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Is the risk for COVID-19 outcomes the same for all patients with chronic kidney disease? A retrospective study

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Abstract. *Coronavirus disease 2019 (COVID-19) emerged at the end of 2019 and quickly spread worldwide. Among the various comorbidities associated with severe disease, chronic kidney disease (CKD) has been identified as one of the leading conditions. However, it is not yet clear whether all stages of CKD pose the same risk for severe COVID-19 infection. Therefore, the objective of this study was to assess the impact of different stages of CKD on the clinical characteristics, disease progression, and outcomes of COVID-19.*

Methods. This retrospective study focused on CKD patients who were admitted with COVID-19. We analyzed various factors including demographic data, comorbidities, symptoms, physical findings, laboratory test results, length of hospital stay, and in-hospital outcomes. These factors were evaluated based on the different stages of CKD.

Results. A total of 284 CKD patients infected with SARS-CoV-2 were evaluated and compared to 395 COVID-19 patients with normal kidney function. Among the CKD patients, 86 were receiving dialysis. We observed significantly higher levels of C-reactive protein, procalcitonin, D-dimer, and ferritin, as well as a significantly lower lymphocyte count, in the CKD groups compared to the control group. There were significant differences among the CKD groups in terms of biochemical markers, duration of hospital stay, rates of ICU admission, and mortality. However, we did not find significant differences between dialysis and non-dialysis CKD patients regarding the length of hospital stay, need for ICU admission, and number of deceased patients.

Conclusions. The presence and severity of CKD should be considered crucial factors for predicting the risk of COVID-19. Patients with late-stage CKD who are hospitalized with COVID-19 require increased awareness and close monitoring to reduce rates of ICU admission and mortality.

Key words: *chronic kidney disease, COVID-19, risk factors.*

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Чи однаковий ризик наслідків COVID-19 для усіх пацієнтів із хронічною хворобою нирок? Ретроспективне дослідження

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Резюме. *Коронавірусна хвороба 2019 (COVID-19) з явилася наприкінці 2019 року і швидко поширилася по всьому світу. Серед різних супутніх захворювань, пов язаних з тяжким перебігом COVID-19, хронічна хвороба нирок (ХХН) була визначена як одна з провідних. Однак, вплив стадії ХХН на тяжкість COVID-19 залишається не визначеним. Метою цього дослідження було оцінити вплив різних стадій ХХН на клінічні характеристики, перебіг та наслідки COVID-19.*

Методи. До цього ретроспективного дослідження залучено пацієнтів з ХХН, які були госпіталізовані з COVID-19. Ми аналізували різні фактори, включаючи демографічні дані, супутні захворювання, симптоми, фізикальні знахідки, результати лабораторних досліджень, тривалість перебування в лікарні та ефективність лікування залежно від стадії ХХН.

Результати. Всього було проаналізовано 284 пацієнта з ХХН, інфікованих SARS-CoV-2, та порівняно з 395 пацієнтами з COVID-19 з нормальною функцією нирок. Серед пацієнтів з ХХН 86 отримували діаліз. Ми спостерігали значно вищі рівні С-реактивного білка, прокальцитоніну, D-димеру та феритину, а також значно нижчу кількість лімфоцитів у групах з ХХН порівняно з контрольною групою. Крім того, спостерігались значні відмінності між групами ХХН з точки зору біохімічних маркерів, тривалості перебування в лікарні, частоти госпіталізації до відділення інтенсивної терапії (ВІТ) та смертності. Однак ми не знайшли значних відмінностей між пацієнтами з ХХН, які отримували діаліз, та тими, хто не отримував діаліз, щодо тривалості перебування в лікарні, потреби в госпіталізації в ВІТ та кількості померлих пацієнтів.

Висновки. Наявність та стадію ХХН слід розглядати як вирішальні фактори для прогнозування ризику COVID-19. Пацієнтам з терміналюною ХХН, які госпіталізовані з COVID-19, потрібна підвищена увага та спостереження для зниження частоти госпіталізації до ВІТ та смертності.

Ключові слова: *хронічна хвороба нирок, COVID-19, фактори ризику.*

Introduction. A mysterious and dangerous viral infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged at the end of 2019 and afterward escalated to a pandemic. This disaster, namely Coronavirus disease 2019 (COVID-19), presents a broad spectrum of clinical symptoms from asymptomatic to respiratory failure and death [1]. Various organs, including the kidneys, may be involved [2]. The underlying factors leading to recovery from the infection or critical illness are being investigated. Several poor prognostic markers have been identified. Lymphopenia, elevated D-dimer, C-reactive protein (CRP), ferritin, and procalcitonin are shown to be useful in predicting the prognosis of COVID-19 [3-7].

Chronic kidney disease (CKD) is defined as a decrease in kidney function, estimated glomerular filtration rate (eGFR), or evidence of kidney damage such as increased albuminuria, abnormal urine deposits, or structural abnormalities that persist for more than three months [8]. Staging of CKD is essential to aid clinicians in management and to predict the risk of progression and complications. Based on eGFR, CKD is grouped into 5 stages.

CKD manifests as the second most common risk factor for severe COVID-19, after advanced age [9-10]. The clinical course and the outcomes of COVID-19 in different CKD stages need to be elucidated. We evaluated the clinical characteristics, course, and outcomes of COVID-19 in patients with CKD and compared them to those without CKD. We aimed to investigate the possible risk stratification for COVID-19 in different stages of CKD.

Materials and methods. ***Study design.*** We conducted this retrospective observational study on COVID-19 patients with CKD, admitted to our hospital with the diagnosis of COVID-19 between March 2020 and February 2021. The study was approved by the Turkish Republic Ministry of Health and the local ethics committee. (Approval number: 514/195/9, 10.02.2021)

Patients. The data of the consecutive patients admitted to dedicated COVID-19 wards in our hospital between March 2020 and February 2021 were collected. SARS-CoV-2 was confirmed by a real-time RT-PCR(reverse transcriptase polymerase-chain-reaction) test. Throat-swab specimens from the oropharynx and nasopharynx were obtained from all patients at admis-

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sion and were put in a viral-transport medium. All the COVID-19 diagnoses were in accordance with guidelines provided by the Ministry of Health, COVID-19 Turkey National Health Commission.

The patients with the diagnosis of CKD were enrolled in the study. CKD was defined as the presence of kidney damage or decreased kidney function for ≥ 3 months, irrespective of the cause. CKD staging was applied with the accepted classification [11]. Inclusion criteria in the study group were as follows: Clinical, laboratory, and/or radiological findings consistent with COVID-19, need for hospital admission, and having been diagnosed as CKD.

For comparison with CKD cases, the data of 395 age and gender-matched COVID-19 patients with normal renal functions have been studied.

The subjects who had no confirmed SARS-coV-2 infection, COVID-19 patients who did not have inpatient admission, patients aged under 18, patients with insufficient data required for the study protocol, and patients with acute kidney injury were excluded from data collection.

Data collection. The demographic data including age and gender, and comorbidities, namely hypertension, cardiovascular disease, and chronic respiratory disease of all patients were recorded. Data collected included the most frequent symptoms (i.e., cough, fever, dyspnea, fatigue, headache, chest pain, gastrointestinal symptoms such as nausea, vomiting, or diarrhea). The physical examination findings on initial admission were examined; these included fever, blood pressure, heart rate, and arterial oxygen saturation. All subjects had been computerized tomography (CT) scanned on admission and radiological findings were recorded. The laboratory test results on the date of admission included complete blood count, renal and hepatic function tests, electrolytes, lactate dehydrogenase, serum albumin, D-dimer, ferritin, and CRP. The estimated glomerular filtration (eGFR) was calculated using Chronic Kidney Disease Epidemiology Cooperation (CKD-EPI) equation [12].

Length of hospital stay, need for admission to intensive care unit, the course, and outcomes during hospitalization were recorded. Treatment protocols were applied according to the COVID-19 guide of the Turkish Ministry of Health [13].

Statistical Analysis. Categorical variables were described as numbers (%). Continuous variables were analyzed parametrically by means and standard deviations, median, minimum and maximum. Differences between categorical variables were calculated using the chi-square method. Differences between continuous variables were calculated using the T-test and ANOVA test. Pearson analysis was used for correlation tests. *A P*-value less than 0.05 was considered statistically significant. Statistical analyses were performed using SPSS software (version 17.0).

Results. We evaluated 284 CKD patients infected by SARS-coV-2 and compared them to 395 COVID-19 patients with normal renal functions. Eighty-six CKD patients were on dialysis. The flowchart of the study population is demonstrated in Figure 1.

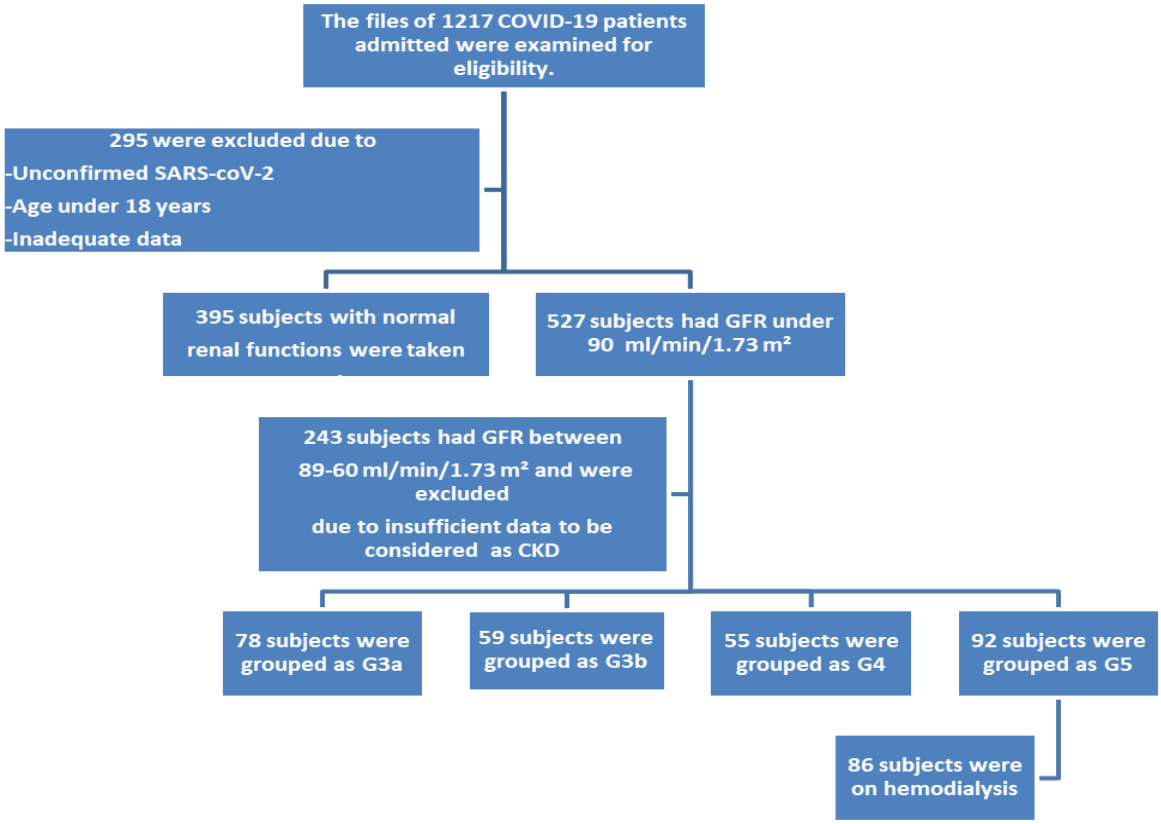


Fig. 1. The flowchart of patient selection and classification.

Table 1 shows the demographics, and comorbidities of the study population.

Table 1

The demographic characteristics of the study population

	Control group	G3a	G3b	G4	G5
Number of cases	395	78	59	55	92
Age(years) Min-Max(Median) Mean±SD	 19-85 (70) 70.18±13.55	 29-93 (74) 71.87±13.03	 47-92 (71) 71.69±11.08	 31-94 (74) 71.96±13.62	 19-92 (67) 62.32±16.09
Gender(female/male)	202/193	41/37	24/35	29/26	46/46
Comorbidities Hypertension DM Chronic lung disease Cardiovascular disease	n (%) 120 (30.4) 143 (36.2) 39 (9.9) 46 (11.6)	n (%) 52 (66.7) 49 (62.8) 18 (23.1) 30 (38.5)	n (%) 47 (79.7) 33 (55.9) 12 (20.3) 30 (50.8)	n (%) 42 (76.4) 30 (54.5) 9 (16.4) 16 (29.1)	n (%) 56 (60.9) 42 (45.7) 10 (10.9) 31 (33.7)

Abbreviations. SD: Standard deviation, DM: Diabetes mellitus
**One-way ANOVA test*

As presented in Table 1, the mean ages were 68.76 (±14.49) and 70.18(±13.55) in the study and control groups, respectively. Women accounted for 49% of the CKD population and 51% of the control group. DM was the leading comorbidity in the control group (36.2%); while hypertension was the most frequent comorbidity in CKD (69.4%). The most common presenting symptoms were cough, fever, shortness of breath, fatigue, headache, chest pain, and gastointestinal disturbances (nausea, vomiting, diarrhea). Cough was the most frequent presenting symptom in the control group, whereas CKD patients presented more commonly with shortness of breath. Nausea, vomiting, and diarrhea were most common in CKD patients in the G4 group (Fig. 2).

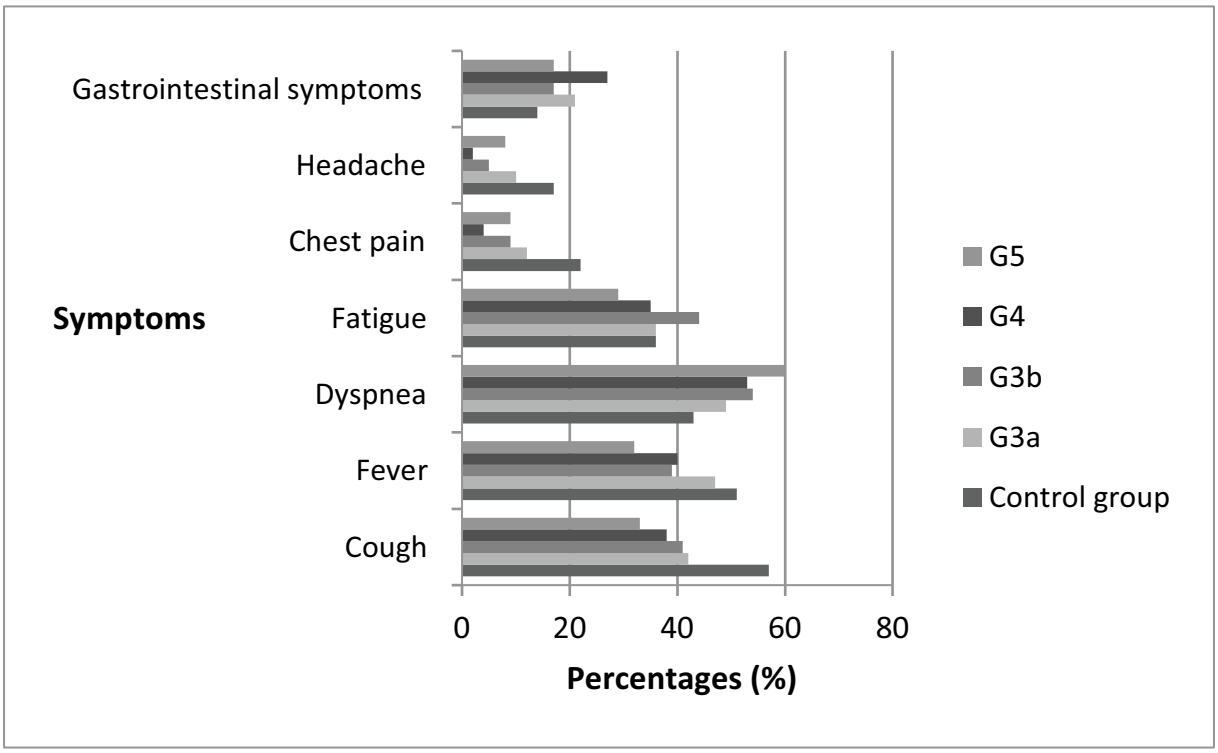


Fig. 2. The percentages of presenting symptoms in control and CKD groups.

The physical findings in different patient groups are demonstrated in Table 2.

Table 2

The physical findings in different groups

	Control group	G3a	G3b	G4	G5	P-value*
Body temperature (°C) *Min-Max(Median)* *Mean±SD*	36.0-39.7(36.8) 37.1±0.79	36.0-39.1(36.7) 36.8±0.65	36.0-39.5(36.7) 36.9±0.75	36.0-39.0(36.7) 36.8±0.57	36.0-40.0(36.7) 36.6±0.79	0.039
Systolic blood pressure (mmHg) *Min-Max(Median)* *Mean±SD*	80-120(110) 119.44±15.83	80-190(120) 119.44±15.97	90-180(110) 117.83±17.29	90-160(115) 117.41±17.82	80-190(120) 121.47±21.46	0.99
Diastolic blood pressure (mmHg) *Min-Max(Median)* *Mean±SD*	40-110(70) 72.24±8.49	50-110(70) 72.86±10.01	55-90(70) 71.33±8.34	50-95(70) 71.09±10.84	40-120(70) 73.80±12.99	0.44
Heart rate (beat/ minute) *Min-Max(Median)* *Mean±SD*	57-130(85) 87.23±14.83	54-140(80) 83.64±12.95	60-140(80) 84.19±17.16	60-132(80) 82.94±13.44	50-140(84) 87.10±17.64	0.10
Arterial oxygen saturation (%) *Min-Max(Median)* *Mean±SD*	64-99(95) 93.79±4.79	38-99(94) 91.51±7.92	60-98(92) 93.79±4.79	70-98(92) 90.81±5.47	60-99(93) 90.42±7.31	<0.001

Body temperature and arterial oxygen saturation showed significant differences between the groups; the latter was found to be lowest in group G5. The results of the laboratory parameters are summarized in Table 3.

Table 3

The comparison of laboratory data

	Control group	G3a	G3b	G4	G5	P-value*
Creatinine(mg/dl) Min-Max(Median) Mean±SD	0.26-0.07(0.66) 0.67±0.14	0.87-1.80(1.19) 1.21±0.20	1.20-2.13(1.57) 1.61±0.24	1.69-5.41(2.38) 2.62±0.79	3.08-20.44(5.77) 6.47±2.92	<0.001
Urea(mg/dl) Min-Max(Median) Mean±SD	7-77(26) 27.35±9.72	29-113(53) 57.75±18.80	10-275(68) 76.63±38.41	39-282(105) 108.56±46.71	46-376(134) 143.14±61.83	
eGFR(ml/min/1.73 m^2) Median Mean±SD	106.00 107.22±11.62	51.50 51.67±4.34	38.30 38.33±4.21	22.20 22.08±4.80	9.00 8.99±3.17	<0.001
Leucocytes(/uL) Min-Max(Median) Mean±SD	900-71200(6100) 6918±4620	3100-33600(7700) 8841±5123	3400-23400(8400) 9643±4649	2600-30600(7800) 9107±4967	1100-36100(8100) 9434±5292	<0.001
Lymphoctes (/mm) Min-Max(Median) Mean±SD	200-6600(1400) 1491±817	400-2900(1100) 1197±521	200-3400(1100) 1170±628	300-4800(850) 1065±727	200-3200(1025) 1156±668	<0.001
Hemoglobin(g/dL) Min-Max(Median) Mean±SD	6.80-17.00(12.90) 12.88±1.79	7.80-14.40(11.50) 11.97±3.43	6.70-15.20(11.50) 11.42±1.76	7.50-14.90(10.45) 10.43±1.70	5.60-16.00(9.75) 9.81±2.11	<0.001
Platelets(/uL) Min-Max(Median) Mean±SD	13000-1630000(210000) 226554±111219	106000-859000(210000) 234324±112825	44000-768000(212000) 239155±110000	61000-748000(192000) 214981±102572	30000-687000(196500) 205025±98878	0.347

Continuation of Table 3

	Control group	G3a	G3b	G4	G5	P-value*
ALT(U/L) Min-Max(Median) Mean±SD	2.-270(24) 32.56±28.81	2-156(17) 23.98±23.61	4-146(17) 24.77±25.47	1-208(16) 30.05±42.71	3-386(14) 23.42±43.46	0.059
AST(U/L) Min-Max(Median) Mean±SD	3-193(29) 34.69±23.21	8-207(25) 30.67±24.47	5-558(27) 39.62±72.36	7-412(26) 40.07±58.54	7-529(19) 30.37±56.38	0.427
LDH(U/L) Min-Max(Median) Mean±SD	20-2900(258) 292.86±203.68	134-651(255) 282.63±102.15	138-842(268) 307.42±142.28	70-1196(274) 311.68±197.69	138.-1587(270) 313.03±193.71	0.808
Sodium(mmol/L) Min-Max(Median) Mean±SD	21-149(136) 134.91±10.07	126-142(136) 134.94±4.01	122-153(135) 135.52±5.86	121-145(134) 133.44±5.16	119-144(135) 134.54±4.62	0.819
Potassium(mmol/L) Min-Max(Median) Mean±SD	2.46-5.85(4.10) 4.09±0.50	2.90-6.40(4.47) 4.46±0.70	2.77-5.40(4.30) 4.23±0.61	2.90-6.88(4.60) 4.65±0.79	2.90-8.20(4.70) 4.81±0.95	<0.001
Albumin(g/L) Min-Max(Median) Mean±SD	17-48(36.50) 35.64±5.81	22-48(35) 34.16±5.85	21-43(34) 33.55±5.40	19-47(33) 32.55±5.42	22-44(31.50) 32.20±5.27	<0.001
CRP(mg/L) Min-Max(Median) Mean±SD	3.00-480.00(21.90) 47.35±61.33	3.00-334.00(45.90) 63.38±70.47	2.90-463.00(61.70) 90.02±84.05	3.00-281.00(63.10) 72.68±59.27	2.40-363.90(102.60) 112.42±90.82	<0.001
Procalcitonin(μg/L) Min-Max(Median) Mean±SD	0.02-3.32(0.07) 0.22±0.49	0.04-9.10(0.16) 0.52±1.45	0.06-8.50(0.28) 1.15±2.12	0.02-73.22(0.40) 3.26±13.03	0.11-236.00(0.88) 10.34±37.22	<0.001
D-dimer(μg/L) Min-Max(Median) Mean±SD	150-30000(575) 1329±2820.90	230-30000(1340) 2512.05±4356.86	190-20000(1195) 2046.78±2874.13	170-14320(1670) 3172.30±3700.23	300-26240(1900) 2912.31±3697.43	<0.001
Ferritin(μg/L) Min-Max(Median) Mean±SD	2.90- 10000.00(162.00) 380.26±764.67	6.20- 1500.00(205.75) 318.55±357.46	12.70- 1581.00(262.20) 461.66±482.46	19.40- 2000.00(277.40) 543.56±558.89	13.60- 2000.00(647.70) 835.26±625.21	<0.001

Abbreviations. eGFR, estimated glomerular filtration rate; ALT, Alanine transferase; AST, Aspartate transferase; LDH, Lactate dehydrogenase; CRP, C-reactive protein.

**One way ANOVA test*

Biochemical tests established to be associated with poor prognosis such as CRP, procalcitonin, D-dimer, and ferritin were significantly higher and lymphocyte count was significantly lower in CKD groups. Compared to the control group, the lymphocyte counts were significantly lower in G3a ($p<0.001$), G3b ($p=0.001$), G4($p<0.001$), and G5 ($p<0.001$). Compared to the control group, CRP values were significantly higher in G3b ($p=0.001$), G4($p<0.004$), and G5 ($p<0.001$). Compared to the control group, the procalcitonin values were significantly higher in G3b ($p=0.013$). D-dimer was significantly increased in G3a($p=0.029$), G4($p=0.001$), and G5 ($p<0.001$), and ferritin was significantly increased in G5 ($p<0.001$) when compared to the control group.

Correlation analysis revealed that eGFR was significantly positively correlated with lymphocyte count($r=0.21$, $p<0.001$) and significantly negatively correlated with CRP($r=-0.30$, $p<0.001$); procalcitonin($r=-0.17$, $p=0.002$); D-dimer($r=-0.19$, $p<0.001$); and ferritin ($r=-0.19$, $p<0.001$).

The duration of hospital stay was 7.03±6.64(1-52) days in the control group, 8.96±7.70(1-39) days in group G3a, 7.97±6.73(1-40) days in group G3b, 10.29±6.86(1-30) days in group G4, and 10.74±9.49(1-46) days in group G5. The difference showed a highly significant difference among groups($p<0.001$). The number of days of hospital admission was negatively correlated with eGFR values ($r=-0.20$, $p<0.001$) (Fig. 3).

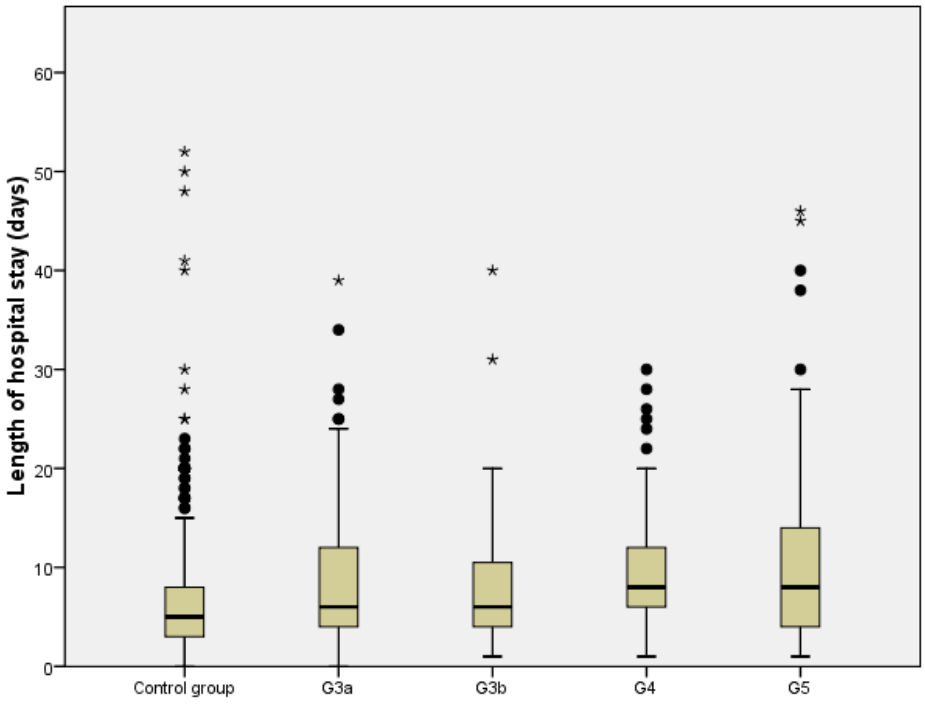
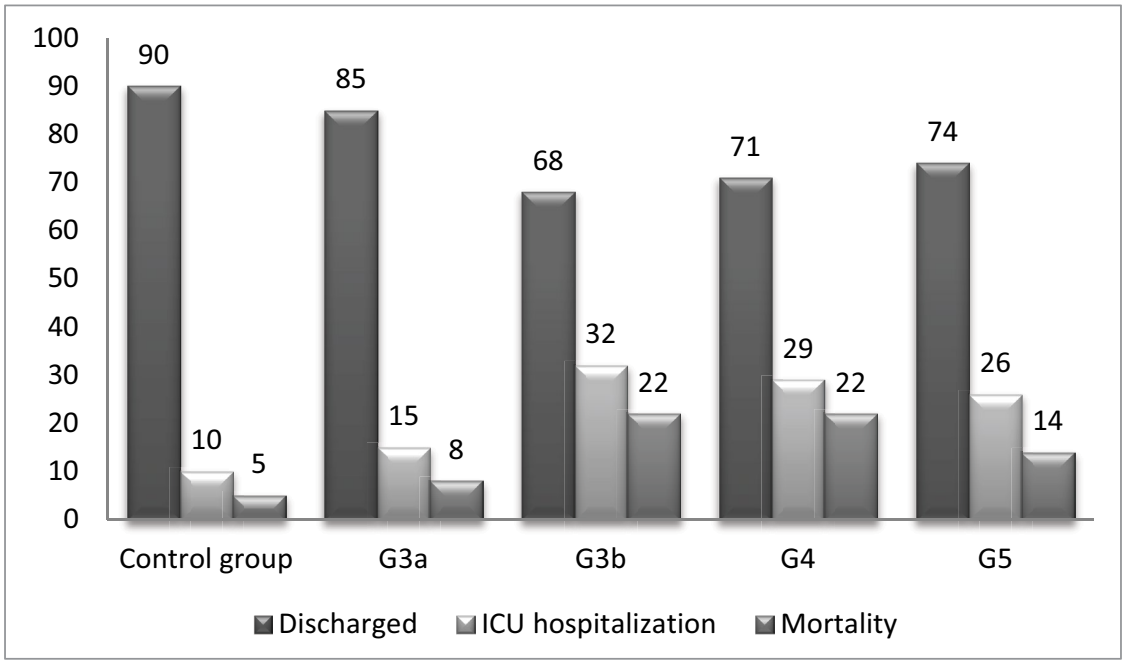


Fig. 3. The distribution of length of hospital stay in control and CKD groups.

The percentages of patients who were discharged from the hospital, who needed ICU hospitalization, and who were deceased are summarized in Figure 4.



Abbreviation. ICU: Intensive care unit.

Fig. 4. The distribution of the outcomes of the groups expressed in percentages

The rate of ICU admission and mortality was lowest in subjects with normal renal functions. The number of deaths tended to increase in patients with eGFR<45 ml/min/1.73 m^2.

The demographic characteristics and laboratory parameters of dialysis patients and CKD patients not receiving dialysis are compared in Table 4.

Table 4

The comparison of laboratory data in dialysis and non-dialysis groups

Dialysis	No	Yes	P-value*
Number of patients	198	86	
Female/male	100/98	40/46	
Age (years) Min-Max(Median) Mean±SD	 29-93(74) 72.02±12.72	 19-94(67) 61.26±15.81	<0.001
Lymphocytes (/mm^3) Min-Max(Median) Mean±SD	 200-4800(1100) 1155±620	 300-3200(1000) 1149±666	0.94
CRP (mg/L) Min-Max(Median) Mean±SD	 2.90-463.00(54.20) 75.80±74.13	 2.40-363.90(102.60) 112.04±89.81	0.001
Procalcitonin (μg/L) Min-Max(Median) Mean±SD	 0.02-236.00(0.24) 3.35±22.37	 0.07-27.88(1.46) 4.91±7.08	0.68
D-dimer (μg/L) Min-Max(Median) Mean±SD	 170-30000(1415) 2762.41±4258.03	 270-10210(1960) 2441.03±2014.30	0.52
Ferritin (μg/L) Min-Max(Median) Mean±SD	 6.20-2000.00(244.00) 403.75±442.69	 29.00-2000.00(794.45) 925.28±623.21	<0.001

Abbreviation. CRP, C-reactive protein
**T-test*

The mean number of days of hospital stay in patients undergoing dialysis, compared to other CKD patients was 9.94±8.30 and 9.43±7.94 days, respectively. The difference was not statistically significant (p=0.62). Of 86 dialysis patients, 21 (24.4%) needed ICU admission and 11 (12.8%) died. In non-dialysis CKD patients, ICU admission and mortality rates were 25.3%(n=50) and 16.7%(n=33), respectively. The differences between dialysis and non-dialysis groups were not statistically significant (p=0.88 for ICU admission and p=0.40 for mortality).

Discussion. Our analyses reveal that the degree of renal function deterioration predicts poor outcomes in COVID-19. Biochemical data proposed to be associated with poor COVID-19 outcomes, namely, lymphopenia, elevated CRP, procalcitonin, D-dimer, and ferritin levels were found to be more pronounced in patients with CKD. One novel finding in our study is that all CKD patients do not share the same risk for COVID-19 outcomes. As the stage of CKD increases, the risk of ICU admission and in-hospital mortality due to COVID-19 increases. We claim that eGFR values account for risk stratification in COVID-19.

CKD has a well-defined link with adverse outcomes in COVID-19. Especially CKD patients who have progressed to kidney failure have an increased risk of death from many causes, including cardiovascular disease (CVD) and infections [**14**]. The Global Burden of Disease collaboration identified that worldwide, CKD is the most prevalent risk factor for severe COVID-19. A recent meta-analysis has confirmed that CKD is associated with an increased risk of COVID-19 infection [**15**]. CKD is an independent risk factor for in-hospital death and poor prognosis of SARS-CoV-2 infection [**16**]. In the study by Yang et al, CKD that does not require renal replacement therapy(RRT) was found to be an independent risk factor for in-hospital death and poor prognosis. Compared to COVID-19 cases without CKD, those with CKD not requiring RRT showed a higher incidence of in-hospital mortality. COVID-19 patients with CKD not undergoing dialysis had higher D-dimer and neutrophil counts, and lower lymphocyte and hemoglobin values. COVID-19 patients with CKD who did not require RRT were prone to neutrophilia at the time of hospitalization and worse clinical outcomes than those without CKD [**17**].

In some European reports, the mortality rate in hemodialysis patients diagnosed with COVID-19 has been reported to be as high as 30-40% [**18,19**]. In-hospital mortality in our dialysis patients was much lower (12.8%). In previous reports, it has been stated that patients receiving dialysis treatment were more vulnerable to SARS-CoV-2, and those who were infected may exhibit worse clinical characteristics than the general COVID-19-infected population. A study found that 2% of patients undergoing dialysis had laboratory-confirmed COVID-19 tests, which is much higher than that of the general population [**2**]. In light of our findings, despite the negative prognostic impact of CKD on mortality, dialysis does not appear to worsen the picture.

It has been presumed that individual risk for COVID-19 patients with kidney abnormalities seems to

be higher in men with advanced age and a worse coagulation profile than those with normal kidney function [20].

The degree of renal impairment is found to be associated with a worse prognosis. In a meta-analysis conducted by Henry et al., higher mortality rates were observed in advanced stages of CKD, namely stages 3-5 [21]. In the study of Gök et al, the risk factors for mortality were determined as CKD stage 3-5, male gender, diabetes mellitus, hypertension, and malignancy. In addition, the mortality rate of patients with CKD stage 3-5 was significantly higher than that of patients with CKD stage 1-2 [22].

Williamson et al recently published that advanced CKD (stages 4 and 5), was among the conditions conveying the highest risk of death and notably higher than that conferred by all other factors. According to the analysis, dialysis and CKD represented two comorbidities associated with the highest risk of death from COVID-19 [9]. Results from the ERA-EDTA Registry further support the high mortality due to COVID-19 in dialysis patients. The 28-day mortality was 20.0% in 3285 patients receiving dialysis [23].

There are some limitations of our study. First, the follow-up period is limited to the duration of hospital stay, therefore long-term outcomes and mortality can not be expressed. Another fact is that the early stages of CKD, namely G1 and G2 were not included in the analyses. Only hospitalized patients have been recruited in the study, in other words, a more severe patient population has been involved. This study does not reflect data from patients who received outpatient treatment.

Conclusions. Physicians should be engaged in close monitoring of CKD patients with COVID-19, for timely detection of signs of disease progression. The presence and degree of CKD should be regarded as an important factor in risk prediction for COVID-19. Late-stage CKD patients hospitalized with COVID-19 require more awareness and close follow-up to reduce ICU admission and mortality rates. We recommend that COVID-19 patients with CKD should be managed closely to prevent severe disease and death.

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Author contributions.
E. Parmaksız: Data collection and analysis;
E. T. Parmaksız: The study design, writing.

References

1. *Petersen E, Koopmans M, Go U, Hamer DH, Petrosillo N, Castelli F, Storgaard M, Al Khalili S, Simonsen L.* Comparing SARS-CoV-2 with SARSCoV and influenza pandemics. Lancet Infect Dis. 2020; 20: e238–e244. doi: 10.1016/S1473-3099(20)30484-9.
2. *Xiong F, Tang H, Liu L, Tu C, Tian JB, Lei CT, Liu J, Dong JW, Chen WL, Wang XH, Luo D, Shi M, Miao XP, Zhang C.* Clinical Characteristics of and Medical Interventions for COVID-19 in Hemodialysis Patients in Wuhan, China. J Am Soc Nephrol. 2020; 31:1387-1397. doi: 10.1681/ASN.2020030354.
3. *Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al.* China Medical Treatment Expert Group for Covid-19. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020 Apr 30; 382(18):1708-1720. doi: 10.1056/NEJMoa2002032.
4. *Huang I, Pranata R.* Lymphopenia and severe coronavirus disease-2019 (COVID-19): systematic review and meta-analysis. J Intensive Care. 2020;8:36. doi: 10.1186/s40560-020-00453-4.
5. *Gallo Marin B, Aghagoli G, Lavine K, Yang L, Siff EJ, Chiang SS, et al.* Predictors of COVID-19 severity: A literature review. Rev Med Virol. 2021;31(1):1-10. doi:10.1002/rmv.2146.
6. *Cheng L, Li H, Li L, Liu C, Yan S, Chen H, Li Y.* Ferritin in the coronavirus disease 2019 (COVID-19): A systematic review and meta-analysis. J Clin Lab Anal. 2020 Oct;34(10):e23618. doi: 10.1002/jcla.23618.
7. *Hu R, Han C, Pei S, Yin M, Chen X.* Procalcitonin levels in COVID-19 patients. Int J Antimicrob Agents. 2020 Aug;56(2):106051. doi: 10.1016/j.ijantimicag.2020.106051.
8. Kidney Disease: Improving Global Outcomes CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Suppl. [Internet]. 2013; 3: 1–150. [cited 2021 April 08]. Available from: https://kdigo.org/wp-content/uploads/2017/02/KDIGO_2012_CKD_GL.pdf.
9. *Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, et al.* Factors associated with COVID-19-related death using OpenSAFELY. Nature 2020; 584: 430–436. doi:10.1038/s41586-020-2521-4.
10. *Clark A, Jit M, Warren-Gash C, Guthrie B, Wang HHX, Mercer SW, et al.* Centre for the Mathematical Modelling of Infectious Diseases COVID-19 working group. Global, regional, and national estimates of the population at increased risk of severe COVID-19 due to underlying health conditions in 2020: a modelling study. Lancet Glob Health. 2020;8: e1003–e1017. doi: 10.1016/S2214-109X(20)30264-3.
11. Chapter 1: definition and classification of CKD. Kidney Int Suppl. (2011); 2013;3:19 –62. doi: 10.1038/kisup.2012.64.

12. *Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI, et al.* A new equation to estimate glomerular filtration rate. Ann Intern Med. 150:604–612. doi: 10.7326/0003-4819-150-9-200905050-00006.
13. COVID-19 (SARS-CoV-2 ENFEKSİYONU) ERİŞKİN HASTA TEDAVİSİ. Republic of Turkey, Ministry of Health. [Internet]. [cited 2021 April 08]. Available from: https://covid19.saglik.gov.tr/TR-66926/eriskin-hasta-tedavisi.html.
14. *Ortiz A, Covic A, Fliser D, Fouque D, Goldsmith D, Kanbay M, et al.* Board of the EURECA-m Working Group of ERA-EDTA. Epidemiology, contributors to, and clinical trials of mortality risk in chronic kidney failure. Lancet. 2014; 383:1831–1843. doi: 10.1016/S0140-6736(14)60384-6.
15. *Brandon MH, Giuseppe L.* Chronic kidney disease is associated with severe coronavirus disease (COVID-19) infection. Int. Urol. Nephrol. 2020 Jun;52(6):1193-1194. doi: 10.1007/s11255-020-02451-9.
16. *Wang X, Fang X, Cai Z, Wu X, Gao X, Min J, Wang F.* Comorbid Chronic Diseases and Acute Organ Injuries Are Strongly Correlated with Disease Severity and Mortality among COVID-19 Patients: A Systemic Review and Meta-Analysis. Research 2020; 2020:2402961. doi: 10.34133/2020/2402961.
17. *Yang D, Xiao Y, Chen J, Chen Y, Luo P, Liu Q, et al.* COVID-19 and chronic renal disease: clinical characteristics and prognosis. QJM. 2020 Nov 1;113(11):799-805. doi: 10.1093/qjmed/hcaa258.
18. *Goicoechea M, Sánchez Cámara LA, Macías N, Muñoz de Morales A, Rojas ÁG, Bascuñana A, et al.* COVID-19: Clinical course and outcomes of 36 maintenance hemodialysis patients from a single center in Spain. Kidney Int. 2020; 98:27-34. doi: 10.1016/j.kint.2020.04.031.
19. *Scarpioni R, Manini A, Valsania T, De Amicis S, Albertazzi V, Melfa L, et al.* Covid-19 and its impact on nephropathic patients: the experience at Ospedale "Guglielmo da Saliceto" in Piacenza. G Ital Nefrol. [Internet]. 2020; 37:2020-vol2. [cited 2021 April 08]. Available from: https://pubmed.ncbi.nlm.nih.gov/32281756/.
20. *Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al.* Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int. 2020; 97(5):829-838. doi: 10.1016/j.kint.2020.03.005.
21. *Henry BM, de Oliveira MHS, Benoit S, Plebani M, Lippi G.* Hematologic, biochemical and immune biomarker abnormalities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chem Lab Med. 2020;58(7):1021–1028. doi: 10.1515/cclm-2020-0369.
22. *Gok M, Cetinkaya H, Kandemir T, Karahan E, Tuncer İB, Bukrek C, Sahin G.* Chronic kidney disease predicts poor outcomes of COVID-19 patients. Int Urol Nephrol. 2021; 53(9):1891-1898. Jan 4:1–8. doi:10.1007/s11255-020-02758-7.
23. *Jager KJ, Kramer A, Chesnaye NC, Couchoud C, Sánchez-Álvarez JE, Garneata L, et al.* Results from the ERA-EDTA Registry indicate a high mortality due to COVID-19 in dialysis patients and kidney transplant recipients across Europe. Kidney Int. 2020 Dec;98(6):1540-1548. doi: 10.1016/j.kint.2020.09.006.