlı Duatepe State Hospital with suspected COVID-19 disease between January 01 and May 05, 2021, and were infected with laboratory-confirmed SARS-COV-2 were included in the study. COVID-19 patients were hospitalized in the COVI-19 ward for 5 to 20 days. This study was approved by the Siirt University non-interventional research ethics committee (Date:26.03.2021 and No: 2021/01.01). The data of 81 patients confirmed with COVID-19 were studied. This study has participated in 39 female and 42 male patients. Demographic, clinical characteristics, pre-existing chronic comorbidities, laboratory and radiological findings, and treatment protocols of the patients were obtained from hospital information system records. All data were checked by two physicians who are experts in internal medicine and infectious diseases. The time from onset of illness to hospitalization was also recorded. All patients participating in this study were laboratory-confirmed COVID-19 patients, and the diagnostic criteria for COVID-19 were based on the positive detection of viral nucleic acids.

White blood cell (WBC), neutrophil (NE), lymphocyte (LY), eosinophil (EO), monocyte (MO), basophil (BA), hemoglobin (HGB), hematocrit (HCT), C-reactive protein (CRP), fasting blood glucose (FBG), lactate dehydrogenase (LDH), urea, creatinine, calcium (Ca), chlorine (Cl), sodium (Na), potassium (K), phosphorus (P), serum creatine kinase (CK), creatine kinase isoenzyme MB (CK-MB), total and direct bilirubin, alanine transaminase (ALT), aspartate transaminase (AST), ferritin, D-dimer, troponin I, international normalized ratio (INR), prothrombin time (PT), and activated partial thromboplastin time (APTT) were determined for each patient. All medical laboratory data were measured by the clinical laboratory of Ankara Polatlı Duatepe State Hospital. Diabetes was defined from the medical history of the patients and type-1 patients were excluded from the study.

Throat-swab specimens obtained from the upper respiratory tract of patients at admission were stored in a viral-transport medium. Total RNA was extracted within two hours using the respiratory sample RNA isolation kit. SARS-CoV-2 was examined by RT-PCR as described previously.

All COVID-19 patients met the following criteria: (a) Epidemiology history, (b) Fever or other respiratory symptoms, (c) Typical CT image abnormities of viral pneumonia, and (d) positive result of RT-PCR for SARS-CoV-2 RNA. Patients were divided into diabetes and non-diabetes groups according to their medical history. Furthermore, CT imaging scores were used to quantify the pathological changes in COVID-19 patients. As a result of the widespread recognition of CT findings, various algorithms on CT and scoring systems that determine the severity of the disease according to CT findings have been developed (16, 17). Despite all this, thoracic CT may be normal, especially in the early stage of the disease, and normal CT does not exclude the disease.

Statistical analysis

Data are presented as the mean ± standard deviation. Statistical analyses were conducted by Kruskal Wallis test and Mann-Whitney U-test (SPSS for Windows 22.0; SPSS, Chicago, IL, USA). A value of $p<0.05$ was defined as significant.

RESULTS

A total of 81 patients participated in this study they were into three groups: COVID-19 (n=26; 10 female, 16 male), COVID-19+DM (n=28; 13 female, 15 male), and COVID-19+ hypertension (HT) (n=27; 16 female, 11 male). There was a statistically significant difference between the groups when they matched for age and gender ($p<0.05$). In this study, the data of 39 female and 42 male patients were studied. The mean age of the COVID-19+DM and COVID-19+HT groups was higher than the COVID-19 group ($p<0.05$).

COVID-19 group 55.96±15.545 years, COVID-19+DM 68.29±12.849 years, COVID-19+HT 71.48±11.416 years.

Only 32 patients had positive PCR tests, and the rate was 39.5%. The number of patients with CT is 69, and the rate is 85.2%. The number of CT-positive patients is 56 and the positivity rate is 81%. The PCR test positivity rate is lower than the CT positivity rate. It suggests that the COVID-19 virus has passed to the lower respiratory tract. The patient may have gone to the hospital long after the symptoms.

Ground-glass opacity, pleural fluid, consolidation, lymphadenopathy, cobblestone appearance, pericardial fluid, air bronchogram, cavitation, airway changes, air cyst, reticular appearance, and nodules (with halo and inverted halo sign) are radiological findings seen in COVID-19 infection.

Of all patients, there were many typically abnormal laboratory test results (Table 1, 2, and 3). The serum FBG and CRP levels were significantly higher in the COVID-19+DM group when compared to the COVID-19 group and COVID-19+HT group ($p<0.05$). The serum Na and Cl levels were significantly lower in the COVID-19+DM group when compared to the COVID-19 group and COVID-19+HT group ($p<0.05$). The serum creatinine and P levels were significantly higher in the COVID-19+DM group when compared to the COVID-19 group ($p<0.05$). The serum Ca levels were significantly lower in the COVID-19+HT group when compared to the COVID-19 group ($p<0.05$).

Table 1. Comparision of laboratory parameters all groups (mean±SD)

	COVID-19 (n=26)	COVID-19+DM (n=28)	COVID-19+HT (n=27)
FBG (mg/dL)	134.04±53.789[a]	230.39±121.165[a,c]	127.19±47.079[c]
CRP (mg/dL)	6.444±7.210[a]	13.329±10.951[a,c]	7.501±6.968[c]
Urea (mg/dL)	39.25±20.561	58.25±41.666	58.03±58.677
Creatinine (mg/dL)	0.794±0.182[a]	1.385±1.302[a]	1.263±1.165
T Bil (mg/dL)	0.520±0.257	0.635±0.402	0.606±0.263
D Bil (mg/dL)	0.172±0.145	0.165±0.829	0.192±0.118
ALT (U/L)	35.85±31.844	26.93±15.251	29.52±28.967
AST (U/L)	43.50±27.946	38.14±23.975	41.44±39.557
LDH (U/L)	390.46±230.216	388.86±156.044	328.93±162.232
Na (mmol/L)	135.69±7.519[a]	134.46±4.880[a, c]	138.07±5.615[c]
K (mmol/L)	4.399±0.625[a]	4.401±0.637[a]	4.232±0.665
Cl (mmol/L)	101.23±3.881[a]	98.29±5.747[a, c]	102.96±4.743[c]
Ca (mg/dL)	9.012±0.592[b]	8.824±0.898	8.530±0.514[b]
CK (U/L)	304.377±428.989	198.521±236.376	112.278±90.755
CK-MB (U/L)	53.35±142.035	22.57±10.039	19.48±7.842
P (mg/dL)	2.462±0.988	2.965±0.818	2.797±0.903

Abbreviations: HT:Hypertension, DM:Diabetes mellitus, FBG:Fasting blood glucose, CRP:C:reactive protein, T Bil:Total bilirubine, D Bil:Direct bilirubine, ALT:Alanine transaminase, AST:Aspartate transaminase, LDH:Lactate dehydrogenase, Sodium:Na, Potassium:K, Chlorine:Cl, Calcium:Ca, CK:Creatine kinase, Creatine kinase isoenzyme MB:CK:MB, Phosphorus:P

[a]FBG, CRP, Creatinine, Na, P, Cl (COVID-19+DM group vs. COVID-19 group)* (p=0.000, p=0.01, p=0.003, p=0.04, p=0.032, p=0.02, respectively)

[b]Ca, (COVID-19+HT vs. COVID-19 group)* (p=0.006)

[c]FBG, CRP, Na, Cl (COVID-19+DM group vs. COVID-19+HT group)* (p=0.000, p=0.04, p=0.01, p=0.001, respectively)

Table 2. Comparision of hemogram parameters all groups (mean±SD)

	COVID-19 (n=26)	COVID-19+DM (n=28)	COVID-19+HT (n=27)
WBC 10^3/mL	7.273±4.032	7.907±3.332	6.730±3.317
LY10^3/mL	1.076±0.526	1.087±0.865	1.444±1.777
MO10^3/mL	3.344±9.481	0.611±0.383	0.591±0.390
NE10^3/mL	5.468±3.610	6.132±2.985	4.989±3.142
EO10^3/mL	0.111±0.153	0.078±0.076	0.064±0.046
BA10^3/mL	0.013±0.011	0.020±0.017	0.028±0.057
HGB g/dL	13.484±1.794[a]	12.245±1.594[a]	12.384±1.987
HCT %	40.735±5.377[a, b]	37.361±4.705[a]	37.511±5.8[b]

Abbreviations: HT-Hypertension, DM-Diabetes mellitus, WBC-White blood cell, LY-Lymphocyte, MO-Monocyte, NE-Neutrophil, EO-Eosinophil, BA-Basophil, HGB-Hemoglobin, HCT-Hematocrit

[a]HGB, HCT (COVID-19+DM group vs. COVID-19 group)* (p=0.017, p=0.03, respectively)

[b]HCT (COVID-19+HT vs. COVID-19 group)* (p=0.046)

Table 3. Comparision of coagulation factors all groups (mean±SD)

	COVID-19 (n=26)	COVID-19+DM (n=28)	COVID-19+HT (n=27)
PT	11.739±0.985	11.800±0.758	16.096±15.602
INR	0.886±0.162	0.939±0.065	1.338±1.491
APTT	20.849±4.564	21.700±5.290	25.959±11.269
D-dimer (mg/L)	2.569±7.179[a]	1.614±1.911	1.987±1.917[a]
Troponin I (ng/mL)	0.043±0.140 [a]	0.061±0.151	0.255±1.157[a]
Ferritin (ng/mL)	355.29±426.902	542.29±791.992	1365.37±3846.767

Abbreviations: HT-Hypertension, DM-Diabetes mellitus, PT-Prothrombin time, INR-International normalized ratio, APTT-Activated partial thromboplastin time

[a]D-dimer, Troponin I (COVID-19+HT vs. COVID-19 group)* (p=0.029, p=0.042, respectively)

The serum HGB and HCT levels were considerably higher in the COVID-19 group compared to the COVID-19+DM group (p<0.05). The serum HCT levels were considerably higher in the COVID-19 group compared to the COVID-19+HT group (p<0.05).

The serum urea levels were lower in the COVID-19 group when compared to the COVID-19+DM and COVID-19+HT groups. However, this was not a significant difference (p>0.05). The serum ALT and AST levels were higher in the COVID-19 group when compared to the COVID-19+DM and COVID-19+HT groups. However, this was not a significant difference (p>0.05).

The serum PT, INR, and APTT levels were higher in the COVID-19+HT group when compared to the COVID-19+DM and COVID-19 groups. However, this was not a significant difference (p>0.05). The serum D-dimer levels were lower in the COVID-19+HT group when compared to the COVID-19 group (p<0.05). The serum troponin I levels were higher in the COVID-19+HT group when compared to the COVID-19 group (p<0.05). The serum ferritin levels were increased in the COVID-19+HT and COVID-19+DM groups when compared to the COVID-19 group. However, this was not a significant difference (p>0.05).

DISCUSSION

Infection with the newly emerging, extremely contagious coronavirus SARS-CoV-2 causes the unique coronavirus illness of 2019 (COVID-19) (18). SARS-CoV-2 mostly infects the lungs and respiratory tract, causing a new kind of coronavirus pneumonia (19). Acute respiratory distress syndrome (ARDS), septic shock, and multiple organ distress syndrome (MODS) can all occur in severe COVID-19 instances (20).

Elderly individuals, along with those with pre-existing conditions, such as hypertension, cancer, cardiovascular diseases, diabetes mellitus, and acute kidney injury, have a demonstrated higher risk for developing more severe cases of COVID-19, as well as suffering a higher risk of mortality (13, 15).

Diabetes is commonly associated with higher mortality and morbidity from infectious diseases, although epidemiologic data to support this claim is surprisingly few. However, it appears to confirm that diabetes increases the risk of infection and death (10-13). However, it is still unclear whether diabetes is a risk factor for COVID-19 prognosis. Type 2 diabetes is commonly thought of as a chronic, low-grade inflammatory disease brought on by a long-term immune system imbalance, metabolic syndrome, or nutrient overload in obese people (21).

It has long been known that diabetic people are more susceptible to infections in general and have a worse prognosis once infected than non-diabetic patients (22). Other coronaviral epidemics have previously shown a similar increase in susceptibility. Pre-existing T2D, for example, was linked to poor outcomes in individuals with severe acute respiratory syndrome (SARS). Patients who died from SARS had a much higher percentage of known T2D history than those who survived (13). T2D was also found to be the predominant comorbidity related to severe or deadly MERS-CoV infections in epidemiological investigations. Regarding the present COVID-19 pandemic, multiple recent studies, though with small sample sizes, have already revealed that T2D is prevalent comorbidity that affects a higher proportion of COVID-19 patients with severe and ICU-admitted cases than those with moderate symptoms (14, 23-25). These links between diabetes and poorer viral infection outcomes are unforeseen, as hyperglycemia deleterious viremia and inflammatory control, increase morbidity and mortality in a variety of patients (26). Overly strict glucose control, on the other hand, can raise the risk of severe hypoglycemia, which can lead to an increase in mortality. Data from human and animal studies, on the other hand, suggests that some viruses are diabetogenic (27). After being infected with chickenpox, Jali et al. (28) reported two patients who developed acute insulin-dependent diabetes mellitus for a brief and temporary duration. In a study of SARS, Yang et al. (13) discovered that fasting blood glucose levels are higher in non-severe patients who had not been treated with glucocorticoids. Another study discovered that ACE2 protein immunostaining is robust in islets of Langerhans but weak in exocrine tissues, implying that coronavirus may cause diabetes by gravely harming islets (13). Sharif et al. found that the risk increased many folds when cardiovascular diseases (CVD) and diabetes coexisted in patients in their study in Bangladesh (29). Harbuwono et al. in a study stated that DM is associated not only with the development of more COVID-19 clinical symptoms but also with a higher risk of COVID-19 mortality. They recommend that this finding may provide a basis for future policy regarding COVID-19 prevention and management among diabetes patients in Indonesia (30). Since viral infection may cause sharp fluctuation of the blood glucose level of diabetes patients, which adversely affects the recovery of patients, there is a reason to suspect that diabetes combined with SARS-CoV-2 pneumonia may form a vicious circle, which is detrimental to the prognosis of COVID-19.

It was demonstrated that FBG level was much higher in the diabetic group compared to the non-diabetic group. The serum FBG level was significantly higher in the COVID-19+DM when compared to the COVID-19 and COVID-19+HT groups in this study.

It is concluded that hypertension increases COVID-19 severity due to underlying endothelial dysfunctions and coagulopathy. COVID-19 might augment the hypertensive complications due to down-regulation of ACE2. The use of ACEIs or ARBs might be beneficial in the management of hypertensive patients with COVID-19 (31). It has been claimed that the interaction between ACEI administration and the inflammatory marker LDH influenced the stay duration (days) at the hospital, which could contribute to improve the clinical/pharmacological management of COVID-19 disease under a personalized medicine approach, where patients with a more severe inflammatory status may probably benefit more specifically by ACEI treatment (32). In a study was found that exposure to ACEIs or ARBs before prior to COVID-19 infection was not associated with an increased risk of hospitalization or all-cause mortality (33).

Aging, cognitive impairment, and higher levels of LDH, K, and FBG were found to be associated with an increased risk of death, while higher platelet levels and oxygen saturation, as well as taking oral glucose-lowering drugs, insulin, statins, and beta-blockers, were significantly associated with a reduced risk of in-hospital mortality (34). The mortality for patients in the older age group and those patients who were admitted to the intensive care unit (ICU) was higher. In addition, six laboratory parameters were positively associated with the odds of mortality: WBC count, NE, creatine kinase myocardial band, CRP, urea, and LDH (35).

The meta-analysis of 305370 patients highlights that patients with cerebrovascular disease (CVD) and COVID-19 have more than 4-fold higher risk of mortality, as well as patients with HT or diabetes (36). The severity of COVID-19 can be suggested to be associated with ALT, AST, FBG, CRP, serum ferritin, segmented %, and NE/LY ratio (NLR) (37).

In another study, although no significant correlation was found between underlying comorbidities HT, coronary artery disease (CAD), DM, chronic obstructive pulmonary disease (COPD) or asthma, those with CT severity scores of the patients with pneumonia had two or more comorbidities (38). In severe COVID-19 patients with diabetes, there were significant sex differences in many laboratory characteristics with a higher risk of mortality among males (39). In another study found that male sex, age, and medical history of obesity, HT, diabetes, immunosuppression, or kidney disease were associated with an increased risk of hospitalization or death (40).

Biochemical results revealed that various suggestive enzymes, such as LDH, HBDH, ALT, and GGT, were abnormally high in the blood of patients with SARS-CoV-2 pneumonia, indicating myocardial, renal, and liver disease. This finding is in line with the widespread distribution of SARS-CoV-2 ACE2 receptors and may help to explain why some patients died of multiple organ failure (1). When comparing the COVID-19 group to the COVID-19+DM and COVID-19+HT groups, serum AST and ALT levels were found to be higher in the COVID-19 group. This was, however, not a significant difference.

Inflammation-related biomarkers such as IL-6, CRP, serum ferritin, coagulation index, and D-dimer were shown considerably higher in diabetic individuals when compared to those without diabetes (41). Cytokine storm is a life-threatening critical condition that requires intensive care and has a very high mortality rate. Early recognition and prompt treatment provide better clinical outcomes (42, 43).

In our study, we demonstrated that the serum CRP levels were higher in the COVID-19+DM group when compared to the COVID-19 and COVID-19+HT groups. The serum ferritin levels were higher in the COVID-19+HT and COVID-19+DM groups when compared to the COVID-19 group. However, this was not a significant difference. The serum HGB and HCT levels were significantly higher in the COVID-19 group compared to the COVID-19+DM group.

In our study, we demonstrated that the number of patients with CT is 69, and the rate is 85.2%. The number of CT-positive patients is 56 and the positivity rate is

81%. The PCR test positivity rate is lower than the CT positivity rate. It suggests that the COVID-19 virus has passed to the lower respiratory tract. The patient may have gone to the hospital long after the symptoms.

Possible reasons for the low positivity of the COVID-19 PCR test in our study are poor quality sample with very little patient material, for example being taken at very early or late stage of infection, for example, not being processed and sent properly, technical reasons inherent in the test such as PCR inhibition or virus mutation, and SARS A negative result was obtained from a patient with a high suspicion of COVID-19, the fluctuating scattering of the CoV-2 virus in symptomatic and asymptomatic cases.

It's noteworthy that for diseases that can induce a cytokine storm. In addition, a significant rise in serum ferritin indicates the activation of the monocyte-macrophage system, which is a crucial part of the inflammatory storm. In the present study, we determined that the serum ferritin, PT, INR, and APTT levels were higher in the COVID-19+HT group when compared to the COVID-19 and COVID-19+DM groups. However, this was not a significant difference. Serum troponin I levels were higher in the COVID-19+HT group when compared to the COVID-19 group. D-Dimer, on the other hand, is a well-known biomarker that has an important place in predicting the prognosis of COVID-19 and shows COVID-related coagulopathy. (34). We determined that the serum D-dimer levels were lower in the COVID-19+HT group when compared to the COVID-19 group. In this respect, it seems that the use of D-dimer in predicting prognosis may be more effective in clinical decision making, especially in patients with a high burden of comorbidity with COVID-19.

Clinical medication showed that the insulin dose increased after the patients were infected with SARS-CoV-2, which shows that the virus affects the patient's glucose metabolism. Dysregulation of glucose metabolism will aggravate diabetes and then affect the severity of pneumonia, which works as an amplification loop. Meanwhile, the diabetic complications signify the seriousness of diabetes, and patients with diabetic complications showed a higher mortality rate, which further proves that diabetes is a risk factor for the prognosis of COVID-19, and the severity of diabetes is correlated positively with the poor prognosis.

Overall, we found that SARS-CoV-2 pneumonia patients with diabetes are more severe than those without diabetes in terms of organ damage, inflammatory variables, and are more likely to advance to a worse prognosis, regardless of whether additional comorbidities are present or not.

As a result, diabetes could be regarded a risk factor for the outcome of SARS-CoV-2 pneumonia, and diabetic patients should be given special attention in the event of rapid worsening. Further studies are required for randomized clinical trials may help confirm in confirming the results and hypotheses.

ETHICS COMITTEE APPROVAL

* The study was approved by the Siirt University Non-Interventional Research Ethics Committee (Date: 26.03.2021 and Number: 2021/01.01).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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