



Post-COVID-19 outcomes of non-dialysis dependent chronic kidney disease patients: a national, multicenter, controlled study

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Abstract

Purpose Coronavirus disease 2019 (COVID-19) has a higher mortality in the presence of chronic kidney disease (CKD). However, there has not been much research in the literature concerning the outcomes of CKD patients in the post-COVID-19 period. We aimed to investigate the outcomes of CKD patients not receiving renal replacement therapy.

Methods In this multicenter observational study, we included CKD patients with a GFR < 60 ml/min/1.73 m² who survived after confirmed COVID-19. Patients with CKD whose kidney disease was due to diabetic nephropathy, polycystic kidney disease and glomerulonephritis were not included in this study. CKD patients with similar characteristics, who did not have COVID-19 were included as the control group.

Results There were 173 patients in the COVID-19 group and 207 patients in the control group. Most patients (72.8%) were treated as inpatient in the COVID-19 group (intensive care unit hospitalization: 16.7%, acute kidney injury: 54.8%, needing dialysis: 7.9%). While there was no significant difference between the baseline creatinine values of the COVID-19 group and the control group (1.86 and 1.9, $p=0.978$, respectively), on the 1st month, creatinine values were significantly higher in the COVID-19 group (2.09 and 1.8, respectively, $p=0.028$). Respiratory system symptoms were more common in COVID-19 patients compared to the control group in the 1st month and 3rd month follow-ups ($p<0.001$). Mortality at 3 months after the diagnosis of COVID-19 was significantly higher in the COVID-19 group than in the control group (respectively; 5.2% and 1.4%, $p:0.037$). Similarly, the rate of patients requiring dialysis for COVID-19 was significantly higher than the control group (respectively; 8.1% and 3.4%, $p: 0.045$).

Conclusions In CKD patients, COVID-19 was associated with increased mortality, as well as more deterioration in kidney function and higher need for dialysis in the post-COVID-19 period. These patients also had higher rate of ongoing respiratory symptoms after COVID-19.

Keywords COVID-19 · CKD · Outcomes

Introduction

Coronavirus disease 2019 (COVID-19) not only affects many systems but is also associated with worse outcomes, especially in patients with comorbidities. Studies conducted during the pandemic period [1–3] have found that

COVID-19 was associated with increased mortality in those with chronic kidney disease (CKD). In addition, it had been observed that COVID-19 caused an increased risk of developing acute kidney injury (AKI), and mortality was significantly increased, especially in the patients with stage 3 AKI [4]. Angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine-type 2 (TMPRSS2) receptors, which play an important role in the entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into the cell, have high expression in the kidneys [5]. Therefore, the

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kidneys are one of the primary target organs of SARS-CoV-2 after the lungs [6]. Increased expression of ACE2 was found to be associated with a higher risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) activity. ACE2 gene polymorphisms may predispose to SARS-CoV-2. The presence of the ACE2 gene on the X chromosome may explain why 66–75% of severe cases are male, and negative outcomes are more common in males including a higher mortality rate. Meanwhile, TMPRSS2 is expressed higher in males, associated with higher androgen levels. In this case, it may be associated with a more severe course of the disease in men [7–9].

In some studies on COVID-19 patients, new-onset proteinuria and high serum creatinine levels were observed in addition to collapsing glomerulopathy (as a result of direct viral effect on podocytes and/or damage due to cytokines) and acute tubular damage findings in the renal biopsy samples. Viral particles were detected in renal tubular cells and podocytes by electron microscopy. These pathological results indicate that SARS-CoV-2 infects [10]. Although there are many studies on COVID-19 and kidney diseases, there are not many studies examining the outcomes of CKD patients with COVID-19 who are not receiving renal replacement therapy (RRT). In this study, we investigated the late-term findings and outcomes of CKD patients who had a COVID-19 infection in Turkey and compared this with a control group of patients with CKD who did not have COVID-19.

Methods

This is a retrospective study where we followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement [11]. Ethics Committee of Health Sciences University Haseki Training and Research Hospital approved the study (number: 12–2021).

Population and setting

This multicenter, retrospective, observational study was supported and announced by the Turkish Society of Nephrology. CKD patients who had at least 3 months of follow-up and did not undergo RRT were included in the study from the national electronic database that was created to follow up the data of all CKD patients in the post-COVID period. Patients with CKD whose kidney disease was due to diabetic nephropathy, polycystic kidney disease and glomerulonephritis were not included in this study. As these patients' demographics, pathophysiology of kidney disease, mechanisms and treatments are different, we created separate data sets for these patients in our registry system. Patients under the age of 18, patients with negative nasopharyngeal

SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR), and patients without outcome data were excluded. The diagnosis and treatment of COVID-19 patients were managed with the guidelines recommended by the Ministry of Health of the Republic of Turkey. At each center, after a patient with a diagnosis of COVID-19 was selected for the study group, the first non-COVID-19 CKD patient with similar kidney disease was selected to the control group at a follow-up visit. Patients with a known diagnosis of CKD and estimated glomerular filtration rates (eGFRs) < 60 mL/min/1.73 m² represented moderate-to-severe CKD. The patient and control groups were selected among patients with at least 3 months of follow-up.

Measurements and definitions

Demographic data (age, gender, smoking, etc.), clinical (CKD etiology, CKD duration, comorbidities, drugs) and laboratory data (creatinine, GFR) of the patient and control groups were recorded in the database. Laboratory and clinical data at the last visit before COVID-19 and at the time of COVID-19 diagnosis and at the 1st and 3rd months after diagnosis were recorded. Similarly, the clinical and laboratory data of the control group at the last visit and the data of the 1st and 3rd months were recorded. Diagnosis dates of COVID-19 patients, complaints of admission, treatments that were given for COVID-19, place of treatment (home, hospital, intensive care), computerized tomography (CT) findings, the outcome of the disease were recorded. In accordance with the national COVID-19 guidelines, the clinical picture at the time of admission was classified as (asymptomatic, mild, moderate-severe and serious-vital disease). Asymptomatic patients were diagnosed during screening in the absence of any symptoms. Patients without symptoms such as fever, cough, and dyspnea were classified as mild disease patients with or without abnormal CT findings. Those with moderate-to-severe disease had dyspnea requiring oxygen therapy and bed rest, among other symptoms. Patients with hypoxia (oxygen saturation below 90% despite oxygen support) or hemodynamic disorders requiring intensive care unit (ICU) were classified as severe vital disease patients. AKI diagnosis and staging were done based on the KDIGO guidelines [12]. Patients who needed dialysis were recorded. At the 1st and 3rd months, the creatinine and eGFR values of the patients were recorded.

Follow-up and outcome

For the inpatients, length of stay, need for ICU and the results were recorded. The primary outcome was the mortality of the patient and control groups in the 3rd month. In addition, the need for RRT during this period, rehospitalization for any reason, continued respiratory symptoms,

need for home oxygen therapy, lower respiratory tract infection, urinary system infection, and emergence of venous or arterial thromboembolic event were also recorded. Serum creatinine, eGFR and proteinuria levels at 3 months were compared.

Statistical analysis

IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA) was used for statistical analysis. We decided the normality of variables using visual methods (histograms and probability plots) and Kolmogorov–Smirnov tests. Categorical variables were presented as numbers and percentages, numeric variables were presented as median and interquartile ranges (25–75%) in descriptive statistics. The comparisons of categorical variables were done using chi-square test. We used the independent *t*-test or Mann–Whitney *U* test as appropriate in the comparison of numerical variables. We used the analysis of variance (ANOVA) test for numerical variables with normal distribution and the Kruskal–Wallis test for numerical variables that were not normally distributed, in the multiple group comparisons of numerical variables. $p < 0.05$ was accepted as the level of significance.

Results

Demographic and baseline characteristics

A total of 380 of 420 submitted patients from 22 centers in Turkey participated in the study. Out of 213 patients in the COVID-19 group, 30 patients with PCR negative and 10 patients without PCR results were excluded, leaving 173 patients. There were 207 patients in the control group. The most common comorbidities in COVID-19 and control groups were hypertension and diabetes. There was no significant difference in creatinine and eGFR values between baseline findings of COVID-19 and control group. However, a significant difference was found between age, CKD duration, heart failure, cerebrovascular disease and sodium levels (Table 1). In addition, the baseline CRP level was significantly higher in COVID-19 group.

The data regarding COVID-19

For the patients in the COVID-19 group, hospital admission symptoms, clinical tables, medications, hospitalization and intensive care unit admission, AKI development and development of RRT need are listed in Table 2. While the most common symptoms were cough and dyspnea, the most common clinical presentation was found to be moderate-to-severe disease. The number of inpatients was 126 (72.8%).

Among the inpatients, the rate of ICU admission was 16.7%, the rate of AKI development was 54.8%, and the rate of patients who needed dialysis was 7.9%. The need for dialysis in patients who developed AKI was 14.5%. The most commonly used drugs were favipiravir and corticosteroids (Table 2, Fig. 1).

Outcomes at 1st month and 3rd months

Mortality in the first month after the diagnosis of COVID-19 was higher in the COVID-19 group than in the control group with similar basal renal function, and the difference was not statistically significant [respectively; 5/173 (2.9%) and 1/207 (0.5%), $p = 0.096$] (Fig. 2). Mortality in the first three months was significantly higher in the COVID-19 group [respectively; 9/173 (5.2%) and 3/207 (1.4%), $p = 0.037$]. Likewise, the rate of patients who initiated dialysis in the first month was higher in the COVID-19 group than in the control group, and the difference was close to the statistical significance limit [respectively; 13/173 (7.5%) and 7/207 (3.4%), $p = 0.072$]. At follow-ups between 1 and 3 months, COVID-19 group patients who had initiated dialysis were significantly higher than the control group patients [14/173 (8.1%) and 7/207 (3.4%), $p = 0.045$, respectively]. While there was no significant difference between baseline creatinine values in the COVID-19 group and control group [1.86 (1.48–2.87) and 1.9 (1.47–2.78), $p = 0.978$, respectively] (Table 1), at first-month follow-up the difference in the creatinine values of the COVID-19 group and control group was statistically significant [1.8 (1.47–2.51) and 2.09 (1.6–2.91), respectively, $p = 0.028$]. No significant difference was observed in creatinine values at the third-month follow-up [1.91 (1.51–2.66) and 2.15 (1.6–3.59), respectively], $p = 0.268$. Respiratory system symptoms were significantly higher in patients who had COVID-19 in the first month and in the first three months compared to the control group (Table 3, Fig. 2). Patients who died in the COVID-19 group were significantly older than survivors (respectively 72.7 ± 6.6 , 66.7 ± 12.8 ; $p = 0.029$).

Discussion

This multicenter national study presented the late outcomes of CKD patients with COVID-19 and also compared these patients with CKD patients without COVID-19. The primary results in this study were a significantly higher third-month mortality, RRT initiation rate, and ongoing respiratory symptoms in patients with COVID-19.

It has been shown in previous studies that COVID-19 disease shows higher mortality in CKD patients compared to non-CKD patients [1, 2, 13]. In our study, the first-month mortality was 2.9% and the third-month mortality was 5.2%.

Table 1 Baseline data of patient and control groups

	COVID-19 group N: 173	Control group N: 207	<i>p</i>
Sex (female/male), <i>n</i> (%)	81/92	96/111	0.096
Age (year), median (IQR)	69 (59–77)	65 (53–73)	0.004
CKD duration (year), median (IQR)	5 (3–8)	5 (3–6)	0.044
BMI (kg/m ²), median (IQR), median (IQR)	26.12 (24.49–29.3)	25.66 (24.01–27.72)	0.096
Systolic blood pressure (mmHg), median (IQR)	135 (123.5–146.5)	140 (130–150)	0.053
Diastolic blood pressure (mmHg), median (IQR)	80 (70–86)	80 (70–90)	0.672
Concomitant diseases, <i>n</i> (%)			
Diabetes mellitus	37/169 (21.9)	60/201 (29.9)	0.083
Hypertension	156/172 (90.7)	175/205 (85.4)	0.115
Ischemic heart disease	61/163 (37.4)	69/180 (20.8)	0.862
Chronic obstructive pulmonary disease	30/166 (18.1)	26/172(15.1)	0.459
Cerebrovascular disease	18/162 (11.1)	4/180 (2.2)	0.001
Heart failure	41/154 (26.6)	26/172 (15.1)	0.001
Malignancy	19/164 (11.6)	15/182 (8.2)	0.297
Autoimmune/autoinflammatory disease	9/165 (5.5)	11/182 (6)	0.814
Chronic liver disease	5/165 (5.5)	1/182 (0.5)	0.106
Medication, <i>n</i> (%)			
ACE-Inhibitors	44/165 (26.7)	61/196 (31.1)	0.353
ARB	43/165 (26.1)	40/195 (20.5)	0.213
Calcium channel blockers	102/166 (61.4)	116/197 (58.9)	0.619
Beta blockers	83/160 (51.9)	98/195 (50.3)	0.761
Other antihypertensives	49/160 (30.6)	76/192 (39.6)	0.080
Insulins	11/165 (6.7)	19/193 (9.8)	0.279
Oral antidiabetic agents	23/166 (13.9)	45/195 (23.1)	0.026
Statin	36/160 (22.5)	61/193 (31.6)	0.056
Antiagregan	72/164 (43.9)	86/188 (45.7)	0.729
Anticoagulant	20/163 (12.3)	15/183 (8.2)	0.210
Smoking, <i>n</i> (%)			
Never smoked	83/159 (52.2)	106/199 (53.3)	0.399
Still smoking	11/159 (6.9)	21/199 (10.6)	
Stopped smoking	65/159 (40.9)	72/199 (36.2)	
Laboratory results, median (IQR)			
Urea (mg/dl)	72 (52–96)	75 (56–92)	0.852
Creatinine (mg/dl)	1.86 (1.48–2.87)	1.9 (1.47–2.78)	0.978
eGFR (ml/min/1.73 m ²)	29 (20–42)	31 (21–42)	0.304
Sodium (mmol/L)	138 (136–141)	139 (137–141)	0.035
Potassium (mmol/L)	4.7 (4.31–5.08)	4.71 (4.3–5.1)	0.945
Calcium (mg/L)	9 (8.3–9.37)	9.1 (8.5–9.5)	0.184
Phosphorus (mg/L)	4 (3.4–4.4)	3.9 (3.5–4.5)	0.403
Albumin (g/dl)	3.9 (3.6–4.2)	4 (3.6–4.2)	0.416
Parathormone (pg/ml)	126.7 (88.2–185)	124.3 (86–184)	0.646
Hemoglobin (g/dl)	11.6 (10.25–12.9)	11.9 (10.5–13.1)	0.421
CRP (mg/L)	7.7 (3–24)	4 (2–10)	<0.001

IQR: interquartile range, *CKD*: chronic kidney disease, *BMI*: body-mass index, *ACE*: angiotensin-converting enzyme, *ARB*: angiotensin receptor blockers, *eGFR*: estimated glomerular filtration rate

In a study conducted on 39 patients with biopsy-confirmed CKD, the COVID-19 mortality rate was found to be 15.4%. These different results may be due to the differences in the

number and groups of patients. Because unlike that study, patients with diabetic nephropathy, patients with glomerular disease, polycystic kidney patients, and patients receiving

Table 2 Symptoms, clinical table, treatment, need for hospitalization and intensive care, development of AKI and need for RRT in COVID-19 group

	n (%)
Symptoms	
Cough	127/168 (% 75.6)
Dyspnea	111/169 (% 65.7)
Fever	105/170 (% 61.8)
Sore throat	64/163 (%39.3)
Loss of taste	22/151 (% 14.6)
Loss of smell	21/153 (%13.7)
Diarrhea	14/157 (% 8.9)
Asymptomatic	5/156 (% 3.2)
COVID-19 related clinical table at the time of diagnosis	
Asymptomatic disease	14/173 (%8.1)
Mild disease	61/173 (%35.3)
Medium-severe disease	89/173 (% 51.4)
Severe-vital disease	9/173 (%5.2)
Treatment for COVID-19	
Favipiravir	144/172 (%83.7)
Glucocorticoid	71/166 (42.8)
Macrolide	57/165 (34.5)
Hydroxychloroquine	51/167 (30.5)
Oseltamivir	22/166 (13.3)
Tocilizumab	7/163 (4.3)
Convalescent plasma	2/163 (1.2)
Apheresis/immunabsorption	1/164 (0.6)
Anakinra/Canakinumab	1/164 (0.6)
JAK2 inhibitor	1/164 (0.6)
Other	8/164 (4.9)
Inpatient treatment	126/173 (% 72.8)
Development of AKI in hospitalized patients	69/126 (% 54.8)
Stage 1 AKI (KDIGO)	40/69 (58)
Stage 2 AKI (KDIGO)	19/69 (27.5)
Stage 3 AKI (KDIGO)	10/69 (14.5)
AKI Development of need for dialysis in hospitalized patients	10/126 (%7.9)
ICU need	21/126 (16.7)
Non-invasive mechanical ventilation	18/22 (81.8)
Intubation	8/22 (36.4)
ECMO	2/21(9.5)
Total length of stay in hospital (days)	10 (8–15)

COVID-19 coronavirus disease 2019, JAK2 janus kinase, AKI acute kidney injury, KDIGO kidney disease improving global outcomes, ECMO extracorporeal membrane oxygenation, RRT renal replacement therapy

RRT were excluded in our study [14]. In a meta-analysis comparing the long-term mortality of patients with CKD who had COVID-19 and those who did not, they found that those with CKD who had COVID-19 had a higher mortality [15]. In the same analysis, mortality was higher in CKD patients under the age of <70 years who had COVID-19. The age of the patients who died in the COVID-19 group was higher compared to those who did not die.

In our CKD patients who had COVID-19, the need for permanent RRT at 3 months was found to be higher than

the control group. In the study of Ng et al. with CKD and non-CKD patients, 6.6% of the patients hospitalized due to COVID-19 developed AKI requiring dialysis, 17% of these patients survived, and 33.3% of the survivors, the kidneys did not improve at discharge [16]. In a study comparing COVID-19 with influenza, mortality and frequency of AKI were found to be higher in those with COVID-19, and 11% of patients with COVID-19 had a $\geq 25\%$ GFR reduction from baseline at ≥ 90 days of follow-up [17]. In another study where patients who developed AKI due to COVID-19

Fig. 1 Presentation of the COVID-19 group in terms of hospitalization and AKI. *AKI* acute kidney injury

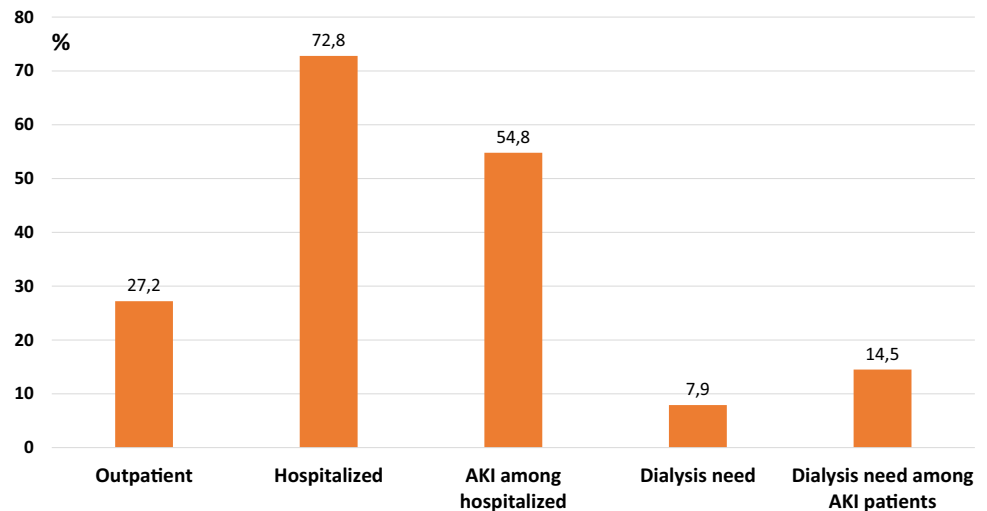
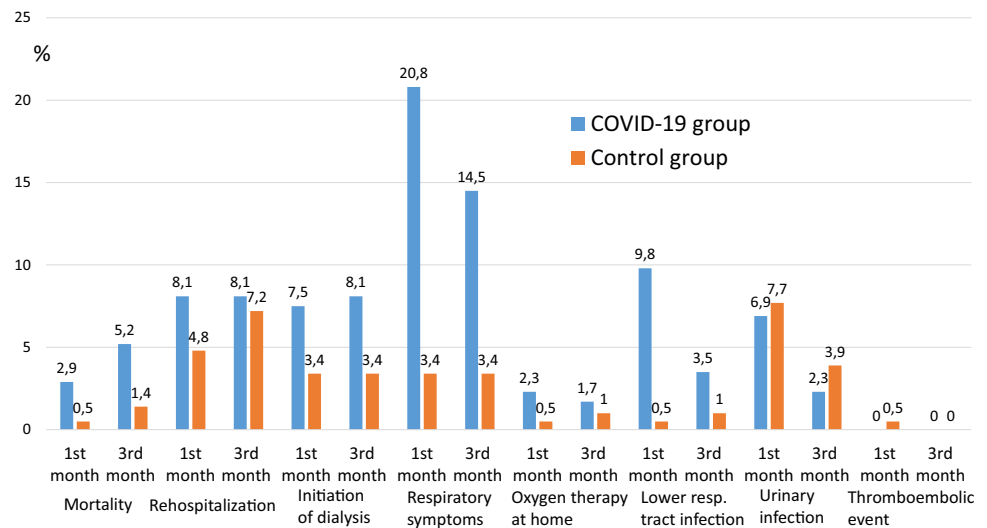


Fig. 2 First and third-month outcomes of study groups



were compared with patients who developed AKI due to another reason and upon follow-up after discharge, a greater decrease was observed in GFR of the COVID-19 patients [18].

In our study, although there was no significant difference between the baseline values of creatinine and GFR, at 1-month follow-up, creatinine and GFR values were significantly different in CKD patients who had COVID-19 compared to CKD patients who did not. In a study with COVID-19 patients [19], one-third of hospitalized patients with AKI due to COVID-19 did not regain their kidney function at discharge. In the same study, it was observed that 36% of the patients who had AKI at discharge and were followed up afterward recovered from AKI.

In our study, respiratory system symptoms were much more common in CKD patients with COVID-19 at 1 month and 3 months compared to the control group. Studies in COVID-19 patients reveal that the lungs were the most

affected organ. Studies on previous coronavirus infections have shown that patients may experience permanent deterioration in respiratory functions in the long term [20]. In the study by Zhao et al., 30.91% of the patients had gastrointestinal symptoms, 18.18% had headache, 16.36% had fatigue, 14.55% had exertional dyspnea, and 81% had cough and sputum at the 3rd month after COVID-19 infection. In the same study, it was also shown that abnormalities persisted in a significant proportion of patients in the HRCT and respiratory tests performed at the 3rd month, and in multivariate analyzes, they found that increased BUN was a risk factor associated with the presence of CT abnormalities [21].

In our study, we found the rate of hospitalization in CKD patients to be 72.8% and the rate of intensive care admission to be 16.7%. The rate of AKI development in hospitalized patients was 54.8%, the rate of patients requiring dialysis was 7.9%, and the need for dialysis was calculated as 14.5% in patients who developed only AKI. In patients who

Table 3 Comparative presentation of the results of the patient and control groups (data presented in numbers and %)

	COVID-19 Group <i>N</i> : 173	Control group <i>N</i> =207	<i>p</i>
30th day after COVID-19			
Number of patients who died, <i>n</i> (%)	5/173 (2.9)	1/207 (0.5)	0.096
Need for chronic RRT, <i>n</i> (%)	13/173 (7.5)	7/207 (3.4)	0.072
Respiratory symptoms, <i>n</i> (%)	36/173 (20.8)	7/207 (3.4)	<0.001
Re-hospitalization for any reason, <i>n</i> (%)	14/173 (8.1)	10/207 (4.8)	0.193
Oxygen therapy at home, <i>n</i> (%)	4/173 (2.3)	1/207 (0.5)	0.182
Lower respiratory tract infection, <i>n</i> (%)	17/173 (9.8)	1/207 (0.5)	<0.001
Urinary tract infection, <i>n</i> (%)	12/173 (6.9)	16/207 (7.7)	0.768
Venous or arterial thromboembolic event, <i>n</i> (%)	0/173 (0)	1/207 (0.5)	1.000
Creatinine (mg/dl)	1.8 (1.47–2.51)	2.09 (1.6–2.91)	0.028
eGFR (ml/min/1.73 m ²)	31.2 (20.6–40.2)	30.9 (20.9–41.0)	0.834
CRP (mg/l)	5.1 (2.99–12.7)	4 (1.36–9)	0.003
Proteinuria (mg/day)	875 (395–2433)	675 (263–1558)	0.123
Hemoglobin (g/dl)	11.4 (10–12.2)	11.86 (10.8–12.9)	0.015
90th day after COVID-19			
Number of patients who died, <i>n</i> (%)	9/173 (5.2)	3/207 (1.4)	0.037
Need for chronic RRT, <i>n</i> (%)	14/173 (8.1)	7/207 (3.4)	0.045
Respiratory symptoms, <i>n</i> (%)	25/173 (14.5)	7/207 (3.4)	<0.001
Re-hospitalization for any reason, <i>n</i> (%)	14/173 (8.1)	15/207 (7.2)	0.757
Oxygen therapy at home, <i>n</i> (%)	3/173 (1.7)	2/207 (1)	0.663
Lower respiratory tract infection, <i>n</i> (%)	6/173 (3.5)	2/207 (1)	0.149
Urinary tract infection, <i>n</i> (%)	4/173 (2.3)	8/207 (3.9)	0.389
Venous or arterial thromboembolic event, <i>n</i> (%)	0/173 (0)	0/207 (0)	–
Creatinine (mg/dl)	1.91 (1.51–2.66)	2.15 (1.6–3.59)	0.268
eGFR (ml/min/1.73 m ²)	28.9 (19.4–39.5)	30.2 (21.5–42.0)	0.220
CRP (mg/l)	5 (2.8–8)	3.07 (2–6)	0.152
Proteinuria (mg/day)	695 (300–1780)	504.7 (123–2006)	0.757
Hemoglobin (g/dl)	11.2 (10.2–12.4)	12.2 (10.5–12.9)	0.079

COVID-19 coronavirus disease 2019, RRT renal replacement therapy, eGFR estimated glomerular filtration rate, CRP C-reactive protein

developed AKI, the rates of stage 1, 2 and 3 AKI was 58%, 27.5% and 14.5%, respectively. Other studies have reported different results, varying between 0.5 and 46%, regarding the rate of AKI development [22]. This is most likely due to the difference in patient groups and diagnostic criteria. In the study by Chan et al., the frequency of AKI development was found to be 46% in hospitalized patients (CKD and non-CKD patients). Dialysis was initiated in 19% of patients who developed AKI. Stage 1, 2, and 3 AKI rates were 39%, 19%, and 42%, respectively [19]. In another study, Arıkan et al. found the frequency of AKI to be 52.1% in patients with CKD and found it higher than those without CKD (39.3%) [23]. The incidence of AKI associated with COVID-19 was found to be higher than in the SARS CoV-1 outbreak in 2005 [24]. In another study, COVID-19 pneumonia showed a higher frequency of AKI when compared to pneumonia due to other causes [25, 26]. Although the reason for this was not fully understood, viral cytopathic effect (ACE-2, TMPRSS2, and CTSL – to which the virus

binds – are highly expressed in the kidney), hemodynamic compromise (patients receiving mechanical ventilation and positive inotropic, insufficient fluid support, pulmonary embolism, myocardial damage), ARDS-AKI axis (hypoxia in ARDS, decrease in cardiac output, systemic inflammation causes AKI), glomerular damage (podocyte damage due to direct viral effect and/or cytokines) and rhabdomyolysis were suggested in the pathogenesis [22].

Another important finding in our study is that baseline and first-month CRP levels in the COVID-19 group were significantly higher than their non-COVID counterparts. This difference disappeared in the third month. The higher baseline CRP level of the COVID-19 group may be explained by the fact that this group has a longer CKD duration, has more heart failure patients, and has different types of recurrent infections due to weaker immunity because it includes older patients. This suggests that these patients may be susceptible to COVID-19. However, our study had not enough data on these subjects. Many treatments, especially corticosteroids,

may have affected the CRP levels of the COVID-19 patients in the first month, but COVID-19 patients with abnormal laboratory tests at the time of diagnosis usually improve during recovery, even in hospitalized patients [27]. Therefore, the high level of CRP in the first month may be due to the ongoing possible inflammation associated with COVID-19 in this group. At the third month, CRP levels did not differ significantly between the groups. These findings were consistent with clinical outcome data in the post-COVID period.

The main shortcomings of our study were it was retrospective, the baseline data of both groups were not exactly similar. However, such problems are common in registry studies. We used random sampling method to avoid possible bias when including control group patients from each center. As a result of this, while the baseline renal function tests of both groups were similar, there were significant differences in some demographic characteristics (age, comorbidity, etc.). Nevertheless, our study provides extremely important data on the late outcomes of COVID-19 in CKD patients who have had it and also offers the opportunity to compare the COVID-19 CKD patients with control group CKD patients.

Conclusions

COVID-19 was related to increased mortality, deterioration in renal functions, increased need for dialysis, and increased respiratory system symptoms in CKD patients in the post-COVID-19 period. Therefore, patients with CKD should be followed closely to manage the diagnosis and treatment of permanent sequelae that may develop after COVID-19.

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Author contributions Conception, design and revised of the study (SO, SK, MA, KA), Data collection and/or processing (NG, EA, IP, DGT, RK, YA, RM, AO, ZA, YB, SA, FY, ST, ABD, IO, AI, AA, NA, TK, HD, TB, TEO, MTD, KT, SU, OG, EAB, AO, NS, AY), Statistical analysis (SO, SK), Interpretation of the data (SO, SK, MA), Article Writing (SK, SO, MA). All authors read and approved the manuscript.

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Declarations

Conflict of interest The authors have declared that no conflict of interest exists.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee at which the studies were conducted [Ethics Committee of Health Sciences University Haseki Training and Research Hospital approved the study (IRB approval number 12–2021)] and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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