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COVID-19 in chronic kidney disease: a retrospective, propensity score-matched cohort study

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Abstract

Background The prognostic factors for COVID-19 in patients with chronic kidney disease (CKD) are uncertain. We conducted a study to compare clinical and prognostic features between hospitalized COVID-19 patients with and without CKD.
Methods Fifty-six patients with stage 3–5 CKD and propensity score-matched fifty-six patients without CKD were included in the study. Patients were followed-up at least fifteen days or until death after COVID-19 diagnosis. The endpoints were death from all causes, development of acute kidney injury (AKI) or cytokine release syndrome or respiratory failure, or admission to the intensive care unit (ICU).
Results All patients were reviewed retrospectively over a median follow-up of 44 days (IQR, 36–52) after diagnosis of COVID-19. Patients with CKD had higher intensive care unit admission and mortality rates than the patients without CKD, but these results did not reach statistical significance (16 vs. 19; $p = 0.54$ and 11 vs. 16, $p = 0.269$, respectively). The frequency of AKI development was significantly higher in predialysis patients with CKD compared to the other group (8 vs. 5; $p < 0.001$), but there was no significant difference between the groups in terms of cytokine release syndrome (13 vs. 8; $p = 0.226$), follow-up in the ICU (19 vs. 16; $p = 0.541$), and respiratory failure (25 vs. 22, $p = 0.566$). Multivariate logistic regression analysis revealed that respiratory failure and AKI were independent risk factors for mortality.
Conclusion The mortality rates of COVID-19 patients with CKD had higher than COVID-19 patients without CKD. Also, AKI and respiratory failure were independently related to mortality.

Keywords COVID-19 · Chronic kidney disease · End-stage kidney disease · Acute kidney injury

Introduction

Coronavirus Disease 2019 (COVID-19) became a pandemic after the first detection in Wuhan, China, in December 2019. Lymphopenia and increased inflammatory markers are prognostic markers in COVID-19 patients [1, 2]. Also, acute kidney injury (AKI) is associated with an unfavorable outcome in COVID-19 patients [3]. The most frequent symptoms are fever, cough, and dyspnea. Also, diarrhea is a usual manifestation in hemodialysis patients with COVID-19 [4]. Pneumonia is the most common manifestation of the infection, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can lead to a cytokine release syndrome that

causes multi-organ dysfunction [5]. Contact history, typical symptoms, laboratory, and radiologic findings can make the diagnosis. A positive PCR result in nasal and oropharyngeal swabs confirms the diagnosis [6].

The treatment regimen for uremic patients consists of managing chronic kidney disease (CKD), viral infection, and complications. Some centers have established treatment regimens for patients with COVID-19, but their effectiveness in large populations has not been proven [7]. Older age, diabetes, and hypertension are well-described risk factors for mortality in COVID-19. Also, CKD is a common chronic condition worldwide. Hypertension, diabetes, and cardiovascular disease are more prevalent in patients with CKD than in the general population. Also, observational studies have shown that high mortality and morbidity rates in CKD patients with COVID-19 than the general population [1]. In

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this study, we compared clinical and prognostic features in COVID-19 patients with and without CKD.

Materials and methods

Study population and design

This retrospective cohort study was conducted on hospitalized patients with the diagnosis of COVID-19 at Istanbul Medical Faculty, Doctor Lütfi Kırdar Training and Research Hospital between February 1 and May 14, 2020. Patients with an estimated creatinine clearance of less than 60 ml/min/1.73 m^2 for more than three months were included in patients with CKD [8]. Those without biochemical and radiological evidence of kidney disease were classified as patients without CKD. Patients with CKD were matched one to one to those without CKD to age and sex by propensity score matching. The estimated creatinine clearance was calculated with the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

Initially, sixty-eight patients with CKD were included in the analysis. The exclusion criteria were patients under immunosuppression (four patients), those with acute kidney injury at admission (six patients), and those lost in the follow-up (two patients) (Fig. 1). The remaining fifty-six patients with CKD were matched with fifty-six those without CKD. All parameters and outcomes were compared between patients with CKD and without CKD.

All the patients were followed-up at least 15 days or until death after diagnosis of COVID-19. The Medical Ethics Committee of the Istanbul Faculty of Medicine approved this study. Clinical data, comorbidities, laboratory, radiological results, antiviral treatments, and CKD management were extracted from electronic medical records. Nasal and oropharyngeal swabs were collected and tested for SARS-CoV-2 ribonucleic acid (RNA) with reverse transcription-polymerase chain reaction (RT-PCR) assay.

Patient management

The COVID-19 diagnosis was based on contact history, symptoms, laboratory, and radiological findings. The positive RT-PCR test was used to confirm the diagnosis. The treatment protocol for CKD patients consists of the management of CKD, viral infection, and anticoagulation. Besides that, cytokine-targeted therapy was used in patients with cytokine release syndrome.

Indications for hospitalization were moderate or severe pneumonia, and cytokine release syndrome (persistent fever, blood lymphocyte count < 800/mm^3, serum C-reactive protein > 40 mg/L, aspartate aminotransferase > 45 IU/L,
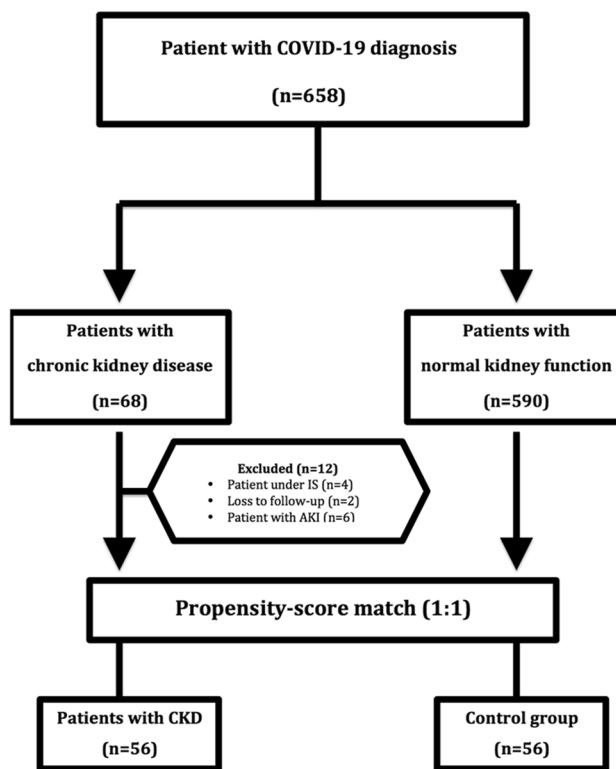
Fig. 1 Flow chart of patients in the study. Abbreviations: *COVID-19* Coronovirus disease 2019, *IS* immunosuppression, *AKI* acute kidney injury, *eGFR* estimated glomerular filtration rate

ferritin > 500 ng/mL, D-dimer > 1000 ng/mL, and triglyceride 150 > mg/dL).

Criteria for admission to the intensive care unit were that the partial pressure of arterial oxygen and the inspiratory oxygen fraction (PaO$_2$/FiO$_2$) ratio less than 300, oxygen saturation under 90% and PaO$_2$ below 70 mm Hg despite 5 L/min oxygen therapy, and persistent hypotension (systolic blood pressure < 90 mm Hg or mean arterial pressure < 65 mm Hg).

Management of chronic kidney disease

Logistics planning is crucial for the management of hemodialysis patients during the COVID-19 outbreak. Twenty beds were used for hemodialysis treatment in Istanbul Medical Faculty and forty beds for Kartal Research and Training Hospital. Dialysis sessions of SARS-CoV-2 infected, and other patients were separated. In the presence of an emergency, dialysis was done after applying disinfection and isolation rules to the patients. Transmission of SARS-CoV-2 was not reported during or after the session in both centers.

Outpatients were followed-up with daily telephone control, weekly examination, and blood analysis. Serum creatinine, electrolytes, C-reactive protein, D-dimer,

pro-calcitonin, fibrinogen, and troponin were followed daily in inpatients. All patients were followed-up within the first week after discharge.

Antiviral and cytokine-targeted therapy

Patients were treated with hydroxychloroquine (400 mg twice a day for one day, then 200 mg twice a day for four days; oral) and azithromycin (500 mg daily for one day, then 250 mg for four days; oral). The hydroxychloroquine dose was reduced (200 mg three times a week after dialysis sessions) in dialysis patients. Tocilizumab (400 mg daily for two days; intravenous) or anakinra (100 mg daily for seven to fourteen days, or until hospital discharge; subcutaneous) were used to treat cytokine release syndrome. Resistant cases were treated with Favipiravir (1600 mg twice a day for one day, then 600 mg twice a day for four days; oral). Antibiotic therapy was administered based on the infection specialist's decision in the presence of confirmed or suspected bacterial infection. Also, patients were monitored for adverse drug reactions, arrhythmias, and changes in the QT interval (Fig. 2).

Anticoagulation and oxygen treatment

Low-molecular-weight heparin was used in all patients unless contraindications. Oxygen treatment was provided to the patients with oxygen saturation below 92% with the nasal cannula and non-rebreather mask. If respiratory failure continues despite these treatments, high flow nasal cannula oxygen therapy was performed before intubation and mechanical ventilation.

Outcomes

The primary endpoint was all-cause mortality. The secondary endpoints were AKI or cytokine release syndrome or respiratory failure, or admission to the intensive care unit (ICU). Definitions of AKI were a 0.3 mg/dl increase in serum creatinine within 48 h or a 1.5-fold increase in serum creatinine in the past seven days.

Statistical analysis

Categorical variables were summarized with counts and percentages. Quantitative variables were summarized with means and standard deviations or medians and interquartile range, where appropriate. The Chi-Square and Fisher's exact test were performed for qualitative variables, whereas the Mann–Whitney U test was used for quantitative variables with the non-parametric distribution. Kaplan–Meier was used for the survival analysis between the patients with and without CKD groups. Logistic regression analysis was
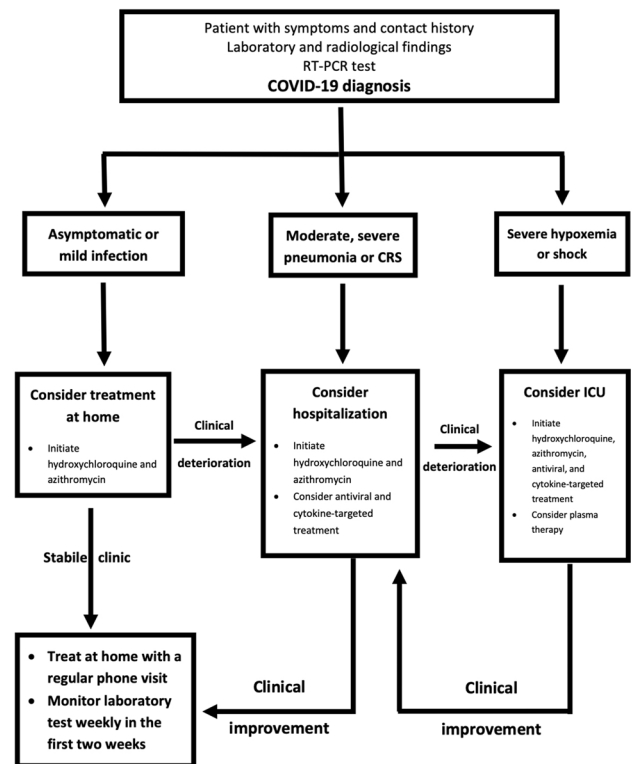
Fig. 2 Diagnosis and treatment of the patients. Abbreviations: *COVID-19* Coronovirus disease 2019, *RT-PCR* reverse transcription-polymerase chain reaction, *CRS* cytokine release syndrome, *ICU* intensive care unit

used to identify patient loss and the associated risk in terms of odds ratio and 95% confidence intervals. Variables were selected by backward elimination using likelihood ratio tests. A p-value of less than 0.05 was considered significant.

Results

Demographics and clinical characteristics

All patients were retrospectively reviewed during a median follow-up period of 44 days (interquartile range, 36–52 days) after COVID-19. The demographic and clinical characteristics of CKD patients and patients without CKD are shown in Table 1. In the CKD group, 44 patients (78.6%) received hemodialysis treatment for end-stage renal disease, and 12 patients (21.4%) had stage three and four CKD.

Hypertension ($n = 46$ [82.1%] vs. $n = 27$ [48.2%]; $p < 0.001$) and previous heart disease history ($n = 29$ [51.8%] vs. $n = 10$ [17.9%]; $p < 0.001$) were more common in patients with CKD compared to patients without CKD. The number of patients with diabetes mellitus and the use of the renin–angiotensin system (RAS) blockade was similar between the groups. Chronic lung disease was more common

Table 1 Baseline demographic, clinical, and laboratory characteristics of the patients

	Patients without CKD ($n=56$)	Patient with CKD ($n=56$)	p value
Demographics features			
Age (Median-IQR 25–75)	64 (51.3–73.8)	63 (50.3–74)	0.94
Sex (*N*, %)			
Male	28 (50%)	28 (50%)	1
Female	28 (50%)	28 (50%)	
Etiology of CKD (*N*, %)			
Diabetic nephropathy		20 (35.7%)	
Hypertensive nephropathy		17 (30.4%)	
Chronic glomerulonephritis		2 (3.6%)	
Others		8 (14.3%)	
Unknown		9 (16.1%)	
Comorbidities (*N*, %)			
Diabetes mellitus	18 (32.1%)	20 (35.7%)	0.69
Chronic lung disease	11 (19.6%)	4 (7.1%)	**0.047**
Previous heart disease	10 (17.9%)	29 (51.8%)	**< 0.001**
Chronic hypertension	27 (48.2%)	46 (82.1%)	**< 0.001**
Usage of RAS blockage	12 (21.4%)	10 (17.9%)	0.406
Clinical characteristics			
Presentation symptoms (*N*, %)			
Fever	28 (50%)	32 (57.1%)	0.448
Cough	41 (73.2%)	32 (57.1%)	0.095
Dyspnea	26 (46.4%)	23 (41.1%)	0.625
Diarrhea	4 (7.1%)	3 (5.4%)	0.714
Initial examination findings (Median-IQR 25–75)			
Heart rate (/min)	89 (82–100)	83 (76–89)	**< 0.001**
SpO$_2$ value (%)	95 (88–97)	95 (90–98)	0.335
Respiratory rate (/min)	19 (17–23)	20 (17–24)	0.264
Blood pressure (mm Hg)			
Systolic	135 (120–145)	130 (120–153)	0.166
Diastolic	83 (70–90)	80 (70–89)	0.3
Laboratory results			
Laboratory results at admission (Median-IQR 25–75)			
Serum creatinine (mg/dL)	0.8 (0.65–1)	3.5 (2–7.3)	**< 0.001**
Leucocyte count (/mm^3)	5710 (4350–8120)	7725 (9128–5433)	0.071
Lymphocyte count (/mm^3)	1150 (758–1478)	940 (520–1355)	0.055
Hemoglobin count (g/dL)	13.2 (11.7–14.6)	12.1 (9.9–13.1)	**< 0.001**
Platelet count (/mm^3)	187 (149–249)	231 (183–257)	0.565
Serum CRP levels (mg/L)	39 (17–93)	55 (18–154)	**0.027**
Serum ALT levels (IU/L)	19 (13–38)	14 (9–31)	0.593
Serum AST levels (IU/L)	29 (20–41)	21 (14–43)	0.178
Serum LDH levels (IU/L)	269 (197–328)	263 (227–445)	0.061
Serum D-Dimer (ng/mL)	755 (520–1833)	1145 (723–2860)	0.993
Serum ferritin (ng/mL)	247 (149–580)	731 (723–2860)	**< 0.0001**
Serum procalcitonin (ng/mL)	0.1 (0.1–0.2)	0.4 (0.2–1.6)	0.118

Bold text indicates a statistically significant difference between the groups

Abbreviations: *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *CKD* chronic kidney disease, *CRP* C-reactive protein, *LDH* lactate dehydrogenase, *SpO2* blood oxygen saturation levels

p values obtained from the chi-square test, Fisher exact test, or Mann–Whitney U test

in patients without CKD than the patients with CKD ($n = 11$ [19.6%] vs. $n = 4$ [7.1%]; $p = 0.047$).

Clinical presentations and laboratory results

Dry cough, fever, and dyspnea were the most common symptoms at presentation in both groups (Table 2). Physical examination findings of the patients in both groups were similar except for heart rate. Heart rate was significantly lower in the patients with CKD compared to the patients without CKD (89 [interquartile range, 82–100] vs. 83 [interquartile range, 76–89]; $p < 0.001$, respectively).

Serum C-reactive protein (55 mg/L [interquartile range, 18–154] vs. 39 mg/L [interquartile range, 17–93]; $p = 0.027$, respectively) and ferritin levels (731 ng/mL [interquartile range, 723–2860] vs. 247 ng/mL [interquartile range, 149–580]; $p < 0.001$, respectively) were significantly elevated in CKD patients compared to the patients without CKD. Anemia was more common in patients with CKD compared to the other group at the time of admission (12.1 [interquartile range, 9.9–13.1] vs. 13.2 [interquartile range, 11.7–14.6]; $p < 0.001$, respectively).

Treatment regimens and complications

The length of hospital stay was similar between groups (9 [interquartile range, 6–12] vs. 13 [interquartile range, 9–18]; $p = 0.089$) (Table 2). Also, the use of cytokine-targeted therapy was similar between groups (13 [23.2%] vs. 8 [14.2%]; $p = 0.324$), but the use of favipiravir (15 [27.3%] vs. 26 [46.4%]; $p = 0.037$) and antibiotics were significantly higher in patients without CKD compared to the other group (13 [23.2%] vs. 38 [67.9%]; $p < 0.001$). No side effects of the drugs were observed in patients, except for hydroxychloroquine related hypoglycemia in two hemodialysis patients.

Outcomes

The mortality rate of COVID-19 in patients with CKD was higher than patients without CKD, but these results did not

Table 2 Treatment modalities and study outcomes in patients with and without CKD

	Patients without CKD ($n = 56$)	Patient with CKD ($n = 56$)	p value
Time			
Post-infection follow-up (Median-IQR 25–75, days)	48 (36–57)	40 (32–47)	**0.038**
Duration of hospitalization .(Median-IQR 25–75, days)	9 (6–12)	13 (9–18)	0.089
Treatment modalities			
Treatment of infection (N, %)			
Favipiravir	26 (46.4%)	15 (26.7%)	**0.037**
Anti-cytokine agents (*N*, %)			
Tocilizumab	5 (8.9%)	1 (1.8%)	0.324
Anakinra	3 (5.4%)	4 (7.1%)	
Tocilizumab + Anakinra	5 (8.9%)	3 (5.4%)	
Antibiotics (*N*, %)	38 (67.9%)	13 (23.2%)	**< 0.001**
Oxygen therapy (*N*, %)			
No support	31 (55.4%)	33 (58.9)	0.703
Low-flow oxygen therapy	25 (44.6%)	10 (17.9%)	**0.002**
High-flow nasal oxygen therapy	16 (28.6%)	20 (35.7%)	0.418
Mechanical ventilation	15 (26.8%)	16 (28.6%)	0.833
Outcomes			
Complications (*N*, %)			
AKI	8 (14.3%)	5 (8.9%)	0.395
Respiratory failure	25 (44.6%)	22 (39.3%)	0.566
CRS	13 (23.2%)	8 (14.3%)	0.226
Follow-up in the ICU	16 (28.6%)	19 (33.9%)	0.541
Number of died patients	11 (19.6%)	16 (28.6%)	0.269

Bold text indicates a statistically significant difference between the groups

Abbreviations: *AKI* acute kidney injury, *CKD* chronic kidney disease, *CRS* cytokine release syndrome, *ICU* intensive care unit

p values obtained from the chi-square test, Fisher exact test, or Mann–Whitney *U* test

reach statistical significance (16 [28.6%] vs. 11 [19.6%]; $p = 0.269$, respectively). There was no significant difference between the groups in terms of cytokine release syndrome (8 [14.2%] vs. 13 [23.2%]; p = 0.226, respectively), follow-up in the ICU (19 [33.9%] vs. 16 [28.6%]; $p = 0.541$, respectively), and respiratory failure (22 [39.3%] vs. 25 [44.6%]; $p = 0.566$, respectively).

In subgroup analysis, mortality rates were higher in patients with the end-stage renal disease compared to the other groups, but these results did not reach statistical significance ([(14/44), 31.8%] vs. [(2/12), 16.7%] vs. [(11/56), 19.6%]; $p = 0.301$, respectively). AKI was more common in patients with stage three and four CKD, compared to the patients without CKD ([(5/12), 41.7%] vs. [(8/56), 14.3%]; $p < 0.001$, respectively). Also, respiratory failure, cytokine release syndrome, and ICU follow-up rates were similar in patients with end-stage renal disease, stage three and four CKD, and without CKD (Table 3).

Multivariate logistic regression analysis revealed that respiratory failure (39.283 [95% CI 7.296–211.519; P < 0.001]

and AKI (10.961 [95% CI 1.688–71.186; $p = 0.012$] were independent risk factors for mortality (Table 4). Kaplan–Meier analysis showed that the mortality of patients with CKD was significantly higher in those without CKD ($p = 0.041$) (Fig. 3).

Discussion

The prognostic factors and outcomes of COVID-19 in chronic kidney disease patients have not been established. Most studies are based on single-arm and retrospective observations [9, 10]. This retrospective and propensity score match analysis is designed to investigate these issues. Fifty-six patients with CKD and the propensity score-matched fifty-six patients without CKD were followed-up for a median of forty-four days in this study.

Previous studies demonstrated that patients with CKD had fewer symptoms, such as fever and cough, compared to the general population, at presentation [9, 10]. Also, CKD

Table 3 Treatment modalities and study outcomes in various groups

	Patients without CKD (n = 56)	Patient with stage 3 and 4 CKD (n = 12)	Patient with ESRD (n = 44)	p value
Time				
Post-infection follow-up (Median-IQR 25–75, days)	48 (36–57)	40 (26–48)	40 (33–47)	0.21
Duration of hospitalization (Median-IQR 25–75, days)	9 (6–12)	13 (9–16)	14 (10–21)	**0.041**
Treatment modalities and outcomes				
Treatment of infection (N, %)				
Favipiravir	26 (46.4%)	6 (50%)	9 (20.5%)	**0.013**
Anti-cytokine agents (N, %)				
Tocilizumab	5 (8.9%)	0	1 (2.3%)	
Anakinra	3 (5.4%)	1 (8.3%)	3 (6.8%)	0.689
Tocilizumab + Anakinra	5 (8.9%)	1 (8.3%)	2 (4.5%)	
Antibiotics (N, %)	38 (67.9%)	6 (50%)	7 (15.9%)	**< 0.001**
Oxygen therapy (N, %)				
No support	31 (55.4%)	8 (66.7)	25 (56.8)	0.771
Low-flow oxygen	25 (44.6%)	4 (33.3%)	6 (13.6%)	**0.004**
High-flow oxygen	16 (28.6%)	3 (25%)	17 (38.6%)	0.482
Mechanical ventilation	15 (26.8%)	3 (25%)	13 (29.5%)	0.931
Complications (N, %)				
AKI	8 (14.3%)	5 (41.7%)	0	**< 0.001**
Respiratory failure	25 (44.6%)	4 (33.3%)	18 (40.9%)	0.759
CRS	13 (23.2%)	2 (16.7%)	6 (13.6%)	0.467
Follow-up in the ICU	16 (28.6%)	3 (25%)	16 (36.4%)	0.625
Number of died patients	11 (19.6%)	2 (16.7%)	14 (31.8%)	0.301

Bold text indicates a statistically significant difference between the groups

Abbreviations: *AKI* acute kidney injury, *CKD* chronic kidney disease, *CRS* cytokine release syndrome, *ICU* intensive care unit

p values obtained from the chi-square test, Fisher exact test, or Mann–Whitney *U* test

Table 4 Univariate and multivariate logistic regression analyses regarding the primary outcome in all patients

	Univariate analysis			Multivariate analysis		
	Odds ratio	Confidence interval	p value	Odds ratio	Confidence interval	p value
Age	1.022	0.991–1.054	0.163			
Male sex	2.474	0.998–6.128	0.05			
Diabetes mellitus	1.036	0.414–2.592	0.94			
Previous lung disease	2.413	0.771–7.547	0.13			
Previous heart disease	2.107	0.87–5.104	0.099			
Chronic hypertension	1.136	0.462–2.796	0.782			
Serum CRP levels	**1.010**	**1.003–1.016**	**0.003**	1.004	0.996–1.012	0.330
Serum LDH levels	1.001	0.998–1.004	0.413			
AKI during hospitalization	**9.333**	**2.344–37.17**	**0.002**	**10.961**	**1.688–71.186**	**0.012**
Usage of anti-cytokine agents	0.361	0.174–1.076	0.052			
Cytokine release syndrome	**3.042**	**1.112–8.322**	**0.030**	2.435	0.661–8.965	0.181
Usage of antibiotics	0.491	0.203–1.186	0.114			
Respiratory failure	**21.565**	**5.924–78.51**	**< 0.001**	**39.283**	**7.296–211.519**	**< 0.001**
Patient with dialysis	1.909	0.765–4.766	0.166			

Bold text indicates a statistically significant difference between the groups

Abbreviations: *AKI* acute kidney injury, *CRP* C-reactive protein, *CKD* chronic kidney disease, *LDH* lactate dehydrogenase
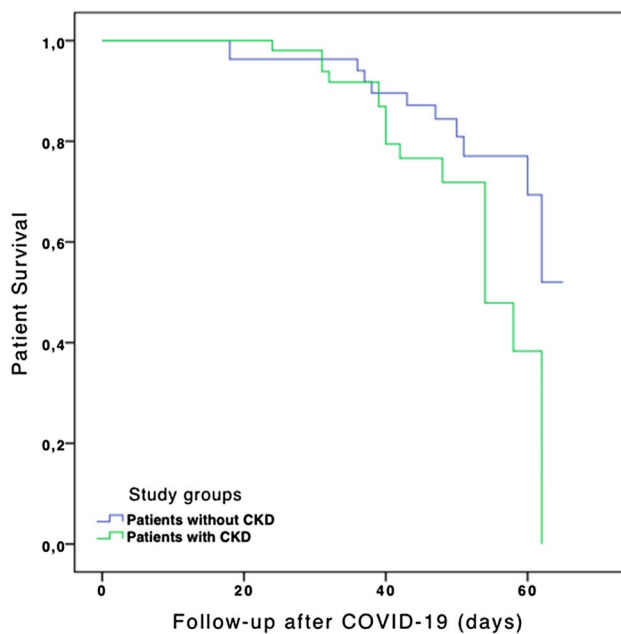
Fig. 3 Kaplan–Meier analysis showed that the mortality of patients according to the groups. Abbreviations: *COVID-19* Coronovirus disease 2019, *CKD* chronic kidney disease

patients had laboratory abnormalities and chest infiltration frequently than those without CKD in previous studies [9, 10]. In our study, patients with CKD had fewer respiratory symptoms than patients without CKD but did not reach statistical significance, which may be explained by two reasons. First, the number of patients in both groups was limited; second, chronic lung disease was more common in patients without CKD. Also, pulse rates were significantly lower

in patients with CKD compared to patients without CKD. These differences may be related to the common usage of non-dihydropyridine calcium channel blockers and beta-blockers in the study group due to increased hypertension and heart disease. Unfortunately, we could not prove that due to a lack of data.

In our study, patients with CKD had elevated serum C-reactive protein and ferritin levels compared to the patient without CKD. Also, lymphocyte count was lower in patients with CKD than the other group however, it did not reach statistical significance.

Many studies defined that patients with CKD had a higher mortality rate than patients without CKD [9–11]. On the other hand, there were conflicting articles on whether CKD is a risk factor for mortality in COVID-19. Some of them have explained that CKD patients are much older, have more cardiovascular events, and a higher prevalence of diabetes mellitus than the general population, so patients with CKD have higher mortality rates than the general population, but CKD is not a risk for death [12]. Also, patients with severe acute respiratory distress syndrome (SARS) had similar mortality rates compared to age and sex-matched non-uremic patients [13]. On the other hand, some of the studies demonstrated that CKD is a risk factor for mortality [9, 10]. In our study, we matched patients with and without CKD in age, gender. Unexpectedly, chronic lung disease was more common in the group without CKD; however, our study showed that patients with CKD have higher mortality rates and longer hospitalization duration than those without CKD, despite similar age and gender. On the other hand, similar to previous studies, our study showed that the prevalence of

chronic heart disease and hypertension is higher in patients with CKD than in patients without CKD. The increased mortality in the CKD group can be explained by more frequent heart disease and hypertension.

AKI is quite common during the COVID-19 outbreak. It occurs via multiple mechanisms involving hypercoagulability, endothelial damage, rhabdomyolysis, and collapsing glomerulopathy. Myocarditis, mechanical ventilation, and cytokine release syndrome are other causal factors [14, 15]. Similar to the earlier research [16], our study demonstrated that AKI was associated with mortality and more common in predialysis patients than patients without CKD.

Previous studies have shown that mortality rates in patients with CKD range from 0 to 34% in COVID-19 [4, 9, 16–18]. In our study, 28.6% of patients with CKD died during the follow-up, and the hemodialysis subgroup had the highest mortality rate (31.8%). These may explain by several reasons. First, all COVID-19 patients had been hospitalized for moderate or severe illness. Second, patients in the dialysis group were older than other studies, and third, there were many comorbid diseases. Therefore, immune dysfunction and secondary opportunistic infection can be associated with a high mortality rate in our patients. .Also, an asymptomatic or mild infection was reported in dialysis patients [19]. However, our study had symptomatic dialysis patients; this may cause higher mortality rates than expected. Favipiravir was approved by Turkish, Chinese, and Indian drug agencies for usage in COVID-19 [20, 21]. Its use has increased recently due to the drawbacks of hydroxychloroquine therapy [21]. Also, the successful usage of favipiravir was reported in dialysis patients in late 2020 [22]. In our study, patients without CKD were treated more frequently with favipiravir than patients with CKD. This issue can be explained by the lack of data for using favipiravir in the early pandemic. Also, although the use of anti-cytokine agents in our study did not differ in terms of the groups, empirical antibiotic use was higher in patients without CKD than in patients with CKD. These can be explained by the increasing frequency of secondary bacterial infections due to structural lung damage in patients without CKD compared to CKD patients. Also, this study is not suitable for testing the efficacy and safety of these drugs.

Our retrospective study has several limitations. The sample size is small, and the follow-up time is short. All COVID-19 patients had been hospitalized for moderate or severe illness. These restrictions did not allow us to draw definitive conclusions from these experiences. Therefore, our findings are preliminary and will need to be confirmed in large-scale prospective cohort studies. Using a standard treatment model and propensity score matching may be considered as the strength of the study.

Consequently, the mortality rates of COVID-19 patients with CKD had higher than those without CKD despite similar age and sex. AKI was more common in patients with stage 3 and 4 CKD than those without CKD. Also, AKI and respiratory failure were associated with mortality. There is not any specific effective antiviral treatment for COVID-19. Hence, drugs should use with caution.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Ethical approval All procedures performed in studies involving human participants were under the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study approved by the Ethics Committee of Istanbul University Istanbul Faculty of Medicine (Date 12/06/2020, number: 860).

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