DOI: 10.5152/turkjnephrol.2021.21045

Original Article

Turkish Journal of Nephrology

COVID-19 Infection in Peritoneal Dialysis Patients: A Comparative Outcome Study with Patients on Hemodialysis and Patients without Kidney Disease

Rümeyza Kazancıoğlu[1], Savaş Öztürk[2], Kenan Turgutalp[3], Meltem Gürsu[1], Mustafa Arıcı[4], Ayşegül Oruç[5], Elbis Ahbap[6], Sibel Gökçay Bek[7], Erkan Şengül[8], Melike Betül Öğütmen[9], Dilek Gibyeli Genek[10], Mehmet Deniz Aylı[11], Yavuz Ayar[12], Engin Onan[13], Serhat Karadağ[2], Ebru Aşıcıoğlu[14], Halil Yazıcı[15], Mehmet Rıza Altıparmak[16], Bülent Tokgöz[17], Ali Rıza Odabaş[18], Halil Zeki Tonbul[19], Siren Sezer[20], Alaattin Yıldız[15], Kenan Ateş[21]

[1]Division of Nephrology, Department of Internal Medicine, Bezmialem Vakif University School of Medicine, Istanbul, Turkey
[2]Department of Nephrology, University of Health Sciences, Haseki Training and Research Hospital, Istanbul, Turkey
[3]Division of Nephrology, Department of Internal Medicine, Mersin University Training and Research Hospital School of Medicine, Mersin, Turkey
[4]Department of Nephrology, Hacettepe University School of Medicine, Ankara, Turkey
[5]Department of Nephrology, Bursa Uludag University School of Medicine, Bursa, Turkey
[6]Department of Nephrology, University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, Istanbul, Turkey
[7]Department of Nephrology, Kocaeli University School of Medicine, Kocaeli, Turkey
[8]Department of Nephrology, University of Health Sciences, Kocaeli Derince Training and Research Hospital, Kocaeli, Turkey
[9]Department of Nephrology, University of Health Sciences, Haydarpasa Numune Training and Research Hospital, Istanbul, Turkey
[10]Division of Nephrology, Department of Internal Medicine, Mugla Sitki Kocman University School of Medicine, Training and Research Hospital, Mugla, Turkey
[11]Department of Nephrology, University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital, Ankara, Turkey
[12]Department of Nephrology, Bursa City Hospital, Bursa, Turkey
[13]Department of Nephrology, Adana City Training and Research Hospital, Adana, Turkey
[14]Division of Nephrology, Department of Internal Medicine, Marmara University Pendik Training and Research Hospital, Istanbul, Turkey
[15]Division of Nephrology, Department of Internal Medicine, Istanbul University School of Medicine, Istanbul, Turkey
[16]Division of Nephrology, Department of Internal Medicine, Istanbul University–Cerrahpasa School of Medicine, Istanbul, Turkey
[17]Department of Nephrology, Erciyes University School of Medicine, Kayseri, Turkey
[18]Department of Nephrology, University of Health Sciences, Sultan Abdulhamid Han Training and Research Hospital, Istanbul, Turkey
[19]Department of Nephrology, Necmettin Erbakan University Meram School of Medicine, Konya, Turkey
[20]Division of Nephrology, Department of Internal Medicine, Atilim University School of Medicine, Ankara, Turkey
[21]Division of Nephrology, Department of Internal Medicine, Ankara University School of Medicine, Ankara, Turkey

ABSTRACT

Objectives: There is limited data about coronavirus disease-19 (COVID-19) characteristics and results in peritoneal dialysis (PD) patients. This study aimed to investigate the characteristics and outcomes among PD patients and compare them with matched hemodialysis (HD) patients and a control group without kidney disease.

Methods: We included 18 PD patients and consecutive age- and gender-matched 18 HD and 18 patients without kidney disease (control group) registered into the Turkish Society of Nephrology database including 1301 COVID-19 patients. We compared demographic, clinical, radiological, laboratory data, and outcomes namely intensive care unit (ICU) admission, mechanical ventilation, mortality, and composite outcome (death and/or ICU admission).

Results: ICU admission, mechanical ventilation, and mortality rates in PD patients (27.8%, 22.2%, and 22.2%, respectively) and the HD group (16.7%, 11.1%, and 16.7%, respectively) were higher than the control group (11.1%, 11.1%, and 5.6%, respectively), but intergroup comparison did not reveal difference. A total of 11 (20.3%) patients had composite outcome (6 PD patients, 3 HD patients, and 2 patients in the control group). In Cox regression analysis, higher age and higher CRP

This work is licensed under a Creative Commons Attribution 4.0 International License.

level were related to increased risk of composite outcome. Adjusted rate of composite outcome in PD group was significantly higher than the control group (*P* = .050). This rate was similar in HD and control groups (*P* = .30).
Conclusions: Combined in-hospital mortality and/or ICU admission of PD patients with COVID-19 was significantly higher than the control patients. There is a need for careful surveillance of PD patients for infection signs and prompt treatment of COVID-19.
Keywords: COVID-19, peritoneal dialysis, hemodialysis, outcome

Corresponding author: Meltem Gürsu ✉ meltem1401@yahoo.com **Received:** February 8, 2021 **Accepted:** August 17, 2021

Cite this article as: Kazancıoğlu R, Öztürk Ş, Turgutalp K, et al. COVID-19 infection in peritoneal dialysis patients: A comparative outcome study with patients on hemodialysis and patients without kidney disease. *Turk J Nephrol.* 2022;31(1):33-42.

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first described in the city of Wuhan, China, in December 2019. Within months, the virus spread around the globe, and a pandemic was declared by the World Health Organization in early March 2020. Coronavirus disease 2019 (COVID-19) is a febrile infection of the respiratory tract, with viral pneumonia and respiratory failure being the most common organ complications leading to hospitalization and frequently requiring ventilation support. It has been shown that mortality progressively increases from the fifth decade of life and is associated with the presence of comorbid conditions, such as hypertension (HT), cardiovascular disease, pulmonary disease, diabetes, and chronic kidney disease (CKD).[1-4]

These situations pose great challenges to patients with stage 5 CKD on dialysis because most of these patients are older and have a significant number of comorbidities. In a cohort of 21 COVID-19 patients admitted to the intensive care unit (ICU), 47.6% had a preexisting CKD and 9.5% had preexisting dialysis dependence.[5] The majority of HD patients are treated in centers, and in essence, an HD ward is quite the opposite of the pursued policy of social distancing, especially of the frail and vulnerable.[6,7] Many countries took measures to reduce potential risks in the spreading of the infection to patients by creating new and working extra shifts, reducing the number of HD patients dialyzing at the same time, allowing at least 6 feet of space between HD chairs/stations, and even decreasing the duration of the sessions at the HD centers.[8]

Currently, more than 369 000 patients receive peritoneal dialysis (PD) worldwide. These patients account for 11% of the global dialysis population.[9] As opposed to HD, PD is home-based and center-free; hence, it reduces the probability of health center-related transmission of COVID-19. However, PD patients have a weakened immune system that is associated with high morbidity of infection.[8] The studies on COVID-19 infection in patients undergoing HD treatment are gradually increasing, as the risk of spread of infection is greater in patients on in-center HD due to the frequent contact with the personnel and other patients in the center. Peritoneal dialysis patients have theoretically less risk of infection due to the home-based nature of the treatment, so the accumulated experience of PD patients is very limited. There is a need for studies comparing PD and HD patients and patients without kidney disease.

The Turkish Society of Nephrology started to collect data of hospitalized COVID patients with varying degrees of kidney dysfunction as well as dialysis patients from multiple centers nationwide with the onset of the pandemic. Herein, we examined the data of PD patients in this data set and compared these with HD and control group patients without kidney disease.

MAIN POINTS

- The Turkish Society of Nephrology started to collect data of hospitalized COVID patients with varying degrees of kidney dysfunction as well as dialysis patients from multiple centers nationwide with the onset of the pandemic. Herein, we examined the data of PD patients in this data set and compared these with HD and control group patients without kidney disease.
- Eighteen PD patients were included in our study, together with age- and gender-matched 18 HD and 18 control patients. Four (22.2%) patients in the PD group died, while 3 (16.7%) patients in the HD group and one (5.6%) patient in the control group died.
- A total of 11 (20.3%) patients had composite outcome meaning death or ICU admission (PD group: 6 patients (33.3%), HD group: 3 patients (16.7%), control group: 2 patients (11.1%)).
- Age, clinically severe disease at presentation, and CRP level at presentation 10 times or above the upper limit of normal were the parameters found to be significantly different between patients grouped according to whether they reached the composite outcome or not. The median time to composite outcome of PD group was significantly shorter than that of the control group (16 days vs 29 days, *P* = 0.022).
- There was no significant difference between the PD and HD groups and between the HD and control groups regarding composite outcome.

METHODS

Data Source

In this multicenter study, the subjects were selected from the national database of the Turkish Society of Nephrology including hospitalized COVID-19 patients with varying stages of CKD, including dialysis (PD and HD) and kidney transplant patients,

as well as consecutive control subjects who had COVID-19 but no kidney disease. The Ethics Committee of Health Sciences University, Istanbul Haseki Training and Research Hospital approved this study (No: 41-2020).

Study Population, Data Collection, and Definitions

The study included all PD patients recorded in this data set. An age- and gender-matched consecutive HD patient and a patient without kidney disease was selected for each PD patient from the database that included only adult patients. The data set included demographic information (age and gender), smoking status, the primary cause of CKD, the duration of renal replacement therapy, the modality of PD, the type of vascular access for HD patients, comorbidities (HT, diabetes mellitus (DM), ischemic heart disease (IHD), heart failure (HF), chronic obstructive pulmonary disease, chronic liver disease, and malignancy), and the medications (angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARB), calcium channel blockers, beta-blockers, any other antihypertensive drugs, insulin, oral antidiabetics, statins, antiaggregants, and anticoagulants)).

The diagnosis and treatment of patients in our country was governed by the "National COVID-19 Diagnosis and Treatment" guideline.[10] We included patients with a positive nasopharyngeal swab testing for SARS-CoV-2 on polymerase chain reaction (PCR) and/or those with clinical symptoms and chest computerized tomography (CT) findings highly suggestive of SARS-COV-2 infection[10] considering the possibility of false-negative results.[11]

The symptoms on presentation, the possible source of the infection, the diagnostic method, and the chest CT findings (normal, solitary lesion, multiple unilateral lesions, or multiple bilateral lesions) were documented. The clinical picture of the patients at presentation was classified based on the national guideline.[10] Asymptomatic patients represented those who were diagnosed during screening in the absence of any symptoms. Patients with symptoms like fever and cough without dyspnea were named to have mild disease whether or not they have abnormal CT findings. Those with the moderate–severe disease had dyspnea necessitating oxygen therapy and bed rest beside other symptoms. Patients who needed follow-up in the ICU due to hypoxia were named as severe patients.

The laboratory findings including serum creatinine, albumin, ferritin, hemoglobin levels, lymphocyte and platelet counts, and CRP levels at presentation, major laboratory abnormalities detected during the follow-up (leucopenia, lymphopenia, anemia, thrombocytopenia, lactate dehydrogenase (LDH), and aspartate transaminase (AST) levels above twice the upper normal limits) were noted. The peak CRP levels observed during the follow-up were also recorded. The medications used for the treatment of COVID-19 were documented.

Outcomes

The need for ICU admission, mechanical ventilation during hospitalization, and the final status of all patients (discharged or death) were recorded as outcome data. Death and/or ICU admission was described as the composite outcome.

Statistical Analysis

Numerical parameters were expressed as median and 25th-75th percentile. Categorical parameters were expressed as numbers and percentages within the group. The chi-square test was used for the comparisons of categorical variables. The Kruskal–Wallis test, with Bonferroni correction for post hoc analyses, was used for non-normally distributed numerical variables. Kaplan–Meier test was used to analyze the composite outcome of the patients during hospitalization, and intergroup comparisons were performed using log-rank test. We formed a multivariate Cox model (stepwise backward LR method) with the parameters that were found to have an effect on the composite outcome in univariate analyses (age, the clinical severity of the disease, and baseline CRP level) to find out the significant independent predictors of composite outcome. Besides, the parameters known to be related to the COVID-19 outcome according to the current literature (gender, presence of DM, HT, cardiac disease, and lymphocyte count) were also included in the model formed because of the limited number of patients included. The final model included also the patient group and SARS-Cov-2 RT-PCR result. Statistical analysis was performed with the IBM SPSS Statistics for Windows (Version 25.0, IBM Corp., Armonk, NY, USA). The statistical significance level was set at $P < .05$.

RESULTS

Baseline Characteristics of the Patients

The whole database included 1301 patients (18 PD patients, 431 HD patients, 310 stage 3–5 CKD patients, and 460 control patients without kidney disease) with COVID-19 infection from 47 centers. Eighteen PD patients were included in our study, together with age- and gender-matched 18 HD and 18 control patients.

The age and gender of the groups were similar (Table 1). Dialysis duration was shorter in the PD group compared to the HD group. Peritoneal dialysis modality was continuous ambulatory in 14 and automated PD in 4 patients. All PD patients were on their previous PD regime during the hospitalization. All HD patients had a thrice weekly dialysis schedule.

Comorbidities and smoking status of the patients are presented in Table 1. The number of patients with DM was higher in the HD group (61.1%) than in the PD (22.2%) and control groups (22.2%). The percentage of patients with HT in the PD group (88.9%) was similar to the HD group (72.2%) and higher than the control group (22.2%). Ischemic heart disease was significantly more prevalent in the HD group (61.1%) than in other groups. Heart failure was

Table 1. Demographic Data, Comorbidities, Medications, Symptoms at Presentation, Possible Source of Infection and Diagnostic Methods, and Laboratory Data at the Time of Hospitalization and During Follow-Up

	PD Group (n = 18)	HD Group (n = 18)	Control Group (n = 18)	*P*
Age (years), median (Q1-Q3)	57 (43-66)	61 (54-67)	62 (41-68)	.401
Duration of dialysis (years), median (Q1-Q3)	3 (1-5)	6 (5-10)	NA	<.001[a]
Gender (male/female), n	7/11	7/11	7/11	1.0
Comorbidities, n (%)				
Diabetes mellitus	4 (22.2)	11 (61.1)	4 (22.2)	.023[a], .008[c]
Hypertension	16 (88.9)	13 (72.2)	4 (22.2)	<.001[b], .008[c]
Ischemic heart disease	6 (33.3)	11 (61.1)	3 (16.7)	.045[a], .019[c]
Heart failure	4 (22.2)	6 (33.3)	0 (0.0)	.02[b], .002[c]
Chronic obstructive pulmonary disease	3 (16.7)	1 (5.6)	2 (11.1)	.133
Chronic liver disease	2 (11.1)	1 (5.6)	0 (0.0)	.195
Malignancy	0 (0.0)	0 (0.0)	1 (5.6)	.226
Smoking status, n (%)				.208
Ex-smoker	2 (11.1)	5 (27.8)	2 (11.1)	
Active smoker	3 (16.7)	0 (0.0)	1 (5.6)	
Never smoked	11 (61.1)	7 (38.9)	10 (55.6)	
Medications, n (%)				
ACE inhibitor	2 (11.1)	0 (0.0)	2 (11.1)	.265
ARB	5 (27.8)	0 (0.0)	1 (5.6)	.018[a]
Calcium channel blocker	8 (44.4)	8 (44.4)	2 (11.1)	.045[b], .007[c]
Beta blocker	6 (33.3)	6 (33.3)	1 (5.6)	.091
Other antihypertensive	2 (11.1)	1 (5.6)	2 (11.1)	.479
Insulin	3 (16.7)	7 (38.9)	2 (11.1)	.005[c]
Oral antidiabetics	0 (0.0)	1 (5.6)	3 (16.7)	.262
Statin	2 (11.1)	1 (5.6)	2 (11.1)	.397
Antiaggregant/anticoagulant	9 (50.0)	8 (44.4)	4 (22.2)	.022[b], .008[c]
Complaints at presentation, n (%)				
Fever	10 (55.6)	11 (61.1)	9 (50.0)	.799
Dyspnea	7 (38.9)	7 (38.9)	5 (27.8)	.723
Cough	9 (50.0)	9 (50.0)	17 (94.4)	.009[b, c]
Possible source of infection, n (%)				.557
Family-house	6 (33.3)	2 (11.1)	6 (33.3)	
Occupational	0 (0.0)	0 (0.0)	1 (5.6)	
Healthy institutions	3 (16.7)	4 (22.2)	2 (11.1)	
Social gatherings	0 (0.0)	3 (16.7)	3 (16.7)	
Unknown	8 (44.4)	9 (50.0)	6 (33.3)	
Laboratory tests, median (Q1-Q3)				
Creatinine (mg/dL)	6.90 (5.8-8.0)	8.06 (5.4-9.4)	0.79 (0.7-0.9)	<.001[b, c]
Albumin (g/dL)	3.05 (2.8-3.4)	3.76 (3.4-4.2)	4.0 (3.6-4.3)	.011[a], .014[b]

(*Continued*)

	PD Group (n = 18)	HD Group (n = 18)	Control Group (n = 18)	*P*
Ferritin (ng/mL)	553 (357-1297)	1099 (806-1535)	178 (94-460)	.009[b], <.01[c]
Hemoglobin (g/dL)	9.6 (8.0-10.4)	10.8 (9.6-11.6)	12.6 (11.2-14.0)	<.001[b], .013[c]
Lymphocyte (/mm^3)	810 (600-1360)	890 (500-1330)	1275 (196-1950)	.41
Platelet count (×1000/mm^3)	202 (151-265)	169 (121-264)	215 (177-293)	.44
Laboratory abnormalities during hospitalization, n (%)				
Leucopenia	7 (38.9)	2 (11.1)	4 (22.2)	.092
Lymphopenia	11 (61.1)	14 (77.8)	6 (33.3)	.022[c]
Anemia	9 (50.0)	9 (50.0)	4 (22.2)	.164
Thrombocytopenia	5 (27.8)	7 (38.9)	3 (16.7)	.213
LDH increase (×2 of upper limit)	4 (22.2)	4 (22.2)	4 (22.2)	.697
AST increase (×2 of upper limit)	2 (11.1)	2 (11.1)	3 (16.7)	.359
Highest CRP level (× of upper limit)				.156
Normal range	0 (0.0)	1 (5.6)	4 (22.2)	
×1-5	3 (16.7)	6 (33.3)	5 (27.8)	
×5-10	4 (22.2)	2 (11.1)	1 (5.6)	
×10-20	3 (16.7)	3 (16.7)	4 (22.2)	
>×20	8 (44.4)	4 (22.2)	4 (22.2)	
Computerized tomography findings, n (%)				.464
Normal	0 (0.0)	0 (0.0)	1 (5.6)	
Solitary lesion	1 (5.6)	1 (5.6)	0 (0.0)	
Unilateral multiple lesions	1 (5.6)	3 (16.7)	2 (11.1)	
Bilateral multiple lesions	13 (72.2)	13 (72.2)	15 (83.30)	
Clinical presentation, *n* (%)				.095
Asymptomatic	0 (0.0)	1 (5.6)	0 (0.0)	
Mild	11 (61.1)	7 (38.9)	15 (83.3)	
Moderate–severe	6 (33.3)	10 (55.6)	3 (16.7)	
Severe	1 (5.6)	0 (0.0)	0 (0.0)	

ACE, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; AST, aspartate transaminase; HD, hemodialysis; LDH, lactate dehydrogenase; NA, not applicable; PD, peritoneal dialysis; RT-PCR, reverse transcription-polymerase chain reaction. [a]Between PD and HD group; [b]Between PD and control group; [c]Between HD and control group.

more frequent in the PD (22.2%) and HD (33.3%) groups than in the control group. The frequency of other comorbidities and smoking status was similar in the 3 groups.

The most common primary kidney disease was hypertensive nephrosclerosis in the PD group and diabetic nephropathy in the HD group. The medications that patients were on at the time of admission were presented in Table 1. Angiotensin receptor blockers were more frequently used by PD patients. Calcium channel blockers, antiaggregant and anticoagulant drugs were more frequently used in the PD and HD groups compared to the control group. The use of insulin was more frequent among patients in the HD group than in the control group due to the high prevalence of DM in the HD group.

Clinical Presentation, Diagnosis, and Tests

The symptoms at presentation, the possible source of infection, and diagnostic methods were also summarized in Table 1. Fever and dyspnea were documented in 55.6% and 38.9% of PD patients, respectively. Cough was present in half of the patients in the PD group that was similar to the HD group and lower than the control group. The possible route of infection was family members in 6 and health institutions in 3 patients and was unknown in others in the PD group. The groups were similar

regarding the route of infection. Diagnostic methods of the COVID-19 were similar in all groups. Polymerase chain reaction positivity was detected in 8 patients (44.4%) in the PD group, 9 patients (50%) in the HD and control groups.

The laboratory data at the time of hospitalization and during follow-up were presented in Table 1. Albumin level was lower in the PD group compared to the other two groups. Hemoglobin level in the PD group was similar to the HD group and lower than the control group. Ferritin levels of PD and HD groups were higher than the control group. Other laboratory parameters were similar. Leucopenia, anemia, thrombocytopenia, increased LDH and AST levels were similar between the groups except for the significant lymphopenia in the control group compared to the HD group. The highest CRP levels were observed in the PD group during the follow-up, but it was not statistically significant.

All patients except one in the PD group had a chest CT. There were no differences in CT findings among the groups (Table 1). Mild clinical presentation was more common in the control group, while the moderate–severe clinical presentation was more common in PD and HD groups (Table 1).

The medications used for the treatment of COVID-19 are given in Table 2. The three groups were similar regarding the medications used. Most of the patients were given oseltamivir, macrolide antibiotics, hydroxychloroquine, favipiravir, glucocorticoids, and/or tocilizumab. None of the patients used lopinavir-ritonavir, canakinumab, or anakinra. Convalescent plasma and/or immunoadsorption were not used for any patient.

Table 2. The Medication Used for the Treatment of COVID-19 Infection and the Outcome Data of the Patients

	PD Group (n = 18)	HD Group (n = 18)	Control Group (n = 18)	*P*
Medications, n (%)				
Oseltamivir	10 (55.6)	11 (61.1)	13 (72.2)	.198
Macrolide antibiotic	13 (72.2)	13 (72.2)	18 (100.0)	.189
Hydroxychloroquine	17 (94.4)	17 (94.4)	18 (100.0)	.595
Favipiravir	1 (5.6)	6 (33.3)	4 (22.2)	.237
Glucocorticoid	2 (11.1)	1 (5.6)	0 (0.0)	.707
Tocilizumab	0 (0.0)	2 (11.1)	0 (0.0)	.380
Outcomes, n (%)				
ICU admission	5 (27.8)	3 (16.7)	2 (11.1)	.424
Mechanical ventilation	4 (22.2)	2 (11.1)	2 (11.1)	.504
Mortality*				.422
Death	4 (22.2)	3 (16.7)	1 (5.6)	
Discharged	14 (77.8)	15 (83.3)	16 (88.9)	

*One patient in the control group was still in ICU. HD, hemodialysis; ICU, intensive care unit; PD, peritoneal dialysis.

Survival

The median follow-up was 7 (5-11) days in the PD group, 10 (5-14) days in the HD group, and 7 (6-13) days in the control group. Intensive care unit admission, mechanical ventilation rates, and in-hospital mortality data were presented in Table 2. Four (22.2%) patients in the PD group died, while 3 (16.7%) patients in the HD group and 1 (5.6%) patient in the control group died (log-rank analyses: PD vs control: $P = .72$, PD vs. HD: $P = .89$, HD vs. control: $P = .43$). Due to the low number of patients and deaths in the groups, we combined death and ICU admission under the name of "composite outcome." Table 3 shows these composite outcome results. A total of 11 (20.3%) patients had composite outcome (PD group: 6 patients (33.3%), HD group: 3 patients (16.7%), control group: 2 patients (11.1%)) (Table 3). Age, clinically severe disease at presentation, and CRP level at presentation 10 times or above the upper limit of normal were the parameters found to be significantly different between patients grouped according to whether they reached the composite outcome or not (Table 3). In the survival analysis related to this composite outcome, the median time to composite outcome of PD group was significantly shorter than that of the control group (16 days vs 29 days, log rank $P = .022$). There was no significant difference between the PD and HD groups and between the HD and control groups regarding composite outcome (Figure 1). The risk of reaching composite outcome was significantly higher in the PD group compared to the control group (hazard ratio (HR): 14.3 (95% CI, 1.0-205), $P = .050$) whereas it was similar in the HD and control groups (HR: 3.9 (95% CI, 0.28-54), $P = .30$). In multivariate Cox regression analysis, age (HR: 1.19 (95% CI, 1.050-1.35)) and CRP level higher than 10-fold the upper limit (HR: 22.5 (95% CI, 1.5-330), $P = .023$) were related to the risk of composite outcome. The RT-PCR test parameter did not show a significant effect on the results in multivariate analysis.

DISCUSSION

In this study, which was composed of age- and sex-matched patient groups, patients in the dialysis (PD and HD) group were found to have a higher mortality rate compared to paired non-uremic control group patients (7/36 (19.5%)) and 1/17 (5.6%), respectively). Moreover, mortality in the PD group was higher than the HD group (22.2% and 16.7%, respectively). Moreover in unadjusted and adjusted composite outcome, analyses revealed that PD patients had a worse outcome than the control group. However, there was no statistical difference between dialysis groups, probably due to the low number of cases. It was also noted that dialysis patients presented with more severe COVID-19 clinical picture had worse laboratory data compared to those without kidney disease.

As far as we know, there is no published study comparing PD patients with HD and non-uremic control patients. Many studies

Table 3. The Data of the Patient According to the Composite Outcome Defined as Death and/or ICU Admission

	Composite Outcome	
	No (n = 43)	Yes (n = 11)
Patient group, n (%)		
Control	16 (37.2)	2 (18.2)
HD	15 (34.9)	3 (27.3)
PD	12 (27.9)	6 (54.5)
*Age (years), median (IQR)	57 (41-67)	66 (57-67)
Gender, n (%)		
Men	15 (34.9)	6 (54.5)
Women	28 (84.8)	5 (15.2)
RRT duration (year), median (IQR)	5 (2-6)	6 (2-7)
Diabetes mellitus, n (%)	13 (30.2)	6 (54.5)
Hypertension, n (%)	24 (55.8)	9 (81.8)
Cardiac disease, n (%)	15 (34.9)	6 (54.5)
SARS-COV-2 RT-PCR positivity, n (%)	18 (41.9)	8 (72.7)
Clinical severity of the disease, n (%)*		
Mild–moderate	30 (69.8)	4 (36.4)
Severe–critical	13 (30.2)	7 (63.6)
Serum creatinine (mg/dL), median (IQR)	5.4 (1-8)	6.5 (5-8)
Albumin (g/dL), median (IQR)	3.74 (3-4)	3.39 (3-4)
Ferritin (ng/mL), median (IQR)	614.9 (262-1279)	409.5 (280-1250)
CRP level (>×2 upper limit), n (%)*		
<×10	28 (65.1)	3 (27.3)
>×10	15 (34.9)	8 (72.7)
Haemoglobin (g/dL), median (IQR)	10.8 (10-12)	11.5 (10-14)
Lymphocyte count (/mm^3), median (IQR)	1000 (200-1460)	1330 (600-1500)
Platelet count (×1000/mm^3), median (IQR)	202 (161-279)	177 (141-224)
ICU admission, n (%)	0 (0)	10 (90.9)
Mechanical ventilation, n (%)**		
Yes	0 (0)	1 (9.1)
No	0 (0)	8 (72.7)
Unknown	0 (0)	1 (9.1)

*$P < .05$; **One patient had missing value. CRP, C-reactive protein; HD, hemodialysis; ICU, intensive care unit; IQR, interquartile range; PD, peritoneal dialysis; RRT, renal replacement therapy; RT-PCR, reverse transcription-polymerase chain reaction.

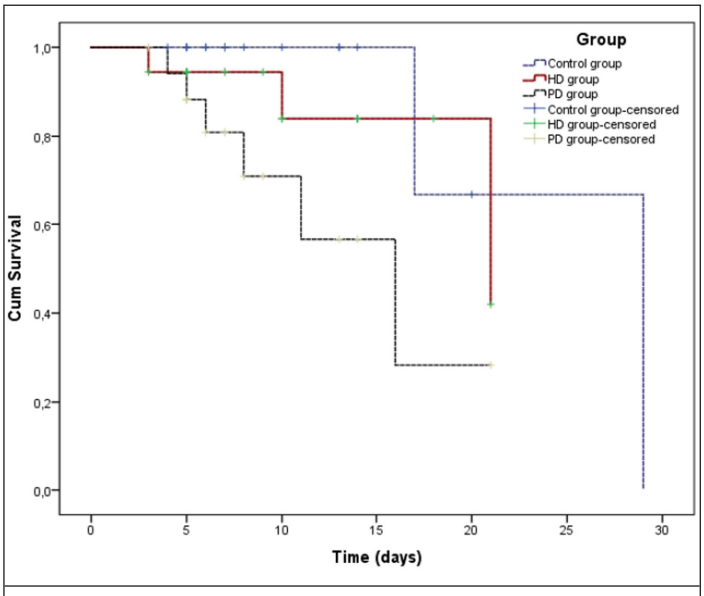

Figure 1. Kaplan–Meier plots of the patient according to the groups. The patient groups were compared in terms of the composite outcome. The median duration for the composite outcome was 29 days in the control group, 21 days in the HD group, and 16 days in the PD group (log-rank P values: control vs HD: .43; control group vs PD group: .22, HD group vs. PD group: .17). HD, hemodialysis; PD, peritoneal dialysis.

reported high mortality in dialysis patients with COVID-19, but the vast majority of these studies included only HD patients. In one study with few PD patients, no comparison was made with the control group.[4,12]

The higher mortality rate in CKD and dialysis patients during the pandemic is not a surprising finding as CKD patients have an unfavorable state regarding their immune status. Alterations in both innate and adaptive immunity have been described in CKD patients, which is believed to be related to the increased risk of infection.[13] Besides, COVID-19 mortality is higher in those with comorbidities.[1,14-16] In our study, the frequency of DM, HT, and cardiovascular disease was higher than the control group in the dialysis patient groups. The relation between the presence of DM and mortality of COVID-19 infection has been reported previously. An example is the study carried on by Guan et al.[13] They analyzed 1590 laboratory-confirmed hospitalized cases with COVID-19 infection. In total, 23.8% of diabetic patients reached the composite end-point compared to 6.8% of patients without DM. Although DM was more prevalent in HD patients compared to PD patients and the control group in our study, this was not found to be correlated with mortality. Similarly, there were intergroup differences regarding the prevalence of HT, IHD, and HF. But again, these factors were found to be not related with the outcome in cox regression analysis. This may be related with the low number of patients.

In the study from the United States by Valeri et al.,[4] including 57 consecutive HD and 2 PD patients, 18 patients (31%) died. Similar to our study, all but 1 patient had HT, 69% had DM, 46%

had coronary artery disease. The patients who died had worse initial and peak lab values. Another paper from Italy reported 21 HD patients with COVID-19 infection, of whom 5 patients died.[17] In a study from Wuhan, China, 154 patients were reported to be COVID-19 positive among 7154 patients undergoing HD.[15] The incidence of COVID-19 in patients undergoing HD was estimated to be 2.15%. In the final analysis, 47 patients were alive and discharged from the hospital, 43 patients were alive but remained in hospital, and 41 patients were deceased. There were 101 mild–moderate patients and 30 severe–critical patients. Cardiovascular disease and the use of renin-angiotensin-aldosteron system (RAAS) inhibitors were more frequent in patients with severe–critical diseases. In our study, HT was highest in the PD group, and calcium channel blockers were the most frequently (44.4%) used antihypertensive drug in these patients.

A recent report from New York shared data of 11 PD patients with COVID-19 infection, 3 of whom required mechanical ventilation, 2 died, 9 were discharged home, and 1 was readmitted for worsening pneumonia.[17] The European Renal Association–European Dialysis and Transplant Association (ERA-EDTA) Registry data on patients receiving kidney replacement therapy in Europe from February 1, 2020, to April 30, 2020, has been reported recently.[18] Twenty-eight days after COVID-19 diagnosis, 628 of 3160 HD patients and 30 of 125 patients on PD had died. The 28-day probability of death was 25.0% in those treated with PD and 23.8% in HD patients. Older age, male gender, HT, DM, and glomerulonephritis were found to be related to increased risk of death in the whole dialysis population. In a single-center study from Madrid, Spain, involving 57 PD and 22 home HD patients between March 10 and May 15, 2020, 12 patients were diagnosed with COVID-19 (9 PD; 3 home HD).[18] There was no statistically significant difference in clinical features between COVID-19 patients and the rest of the unit. All patients except 1 were hospitalized. In total, 10 patients (83%) were discharged and 2 patients (17%) died. The deceased were older than the survivors.

A more recent analysis from Turkey reported the mortality rate of maintenance HD patients hospitalized for COVID-19 infection as 16.3% (93 of 567 patients), and 67.9% of the patients needed mechanical ventilation in this study population.[19]

Ozturk et al. analyzed the outcome of 1210 patients with CKD, HD patients, and renal transplant patients. They reported the rates of admission to ICU and mortality of the groups as 28.4%, 16.2%, and 11.1%, respectively. Adjusted mortality in CKD and HD groups was significantly higher than the control group.[20]

With the accumulation of data with HD patients, guidelines have been revised for the care of HD patients regarding their daily life, transfer to HD unit, treatment in the unit, and so on. Coronavirus disease-19 experience with PD patients is very limited in the literature. Peritoneal dialysis regimen itself can have a dramatic impact on a patients' life. Doing several exchanges per day, hooking up to a cycling machine at night, following detailed instructions on how to avoid infections can have a major effect on the patient, caregiver, and family.[21] However, this home therapy was an advantage for our patients at times of crisis, such as mass disasters like earthquakes, hurricanes, or ongoing conflicts.[22] Coronavirus disease-19 pandemic may be considered as a situation similar to these. Moreover, PD patients have some hypothetical advantage of having a home therapy that may continue uninterrupted. Remote monitoring of PD patients also gives the physician the opportunity to monitor patients' symptoms, dialytic issues while limiting hospital visits during the pandemic.[7]

In Turkey, the number of prevalent PD and HD patients was 3192 and 60 643, respectively, in 2018, according to the Registry Report of the Turkish Society of Nephrology.[16,23] Hence, the PD patients constitute 5.0% of the dialysis population. In our database, 18 PD patients consisted of 4.0% of the entire dialysis group (449 patients), actually most probably reflecting the national PD patients more accurately than the HD patient group. Therefore, based on these data, it can be said that PD patients in our country have less COVID-19 infection than HD patients.

In addition, the clinical and laboratory findings of our dialysis group patients at presentation were worse than the control group, but their images on chest CT were generally not different from the control group. The chest CT scans in HD group, in the study of Xiong et al.,[15] from Wuhan, China, were also similar to those in the general population. These suggest that in the COVID-19 outbreak, uremic patients may have less reflection of the severe inflammatory response to chest radiology.

The COVID-19 treatment administered to our patients included hydroxychloroquine, macrolide, and oseltamivir in accordance with the relevant version of the COVID-19 treatment recommendations of the Turkish Ministry of Health. These practices were not different between groups. Other treatments were rarely used for our study population to conclude any suggestions.

Peritoneal dialysis patients have been relatively less affected during the pandemic, so the number of PD patients infected with COVID-19 is limited. The low number of events in these patients made the significance of statistical analysis difficult. Also, the comparative analysis of these PD cases with HD and control groups revealed statistical difficulties. To overcome this limitation and to be able to make multivariate analysis, mortality and ICU admission were together defined as "composite outcome." However, as we have presented in the results of the Cox regression analysis, the HR values were quite high and the CI values were quite wide. These values are important in terms of showing the existence of a relationship rather than the quantity of the relationship.

Another concern in the study was the inclusion of patients who did not have a positive RT-PCR. We included the RT-PCR negative patients in the study only if their clinical findings and CT findings strongly suggested COVID-19. Serological testing may not be sufficient in the diagnosis of COVID-19 infection. In a recent report supporting this fact from London, 356 patients have been screened for COVID-19 infection. Of the 42 patients who were tested negative for PCR, 8 patients had positive antibody testing. Among 235 patients without symptoms before, 44 patients were positive for antibody. This is a valuable finding in terms of reflecting the real situation.[22] Our study is another proof for the insufficiency of PCR testing alone in COVID-19 diagnosis in dialysis patient. In addition, the RT-PCR test parameter did not show a significant effect on the results in multivariate analysis. The ERA-EDTA Registry also included patients with COVID-19 infection diagnosed either clinically or proved by testing, although the authors did not report the ratio of test negative patients with clinical findings consistent with COVID-19 infection.[18]

This study has several limitations, such as having a relatively small sample size and retrospective nature. Additionally, we were unable to determine the true total number of dialysis patients affected with COVID-19, including those who were asymptomatic or only mildly symptomatic and never tested due to the limited availability of testing for patients with mild cases at that time.

CONCLUSIONS

Combined in-hospital mortality and/or ICU admission of PD patients with COVID-19 is significantly higher than the control patients. This finding increases the need for careful surveillance of PD patients for infection signs and prompts treatment of COVID-19. Due to the relatively small sample size, we could not evaluate whether PD patients were at increased risk of in-hospital outcomes compared to HD patients in this study.

Ethics Committee Approval: The ethics committe was received from the Ethics Committee of Health Sciences University, Istanbul Haseki Training and Research Hospital (No: 41-2020).

Informed Consent: Informed consent was not obtained for each patient due to the conditions of pandemic.

Peer Review: Externally peer-reviewed.

Author Contributions: Concept - R.K., S.Ö., M.G., K.T., M.A., S.S., A.Y., H.Z.T., A.R.O.; Design - R.K., S.Ö., M.G., K.T., M.A., K.A.; Supervision - R.K., S.Ö., M.A., K.A.; Resource - S.Ö., M.A., A.Y., K.A.; Materials - S.Ö., M.G., K.T., M.A., A.O., E.A., S.G.B., E.S., M.B.O., D.G.G., M.D.A., Y.A., E.O., S.K., E.A., H.Y., M.R.A., B.T., A.R.O., H.Z.T., S.S., A.Y., K.A.; Data Collection and/or Processing - S.Ö., M.G., K.T., M.A.; Analysis and/or Interpretation - R.K., S.Ö., K.T., M.A., K.A., M.G.; Literature Search - R.K., S.Ö., M.G.; Writing - M.G., S.Ö., R.K.; Critical Reviews - R.K., S.Ö.

Acknowledgments: The original database was designed and developed by the Turkish Society of Nephrology.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. *Kidney Int*. 2020;97(5):829-838. [CrossRef]
2. Naicker S, Yang CW, Hwang SJ, et al. The novel coronavirus 2019 epidemic and kidneys. *Kidney Int*. 2020;97(5):824-828. [CrossRef]
3. Anders HJ, Bruchfeld A, Fernandez Juarez GM, et al. Recommendations for the management of patients with immune-mediated kidney disease during the severe acute respiratory syndrome coronavirus 2 pandemic. *Nephrol Dial Transplant*. 2020;35(6):920-925. [CrossRef]
4. Valeri AM, Robbins-Juarez SY, Stevens JS, et al. Presentation and outcomes of patients with ESKD and COVID-19. *J Am Soc Nephrol*. 2020;31(7):1409-1415. [CrossRef]
5. Arentz M, Yim E, Klaff L, et al. Characteristics and outcomes of 21 critically ill patients with COVID-19 in Washington State. *JAMA*. 2020;323(16):1612-1614. [CrossRef]
6. Meijers B, Messa P, Ronco C. Safeguarding the maintenance hemodialysis patient population during the coronavirus disease 2019 pandemic. *Blood Purif*. 2020;49(3):259-264. [CrossRef]
7. En Khoo BZ, See YP, Kam Koh TJ, Yeo SC. Coronavirus Disease 2019 (COVID-19) and dialysis: the experience in Singapore. *Kidney Med*. 2020;2(4):381-384. [CrossRef]
8. El Shamy O, Tran H, Sharma S, et al. Telenephrology with remote peritoneal dialysis monitoring during coronavirus disease 2019. *Am J Nephrol*. 2020;51(6):480-482. [CrossRef]
9. Jain AK, Blake P, Cordy P, Garg AX. Global trends in rates of peritoneal dialysis. *J Am Soc Nephrol*. 2012;23(3):533-544. [CrossRef]
10. Republic of Turkey Ministry of Health. *Guidance to COVID-19 (SARS Cov2 Infection) (Scientific Board Study)*. 2020. Turkey: Directorate General of Public Health. (Accessed April 18, 2020). https://covid19.saglik.gov.tr/Eklenti/40719/0/covid-19rehberieriskinhastayonetimivetedavipdf.pdf.
11. Wang W, Xu Y, Gao R, et al. Detection of SARS-CoV-2 in different types of clinical specimens. *JAMA*. 2020;323(18):1843-1844. [CrossRef]
12. Jiang HJ, Tang H, Xiong F, et al. COVID-19 in peritoneal dialysis patients. *Clin J Am Soc Nephrol*. 2020;16(1):121-123. [CrossRef]
13. Kato S, Chmielewski M, Honda H, et al. Aspects of immune dysfunction in end-stage renal disease. *Clin J Am Soc Nephrol*. 2008;3(5):1526-1533. [CrossRef]
14. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. *Eur Respir J*. 2020;55(5). [CrossRef]
15. Xiong F, Tang H, Liu L, et al. Clinical characteristics of and medical interventions for COVID-19 in hemodialysis patients in Wuhan, China. *J Am Soc Nephrol*. 2020;31(7):1387-1397. [CrossRef]
16. Kulkarni S, Jenner BL, Wilkinson I. COVID-19 and hypertension. *J Renin Angiotensin Aldosterone Syst*. 2020;21(2):1470320320927851. [CrossRef]
17. Alberici F, Delbarba E, Manenti C, et al. Management of patients on dialysis and with kidney transplant during SARS-COV-2

(COVID-19) pandemic in Brescia, Italy. *Kidney Int Rep*. 2020;5(5):580-585. [CrossRef]
18. Maldonado M, Ossorio M, Del Peso G, et al. COVID-19 incidence and outcomes in a home dialysis unit in Madrid (Spain) at the height of the pandemic. *Nefrologia*. 2021;41(3):329-336. [CrossRef]
19. Turgutalp K, Ozturk S, Arici M, et al. Determinants of mortality in a large group of hemodialysis patients hospitalized for COVID-19. *BMC Nephrol*. 2021;22(1):29. [CrossRef].
20. Ozturk S, Turgutalp K, Arici M, et al. Mortality analysis of COVID-19 infection in chronic kidney disease, haemodialysis and renal transplant patients compared with patients without kidney disease: a nationwide analysis from Turkey. *Nephrol Dial Transplant*. 2020;35(12):2083-2095. [CrossRef].
21. Finkelstein FO, Foo MWY. Health-related quality of life and adequacy of dialysis for the individual maintained on peritoneal dialysis. *Perit Dial Int*. 2020;40(3):270-273. [CrossRef]
22. Gorbatkin C, Finkelstein FO, Kazancioglu RT. Peritoneal dialysis during active war. *Semin Nephrol*. 2020;40(4):375-385. (doi: [CrossRef])
23. Turkish Society of Nephrology. *Registry of the Nephrology, Dialysis and Transplantation in Turkey Registry 2018*. 2018. Available at: http://www.nefroloji.org.tr/folders/file/REGISTRY_2018.pdf.