

COVID-19 & Chronic Renal Disease: Clinical characteristics & prognosis

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Number of Tables: 4

Number of Figures: 0

Number of Supplementary Material: 1 (9 supplementary tables and 2 supplementary figures)

Word count for the article's text: 2494

Word count for abstract: 250

Abstract

Background: Patients on dialysis were susceptible to COVID-19 and were prone to severe clinical characteristics after infection; acute kidney injury was related to mortality in COVID-19 cases. Limited is known about the characteristics of COVID-19 patients with end-stage renal disease not requiring renal replacement therapy (RRT).

Aim: Evaluate clinical characteristics, course and outcomes of COVID-19 patients with chronic kidney disease (CKD) who did not require RRT and those on dialysis.

Design: A two-center retrospective study.

Methods: 836 adult patients with COVID-19 (24 CKD not on dialysis; 15 dialysis-dependent CKD) were included. The study includes no patients with renal transplantation. Risk factors were explored.

Results: CKD not requiring RRT is an independent risk factor for in-hospital death [adjusted OR (aOR) 7.35 (95%CI 2.41-22.44)] and poor prognosis [aOR 3.01 (95%CI 1.23-7.33)]. Compared to COVID-19 cases without CKD, those with CKD not requiring RRT showed similar percentage of initial moderate cases (75.00% vs. 73.65%) but higher incidence of in-hospital neutrophilia (50.00% vs. 27.30%) or death (50.00% vs. 9.03%). The odds ratio of dialysis associated to mortality in CKD patients was 2.00 (95%CI 0.52-7.63), suggesting COVID-19 patients with dialysis-dependent CKD were at greater risk of in-hospital death. For COVID-19 patients with CKD not requiring RRT, statins reduced the risk of neutrophilia [OR 0.10 (95%CI 0.01-0.69)] while diuretics increased the risk of neutrophilia [OR 15.4 (95%CI 1.47-160.97)], although both showed no association to mortality.

Conclusion: COVID-19 patients with CKD presented high incidence of neutrophilia, poor prognosis and in-hospital death, with dialysis patients being more vulnerable.

Keywords: chronic kidney disease, COVID-19, dialysis, neutrophils, inflammation

Introduction

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),¹ primarily manifests as an acute respiratory illness, but it can affect multiple organs including kidney;² in cases COVID-19 may also be presented asymptotically without organ manifestations.³ Kidney was reported with high expression of ACE2, an important target of SARS-CoV-2;^{4,5} moreover, SARS-CoV-2 has been identified in urine and kidney of COVID-19 patients, suggesting kidney as a target of this coronavirus.^{6,7}

Amounting evidence has indicated correlation between kidney abnormalities and COVID-19. Acute kidney injury (AKI) occurred in 5.1% of 701 COVID-19 patients, and the risk of mortality increased 4-fold among patients with stage 3 AKI.⁸ COVID-19 patients with renal involvement showed higher overall mortality than those without (11.2% vs.1.2%).⁹ Patients receiving dialysis therapy were more vulnerable to SARS-CoV-2, and those who infected may present worse clinical characteristics than general COVID-19-infected population.^{3,10,11} The morbidity of COVID-19 in 7154 patients undergoing hemodialysis was 4 times higher than that of the general population during the same period.³ Of 36 hospitalized maintenance hemodialysis patients from Spain who were diagnosed with COVID-19, 50% underwent radiological worsening during the first week after admission and 30.5% died,¹⁰ and high mortality (41%) was also reported in another cohort from Italy.¹¹ CKD was among common comorbidities in COVID-19 patients.¹²⁻¹⁴ However, when it comes to the specific clinical characteristics of COVID-19 patients with underlying CKD not requiring renal replacement therapy (RRT), much remains unclear.

In this two-center retrospective cohort study, we describe the clinical characteristics, course and

outcomes of patients with COVID-19 and CKD not requiring RRT (CKD not on dialysis), and compared them to those of COVID-19 patients with dialysis-dependent CKD and of those without CKD. Patients with renal transplantation were not included. We also present information about in-hospital medications and laboratory finding changes among CKD patients not requiring RRT and among those on dialysis, with association to their clinical outcomes.

Materials and Methods

Study design and participants

836 patients aged 20 to 99 were included in this cohort, who were admitted in two tertiary comprehensive hospitals (437 from the Central Hospital of Wuhan and 399 from Wuhan Third Hospital) in China from January 1, 2020, and enrolled with a definite outcome (discharged or died in hospital); the data cutoff was March 23, 2020. Both hospitals were designated hospitals to treat moderate, severe and critical COVID-19 patients. Mild cases, which accounted for the majority of COVID-19 cases and were cared in Fangcang shelter hospitals,¹⁵ were not included, thus this study represents the severe end of COVID-19.

All patients were diagnosed as confirmed COVID-19 according to the Diagnosis and Treatment Plan for COVID-19 (Seventh Edition).¹⁶ CKD ascertainment was based on medical records of CKD diagnosis according to KDIGO CKD guidelines¹⁷ with 39 patients identified. There is no patient with renal transplantation. Of the 39 COVID-19 patients with CKD, 24 did not require RRT, among whom 20 were category G3-G5, 1 was category G1, 2 were category G2, and 1 was not specified in the medical record; the other 15 COVID-19 patients with CKD were category

G3-G5 and were on dialysis. Patients not requiring RRT at admission did not receive RRT during hospitalization.

All clinical investigations were conducted in accordance with the guidelines of the Declaration of Helsinki. The Research Ethics Commissions of both hospitals approved this study [2020-76 (April 29, 2020) and KY2020-20 (March 8, 2020)] and granted waiver of informed consent from study participants due to the study's retrospective design.

Data collection and definitions

The demographics, baseline characteristics, laboratory findings, treatment, and outcome data were extracted from electronic medical records and reviewed by co-author Dr. Luo and two other physicians (Drs. B. Shu and G. Li). Estimated glomerular filtration rate (eGFR) was calculated by the CKD-EPI equation.¹⁸ COVID-19 were defined as 4 grades,¹⁶ this cohort includes moderate, severe and critical cases. Fever was defined as axillary temperature of at least 37.3°C. Poor prognosis included progress to severe or critical illness, and in-hospital death. Lymphopenia was defined as number of lymphocytes $<1.0 \times 10^9/L$, neutrophilia was defined as neutrophil counts $\geq 7.5 \times 10^9/L$.

Statistical analysis

Categorical and continuous variables were respectively described as number (%) and median [interquartile range (IQR)]. Characters between groups were compared using χ^2 test, Fisher exact test, t-test or Mann-Whitney U test as appropriate. Logistic regression was used for exploring

risk factors. CKD or CKD not requiring RRT, and the other 6 variables [age, gender, neutrophils, D-dimer, eGFR, C-reactive protein (CRP)] were chosen as seven variables in multivariable regression models for all patients. For COVID-19 patients with CKD, risk factors were explored using univariable regression due to limited number of cases. 2-sided P value less than 0.05 was considered statistically significant. Analyses were performed with SPSS (version 22.0) and GraphPad Prism 8.0.

Results

Demographics, clinical characteristics and outcomes of the study population

Women accounted for 51.56% of the study population. 39 of the 836 confirmed COVID-19 cases had pre-existing CKD, 15 of the 39 patients were on dialysis while the other 24 were not. Compared to COVID-19 patients without CKD, fewer percentage of patients presented fever on admission in CKD cases (Table 1). In COVID-19 patients with CKD requiring no RRT, who showed higher prevalence of other comorbidities than those without CKD, hypertension was the leading comorbidity [15 (62.50%) patients]. The median age [73.5 (IQR 64.5-86.6) years] of COVID-19 patients with CKD not requiring RRT were older than that of patients on dialysis [58.0 (47.0-68.0) years] or without CKD [61.0 (45.0-69.0) years]. Notably, similar proportions of patients with CKD not requiring RRT and those without CKD were diagnosed as moderate COVID-19 cases on admission (75.00% vs. 73.65%, $P = 1.000$), which were much higher than the percentage of initial moderate cases (40.00%) in COVID-19 patients with dialysis-dependent CKD. However, in-hospital mortality (50.00% vs. 66.67%, $P = 0.343$) and poor prognosis rate

(83.33% vs. 80.00%, $P = 1.000$) of CKD cases not on dialysis vs. dialysis cases were similar, and were all significantly higher than those of COVID-19 patients without CKD (in-hospital mortality, 9.03%; poor prognosis rate, 39.40%; Table 1).

Initial laboratory findings

Compared to COVID-19 patients without CKD, the values of D-dimer and neutrophils of COVID-19 patients with CKD not on dialysis were higher, and lymphocytes and hemoglobin were lower (Table 2). Dialysis patients with COVID-19, comparing to the CKD cases not requiring RRT, suffered from even severe kidney abnormalities, anemia, and infection, and showed abnormally increased creatine kinase and lactate dehydrogenase (LDH) on admission (Table 2).

Characteristics according to age and gender subgroups

The percentages of initial critical cases (33.33% vs. 3.14%, $P = 0.016$) were higher in COVID-19 patients with CKD not on dialysis than those without CKD in <65 group (Supplementary Table S1). In ≥ 65 group, COVID-19 patients with CKD not on dialysis showed higher prevalence of poor prognosis than those without CKD (Supplementary Table S1).

Men accounts for the majority of COVID-19 cases with CKD not requiring RRT (75%) and of those on dialysis (66.67%). Within male but not female COVID-19 patients, CKD cases not on dialysis vs. cases without CKD had significantly higher poor prognosis rate, larger percentage of hypertension and diabetes, and lower albumin (Supplementary Table S2). In addition, the

differences of laboratory findings between COVID-19 patients with CKD that on and not on dialysis were overall age- and gender-independent.

Risk factors

CKD is an independent risk factor for either in-hospital death or poor prognosis (Supplementary Table S3). Furthermore, patients with CKD not requiring RRT had greater risk for in-hospital death [adjusted OR (aOR) 7.35 (95%CI 2.41-22.44), $P < 0.001$] and poor prognosis [aOR 3.01 (95%CI 1.23-7.33), $P = 0.016$]. Besides, patients ≥ 65 years old and men were prone to higher mortality, while higher initial neutrophils and CRP were associated to increased odds of in-hospital death and poor prognosis among the study population (Table 3). Lineal models showed similar results when adjusting for study center (Supplementary Table S4).

Lymphopenia and neutrophilia during hospitalization

Univariable analyses suggested that low initial lymphocytes [OR 0.11 (95%CI 0.02-0.73), $\times 10^9/L$, $P = 0.022$] was significantly associated to higher odds of in-hospital death within COVID-19 patients with CKD (Supplementary Table S5). We further analyzed the incidence of in-hospital lymphopenia or neutrophilia that associated with cytokine storm and COVID-19 severity.^{2,19} Patients with CKD are prone to be lymphopenic. At admission, the proportion of patients presenting lymphopenia was 43.77% amongst those without CKD, and 71.79% amongst those with CKD (62.50% of CKD cases not requiring RRT and 86.67% of dialysis cases). During hospitalization, 51.57% of COVID-19 patients without CKD, and over 90% of those with CKD

(95.83% of CKD cases not requiring RRT and 93.33% of dialysis cases) underwent lymphopenia. Moreover, the prevalence of in-hospital neutrophilia was smaller in COVID-19 patients without CKD (27.30%) than in CKD cases not requiring RRT (50.00%) and dialysis cases (46.67%) (Supplementary Table S6).

Laboratory findings during hospitalization

Univariable regression among COVID-19 patients with CKD showed the odds ratio of dialysis associated to mortality was 2.00 (95%CI 0.52-7.63, $P = 0.310$; Supplementary Table S5), suggesting COVID-19 patients with dialysis-dependent CKD were at greater risk of in-hospital death than those with CKD not on dialysis. Notably, one week after admission, worsening changes in neutrophils and LDH were observed in COVID-19 patients with dialysis-dependent CKD, but not in those with CKD not requiring RRT (Supplementary Figure S1). For both groups, no significant differences were observed between initial and one-week-after-admission test results in other laboratory indices (Supplementary Figure S2).

On day 7 after admission, non-survivors vs. survivors with CKD not requiring RRT showed significantly lower concentration of platelets and elevated level of creatine kinase (Table 4). For dialysis patients with COVID-19, lymphocytes level on admission were significantly lower in non-survival group than in survival group (Table 4). Other one-week-after-admission laboratory findings were provided in Supplementary Table S7.

Medications

Among COVID-19 patients with CKD not on dialysis, usages of glucocorticoid, antibiotics, blood glucose-lowering drugs, statins, diuretics and calcium antagonists showed no significant difference between survivors and non-survivors (Table 4). Univariable regression suggested that most of the analyzed medications had no association with in-hospital mortality, except for usage of beta blocker which was a risk factor, however, whether this was due to effect of beta blocker or to characteristics of the patients for whom it was prescribed is unclear (Supplementary Table S8). None of the 3 patients with CKD not requiring RRT who were taking angiotensin-converting-enzyme inhibitor or angiotensin receptor blocker, which may increase the level of ACE2,²⁰ underwent in-hospital neutrophilia or death (Table 4). In addition, among patients with COVID-19 and CKD that not on dialysis, 8 (66.67%) of patients without neutrophilia and 2 (16.67%) of those who underwent in-hospital neutrophilia used statins, and usage of statins reduced the risk of developing in-hospital neutrophilia [OR 0.10 (95% 0.01-0.69), $P = 0.020$]. Moreover, usage of diuretics increased the risk of developing in-hospital neutrophilia [OR 15.4 (95%CI 1.47-160.97), $P = 0.22$; Supplementary Table S9].

Discussion

Information about patients with CKD not requiring RRT who infected with COVID-19 is limited. This two-center retrospective study identified that CKD not requiring RRT is an independent risk factor for in-hospital death and poor prognosis of patients with COVID-19 (Table 3), which is consistent to previous meta-analyses revealing the association of CKD and severe COVID-19 illness.^{14, 21} Besides, age ≥ 65 years old, higher neutrophils, CRP and men were associated to

higher mortality, echoing to previous reports regarding COVID-19.^{22,23}

The incidence of fever on admission were lower in COVID-19 patients with either CKD not requiring RRT or dialysis-dependent CKD than in those without CKD (Table 1), and similar findings were observed in dialysis population, which may be related to their reduced immune function.^{3,10,24} COVID-19 patients with CKD not requiring RRT vs. those with dialysis-dependent CKD presented overall less severe clinical features, however, no significant difference in poor prognosis rate or in-hospital mortality was identified between these two groups, which may be partly attributed to the older age of the CKD population who were not on dialysis (Table 1).

Although patients with CKD not requiring RRT, compared to patients without CKD, had similar proportions of moderate cases on admission, they showed significantly higher incidence of in-hospital death and poor prognosis (Table 1). This may be explained by our findings that lymphopenia and neutrophilia, which were associated to cytokine storm as well as worse clinical progress in COVID-19 cases,^{19,23} occurred more commonly in patients with CKD not requiring RRT than in those without CKD (Supplementary Table S6). Notably, among CKD cases not requiring RRT, non-survivors comparing to the survivors presented significantly increased creatine kinase after one-week hospitalization (Table 3), suggesting worse multi-organ damage which also relate to inflammation.^{25,26} These findings together indicated that the disease tend to progress to more severe illness in COVID-19 patients with CKD not requiring RRT, and in clinical management of this kind of patients, attention needs to be paid to laboratory parameters relating to inflammation, such as lymphocytes, neutrophils and creatine kinase.

After 7-day hospitalization, patients on dialysis, but not those with CKD requiring no RRT, presented significant increases in LDH and neutrophils, indicating they were prone to more severe status. In addition, lymphopenia was common in dialysis patients, and non-survivors in CKD patients on dialysis presented significantly lower lymphocytes on admission than survivors, echoing to another study on dialysis patients which suggested lymphopenia and high LDH at 7 days after clinical onset as predictors of mortality.¹⁰

Interestingly, although showing no association with mortality, usage of diuretics increased the risk of in-hospital neutrophilia for patients with CKD and COVID-19 who were not on dialysis; whereas statins reduced the risk of in-hospital neutrophilia, which may be due to its anti-inflammatory and immunomodulatory activities,²⁷ echoing to a recent finding that statin use is associated with lower risk of mortality in COVID-19 patients.²⁸ However, investigations on larger population are still necessary to confirm these effects. Moreover, consistent to recent consensus,^{29,30} our data suggest no evidence for the need of discontinuing the chronic drugs that patients took before admission due to chronic diseases.

Strengths of our study include a cohort of CKD patients with COVID-19 from two study centers, and a detailed presentation focusing on clinical characters, course and outcomes of COVID-19 patients with underlying CKD who were not on dialysis. There are also limitations. Our results only presented short-term outcomes in this cohort, and it was not a randomized, controlled trial, the analyses were based on clinically available data, rather than protocol-driven timed measurements.

In conclusion, CKD not requiring RRT as an independent risk factor for in-hospital death and

poor prognosis in COVID-19 patients. COVID-19 patients with CKD not requiring RRT compared to those without CKD were prone to neutrophilia during hospitalization and worse clinical outcomes. Among patients with CKD and COVID-19, dialysis-dependent cases vs. CKD cases that not on dialysis presented higher risk of in-hospital death, more malignant laboratory findings on admission, and worsen changes of neutrophilia and LDH within first week after admission. For patients with CKD and COVID-19, neutrophils, creatine kinase and lymphocytes were noteworthy laboratory indices when treating those who were not on dialysis.

Funding

None.

Acknowledgements

We thank Tongji-Rongcheng Center for Biomedicine, Huazhong University of Science and Technology for support. We also appreciate Dr. B. Shu and Dr. G. Li (Department of Urological Surgery, The Central Hospital of Wuhan) for their help in extracting and reviewing electronic medical records.

Conflict of interest

The authors declare that they have no conflicts of interest.

Authors' contributions

A.P. and C.B. designed the study; D.Y., Y.X., J.C., P.L., Q.L., A.D., C.B., and A.P. extracted the data; D.Y., Y.X., J.C., Y.C., B.C., A.P., C.Y., M.X., Y.Z., X.L., and H.C. analyzed the data; D.Y., Y.X., Y.C., K.H., C.B., and A.P. drafted the paper; all authors revised the paper and approved the final version of the manuscript

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Table 1. Demographic and baseline characteristics of COVID-19 patients with non-CKD and CKD (not on dialysis or on dialysis)

	Non-CKD	CKD not on dialysis	<i>P</i> value	CKD on dialysis	<i>P</i> value	*<i>P</i> value
No. of Patients	797	24		15		
Age, years	61.0 (45.0-69.0)	73.5 (64.5-86.0)	<0.001	58.0 (47.0-68.0)	0.984	0.002
Hospital stay, days	18.0 (15.0-25.5)	25.5 (22.3-47.8)	<0.001	12.0 (7.0-18.0)	0.008	<0.001
Gender						
Male	377 (47.30%)	18 (75.00%)	0.011	10 (66.67%)	0.192	0.718
Female	420 (52.70%)	6 (25.00%)		5 (33.33%)		
Initial common symptoms						
Fever on admission	455 (57.09%)	2 (8.33%)	<0.001	5 (33.33%)	0.112	0.085
Cough	555 (69.64%)	10 (41.67%)	0.005	11 (73.33%)	1.000	0.098
Fatigue	310 (38.9%)	12 (50.00%)	0.293	5 (33.33%)	0.792	0.343
Dyspnea	162 (20.33%)	2 (8.33%)	0.197	4 (26.67%)	0.523	0.180
Myalgia	94 (11.79%)	4 (16.67%)	0.516	0 (0.00%)	0.240	0.146
Sputum	259 (32.50%)	6 (25.00%)	0.513	4 (26.67%)	0.784	1.000
Diarrhoea	163 (20.45%)	2 (8.33%)	0.197	4 (26.67%)	0.525	0.180
Nausea or vomiting	85 (10.66%)	2 (8.33%)	1.000	1 (6.67%)	1.000	1.000
Comorbidities						
Hypertension	268 (33.63%)	15 (62.50%)	0.005	12 (80.00%)	<0.001	0.305
Diabetes	115 (14.43%)	9 (37.50%)	0.005	2 (13.33%)	1.000	0.150
Cardiovascular disease	78 (9.79%)	13 (54.17%)	<0.001	3 (20.00%)	0.182	0.049
Nervous system disease	36 (4.52%)	9 (37.50%)	<0.001	0 (0.00%)	1.000	0.007
Chronic lung disease	19 (2.38%)	8 (33.33%)	<0.001	0 (0.00%)	1.000	0.015
Tumor	20 (2.51%)	3 (12.50%)	0.026	0 (0.00%)	1.000	0.271
Initial disease severity status						

Moderate	587 (73.65%)	18 (75.00%)	1.000	6 (40.00%)	0.007	0.044
Severe	160 (20.08%)	2 (8.33%)	0.198	4 (26.67%)	0.519	0.180
Critical	50 (6.27%)	4 (16.67%)	0.066	5 (33.33%)	0.002	0.266
Clinical outcomes						
In-hospital death	72 (9.03%)	12 (50.00%)	<0.001	10 (66.67%)	0.000	0.343
Poor prognosis	314 (39.40%)	20 (83.33%)	<0.001	12 (80.00%)	0.002	1.000

Data were n (%) or median (IQR). *CKD not on dialysis vs CKD on dialysis. Data were collected on admission, except for clinical outcomes. CKD, chronic kidney disease.

Table 2. Initial laboratory findings of COVID-19 patients with non-CKD and CKD (not on dialysis or on dialysis)

	Non-CKD	CKD not on dialysis	<i>P</i> value	CKD on dialysis	<i>P</i> value	* <i>P</i> value
Biochemical						
Blood urea nitrogen, mmol/L	4.20 (3.26-5.38)	9.26 (6.28-15.45)	<0.001	31.40 (27.83-45.9)	<0.001	<0.001
Serum creatinine, μmol/L	66.15 (52.13-78.38)	115.10 (95.88-159.40)	<0.001	1311.70 (1039.20-1585.30)	<0.001	<0.001
Blood uric acid, μmol/L	256.00 (207.00-324.00)	350.00 (258.25-473.25)	<0.001	561.00 (407.00-601.00)	<0.001	0.030
eGFR, ml/min per 1.73 m ²	95.93 (83.09-108.07)	47.96 (29.17-63.6)	<0.001	3.06 (2.09-3.99)	<0.001	<0.001
Hemoglobin, g/L	126.00 (116.00-137.00)	113.50 (96.25-132.00)	0.013	96.00 (78.00-122.00)	<0.001	0.066
Albumin, g/L	37.70 (34.30-41.50)	33.50 (29.8-37.00)	0.001	38.10 (34.10-39.80)	0.781	0.038
ALT, U/L	22.40 (14.43-36.08)	17.90 (10.00-27.40)	0.033	14.30 (10.00-35.00)	0.182	0.930
AST, U/L	25.00 (18.40-37.08)	26.30 (19.15-36.20)	0.772	17.00 (13.90-38.00)	0.158	0.212
Total bilirubin, μmol/L	9.20 (6.93-12.50)	6.30 (3.40-10.10)	0.012	4.00 (2.70-7.00)	<0.001	0.107
Alkaline phosphatase, U/L	56.50 (44.75-70.00)	55.00 (39.25-70.75)	0.603	71.00 (60.00-129.50)	0.014	0.083
Creatine kinase, U/L	76.00 (46.00-136.00)	97.00 (48.25-117.45)	0.766	218.10 (107.00-367.00)	0.001	0.007
LDH, U/L	206.00 (165.00-282.00)	229.50 (162.75-279.50)	0.843	257.00 (183.00-353.00)	0.137	0.258
Glucose, mmol/L	5.57 (4.83-7.08)	7.46 (5.19-8.39)	0.018	5.51 (4.94-6.55)	0.753	0.081
TG, mmol/L	1.20 (0.86-1.66)	1.26 (0.91-2.01)	0.657	1.53 (1.22-2.01)	0.162	0.555
TC, mmol/L	3.94 (3.38-4.56)	3.37 (2.8-4.18)	0.036	3.34 (2.49-4.26)	0.034	0.528
HDL-C, mmol/L	1.00 (0.82-1.21)	0.9 (0.74-1.11)	0.114	0.81 (0.55-0.88)	0.004	0.183
LDL-C, mmol/L	2.32 (1.85-2.78)	1.87 (1.47-2.31)	0.010	1.84 (1.18-2.71)	0.058	0.951
Hematologic, ×10⁹/L						
White blood cells	4.97 (3.80-6.55)	5.93 (4.64-7.45)	0.063	4.80 (3.70-5.20)	0.347	0.066
Neutrophils	3.21 (2.30-4.70)	4.50 (2.77-6.22)	0.020	3.69 (2.59-4.46)	0.695	0.182
Lymphocytes	1.06 (0.77-1.48)	0.94 (0.66-1.07)	0.049	0.36 (0.28-0.85)	<0.001	0.005
Monocytes	0.36 (0.26-0.49)	0.33 (0.25-0.50)	0.593	0.26 (0.20-0.44)	0.092	0.338
Platelets	189.00 (146.00-255.00)	165.00 (122.75-210.25)	0.065	120.00 (90.00-182.00)	0.001	0.091
Coagulation function						

APTT, s	28.90 (25.60-32.53)	32.05 (26.40-38.58)	0.110	34.60 (31.05-55.78)	<0.001	0.113
PT, s	11.60 (11.10-12.20)	12.00 (10.93-12.60)	0.431	12.55 (11.60-13.28)	0.006	0.120
D-dimer, mg/L	0.59 (0.30-1.32)	1.09 (0.66-3.30)	0.003	0.93 (0.51-1.68)	0.127	0.313
Infection-related indices						
Procalcitonin, ng/mL, ≥ 0.05 , < 0.5	301 (37.77%)	15 (62.50%)	0.018	4 (26.67%)	0.434	0.048
Procalcitonin, ng/mL, ≥ 0.5	33 (4.14%)	5 (20.83%)	0.004	10 (66.67%)	<0.001	0.007
CRP, mg/L	15.12 (2.60-50.00)	29.00 (3.60-81.41)	0.113	61.75 (13.42-145.38)	0.002	0.153

Data were n (%) or median (IQR). *CKD not on dialysis vs CKD on dialysis. Data were collected on admission. Abbreviations: CKD, chronic kidney disease; eGFR, estimated globular filtration rate; ALT, Alanine aminotransferase; AST, Aspartate aminotransferase; LDH, Lactate dehydrogenase; TG, Total triglycerides; TC, Total cholesterol; HDL-C, High-density lipoprotein cholesterol; LDL-C, Low-density lipoprotein cholesterol; APTT, Activated partial thromboplastin time; PT, Prothrombin time; CRP, C-reactive protein.

Table 3. Multivariable logistic regression for risk factors associated with in-hospital death and poor prognosis of the study population

	Risk factors associated with in-hospital death		Risk factors associated with poor prognosis	
	Multivariable OR (95% CI)	<i>P</i> value	Multivariable OR (95% CI)	<i>P</i> value
Age, ≥65 vs <65	3.26 (1.79, 5.94)	<0.001	1.01 (0.72, 1.41)	0.961
Gender, Female vs Male	0.36 (0.20, 0.65)	0.001	0.65 (0.48, 0.88)	0.006
Neutrophils, ×10 ⁹ /L	1.17 (1.07, 1.27)	<0.001	1.07 (1.01, 1.14)	0.026
D-dimer, mg/L	1.05 (1.00, 1.09)	0.036	1.02 (0.99, 1.05)	0.293
CRP, mg/L	1.01 (1.01, 1.02)	<0.001	1.01 (1.00, 1.01)	<0.001
eGFR, ml/min per 1.73 m ²	0.97 (0.96, 0.98)	<0.001	0.99 (0.98, 1.00)	0.004
CKD not on dialysis, Yes vs No	7.35 (2.41, 22.44)	<0.001	3.01 (1.23, 7.33)	0.016

Data were odds ratio (95% confidence intervals). Poor prognosis included progress to severe or critical illness, and in-hospital death. Age, gender, neutrophils, D-dimer, CRP, eGFR and CKD (not on dialysis) were chosen variables for the multivariable model of all COVID-19 cases. 94 of all COVID-19 patients (22 with CKD, 12 with CKD and not on dialysis) underwent in-hospital death. 346 of all COVID-19 patients (32 with CKD, 20 with CKD and not on dialysis) underwent poor prognosis. *P* < 0.05 were considered significant. Abbreviations: OR, Odds ratio; CI, Confidence interval; CKD, chronic kidney disease; eGFR, estimated globular filtration rate; CRP, C-reactive protein.

Table 4. Laboratory findings on admission and one week after admission, and medications of CKD patients with COVID-19 (not on dialysis or on dialysis) according to survival and non-survival subgroups.

	CKD not on dialysis			CKD on dialysis		
	Survivors	Non-survivors	<i>P</i> value	Survivors	Non-survivors	<i>P</i> value
No. of cases	12	12		5	10	
Laboratory finding , Median (IQR)						
Lymphocytes, ×10 ⁹ /L						
On admission	0.96 (0.83-1.09)	0.82 (0.49-1.07)	0.319	0.86 (0.61-1.23)	0.32 (0.27-0.40)	0.005
Day 7	0.93 (0.77-1.18)	0.66 (0.38-1.38)	0.400	0.56 (0.26-0.97)	0.35 (0.15-0.51)	0.230
Platelets, ×10 ⁹ /L						
On admission	165.00 (138.75-200.5)	172.50 (102.75-262.75)	1.000	120.00 (88.00-208.50)	131.50 (99.25-179.50)	0.950
Day 7	199.00 (168.50-309.25)	139.00 (105.50-197.50)	0.028	NA	151.00 (111.00-225.00)	NA
Creatine kinase, U/L						
On admission	81.50 (35.08-104.00)	104.00 (66.25-161.65)	0.266	107.00 (57.50-256.05)	309.50 (133.95-426.40)	0.075
Day 7	26.00 (24.00-75.00)	223.20 (172.00-673.70)	0.026	NA	256.00 (60.00-652.00)	NA
In-hospital medications						
Metformin	2 (16.67%)	1 (8.33%)	1.000	0 (0.00%)	0 (0.00%)	NA
Insulin	4 (33.33%)	5 (41.67%)	1.000	1 (20.00%)	5 (50.00%)	0.580
Calcium Antagonists	7 (58.33%)	6 (50%)	1.000	2 (40.00%)	4 (40.00%)	1.000
Beta blocker	1 (8.33%)	7 (58.33%)	0.027	2 (40.00%)	2 (20.00%)	0.560
ACEI/ARB	3 (25.00%)	0 (0.00%)	0.217	0 (0.00%)	3 (30.00%)	0.505
Heparins	8 (66.67%)	10 (83.33%)	0.640	5 (100.00%)	10 (100.00%)	NA
Statins	5 (41.67%)	5 (41.67%)	1.000	0 (0.00%)	0 (0.00%)	NA
Antibiotics	10 (83.33%)	9 (75.00%)	1.000	4 (80.00%)	8 (80.00%)	1.000
Glucocorticoids	10 (83.33%)	10 (83.33%)	1.000	2 (40.00%)	5 (50.00%)	1.000
Diuretics	7 (58.33%)	9 (75.00%)	0.667	1 (20.00%)	3 (30.00%)	1.000

Data were n (%) or median (IQR). NA, not available due to lacking of laboratory test results for analysis. Abbreviations: CKD, chronic kidney disease; AST, Aspartate aminotransferase; LDH, Lactate dehydrogenase. * Significant difference between values at admission and one week after on admission.

A list of definitions

CKD	Chronic kidney disease
COVID-19	Coronavirus disease 2019
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
AKI	Acute kidney injury
ALT	Alanine aminotransferase
APTT	Activated partial thromboplastin time
AST	Aspartate aminotransferase
CRP	C-reactive protein
eGFR	Estimated globular filtration rat
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
LDH	Lactate dehydrogenase
PT	Prothrombin time
RRT	Renal replacement therapy
TC	Total cholesterol
TG	Total triglycerides