Clinical and Radiologic Characteristics of COVID-19 in Patients With CKD

Alireza Abrishami,[1] Nastaran Khalili,[2] Nooshin Dalili,[3,4] Reza Khaleghnejad Tabari,[5] Reza Farjad,[1] Shiva Samavat,[3,4] Ali Neyriz Naghadehi,[1] Hamidreza Haghighatkhah,[6] Mohsen Nafar,[7] Morteza Sanei-Taheri[8,9]

[1]Department of Radiology, Shahid Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Nephrology, Shahid Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Chronic Kidney Disease Research Center, Shahid Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[5]Gandi hospital, Tehran, Iran
[6]Department of Diagnostic Imaging, Shohada-e-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[7]President of Iranian Society of Nephrology, Tehran, Iran
[8]Department of Radiology, Shohada-E-Tajrish Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[9]President of Iranian Society of Radiology, Tehran, Iran

Keywords. chronic kidney disease; COVID-19; computed tomography; mortality

Introduction. In this study, we aimed to evaluate the presentation and outcome of COVID-19 in patients with chronic kidney disease (CKD).
Methods. We included 43 patients with a past history of CKD and confirmed diagnosis of COVID-19. Patients were evaluated for demographic characteristics, clinical and laboratory data and findings of initial chest computed tomography (CT) and were followed until either death or discharge occurred. Then, study variables were compared based on final outcome and stage of CKD.
Results. Mean age ± SD of patients was 60.65 ± 14.36 years; 65.1% were male. Five of 43 patients (11.6%) died on follow-up and the rest were discharged. Disease outcome did not differ across CKD stages ($P > .05$). More than half of the patients (58.1%) presented with severe disease on admission. Clinical symptoms were similar to those of non-CKD individuals. Mean duration of hospitalization was higher in those who died, although not significant (16.6 ± 8.38 vs. 11 ± 6.26, $P > .05$). The only hematologic parameter that significantly differed between survivors and non-survivors was lactase dehydrogenase level ($P < .05$). Ground-glass opacification and reticular pattern were the most frequent patterns on CT and pleural effusion existed in about one-fifth of all patients. A greater lower zone score was noted in deceased patients ($P < .05$).
Conclusion. Patients with CKD are vulnerable to a more severe form of COVID-19 and experience a higher mortality rate than the general population; however, higher CKD stage is not related to worse prognosis or different imaging manifestation compared with lower stage.

IJKD 2020;14:267-77
www.ijkd.org

Original Paper

INTRODUCTION

In December 2019, an outbreak of pneumonia caused by a novel beta-coronavirus, currently named as the "severe acute respiratory syndrome coronavirus 2" (SARS-CoV-2), occurred in Wuhan, China. The disease caused by this virus was subsequently named Coronavirus Disease 2019 (COVID-19).[1] The most common clinical presentations of COVID-19 include fever, cough, dyspnea, and fatigue along with ground glass opacification (GGO) on chest computed tomography (CT) imaging.[2,3] Although the majority of patients with COVID-19 develop mild form of the disease, specific patient populations are at a risk of severe disease and require more attention. According to published studies, patients with underlying

conditions such as diabetes, cardiovascular disease, liver cirrhosis, and chronic kidney disease (CKD) are not only at a higher risk of infection, but also prone to a more serious outcome once infected. These patients are more likely to progress to forms of disease requiring admission to intensive care unit, mechanical ventilation or death.[4,5] Of note, patients with CKD are most likely to suffer from other concurrent comorbidities, such as hypertension, diabetes, and cardiovascular diseases.

Hence, it is likely that patients with CKD, in particular those on dialysis, will be at an excessive risk by the current COVID-19 pandemic[5] and as the crisis tends to remain, increased emphasis should be given to understanding disease presentation in high-risk subgroups for better patient management. While there is relatively extensive data regarding acute kidney injury triggered by COVID-19,[6,7] only few studies have investigated the characteristics of COVID-19 in patients with pre-existing kidney failure. Thus, in this study, we aimed to evaluate the clinical, laboratory and imaging findings, as well as disease outcome of a series of CKD patients with confirmed diagnosis of SARS-CoV-2 infection.

MATERIALS AND METHODS

Study Population And Design

This was a single-center study conducted on 43 consecutive patients with confirmed COVID-19 who were admitted from 20 February, 2020 to 15 April, 2020 to our academic tertiary hospital. Figure 1 shows the flowchart for patient enrollment. Inclusion criteria were as follows: 1) confirmed diagnosis of COVID-19 through real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay with samples obtained from nasopharyngeal swab; 2) chest CT images suggestive for COVID-19 pneumonia; 3) confirmed diagnosis of CKD based on Kidney disease: Improving Global Outcomes (KDIGO) CKD Work Group (2012) classification;[8] and 4) age older than 18 years old. All patients were receiving standard therapy for CKD based on national and international guidelines. On admission, patients' information regarding demographic data, past medical history, and presenting signs and symptoms was obtained through a pre-designed questionnaire filled by an independant investigator. Also, vital signs including patients' pulse rate and oxygen saturation (SpO2) were measured by a fingertip pulse oximeter and respiratory rate was measured by counting chest movements in one minute. Furthermore, the imaging findings of patients' initial chest CT were recorded. According to diagnosis guidelines of COVID-19 in Iran, all patients had undergone at least one low-dose CT scan at admission as part of their initial work-up.[9]

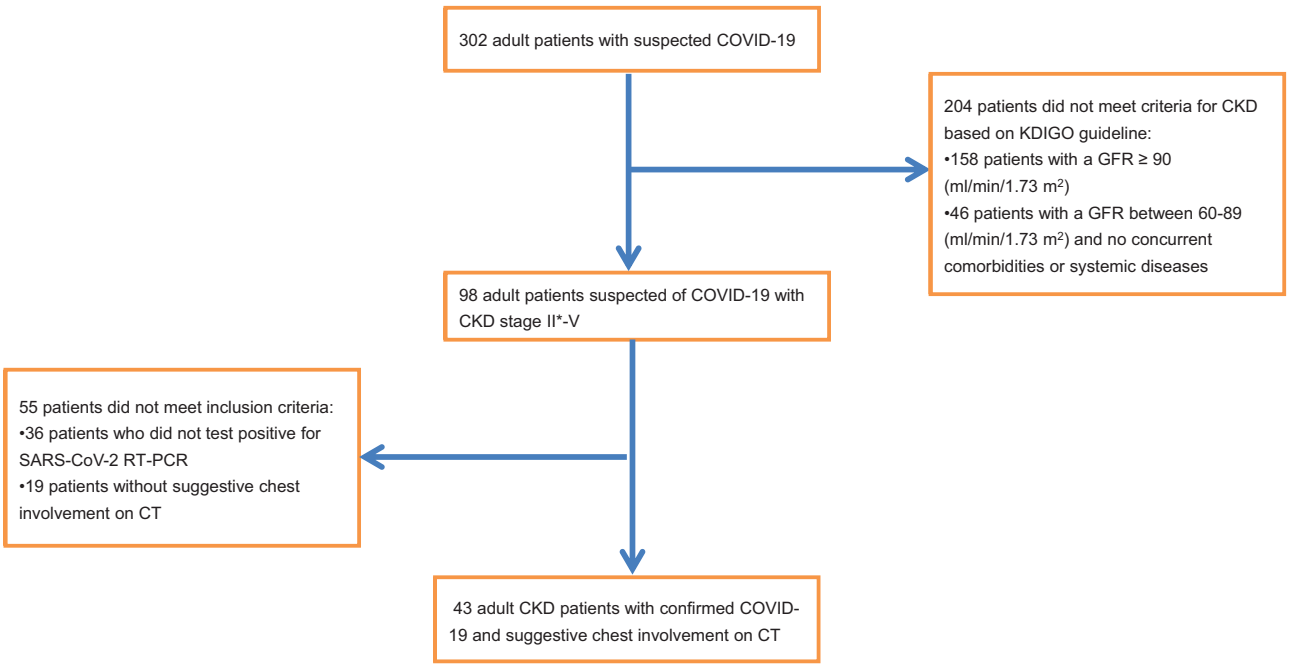

Figure 1. It shows flowchart of patient enrollment.
*G2 category with concurrent comorbidity/systemic disease

All patients were followed until one of the study endpoints (determined as either death or complete recovery and discharge) were reached. Estimated glomerular filtration rate (eGFR) was calculated for each case according to the Modification of Diet in Renal Disease (MDRD) equation.[10] According to the interim guideline of the WHO, published on 13 March, 2020, severe disease was defined as fever or suspected respiratory infection, plus either respiratory rate > 30 breaths/min; severe respiratory distress; or SpO2 ≤ 93% on room air.[11] Lymphocytopenia was considered as absolute lymphocyte count < 1×10^9, thrombocytopenia as platelet count < 150×10^9, neutrophilia as absolute neutrophil count > 7.5×10^9, and eosinopenia as < 0.01×10^9 in per liter of blood.

Ethical Considerations

The study protocol was approved by the ethics committee of our institutional review board. Informed consent was obtained from all patients prior to enrollment and all personal data was anonymized. All procedures performed in this study was in accordance with 1964 Helsinki declaration and its later amendments.

Chest CT Imaging

As part of national COVID-19 guidelines, all patients underwent non-contrast chest CT scan with a low-dose protocol.[18] All CT scans were performed using a 64-slice scanner (Siemens sensation; Siemens Healthineers, Erlangen, Germany) in a supine position during end-inspiration. For every patient, a low-dose CT protocol with the following scanning parameters was performed: gantry rotation time of 0.5 seconds, 0.625 mm × 64-detector array, pitch of 1.4, table speed of 45.2 mm/rotation, 20 mAs, 120 kVp, and a 300 × 300 matrix. CARE Dose4D; CARE kV scanning parameters were off. For the purpose of sagittal and coronal image reconstruction, 1 mm slice thickness and 1 mm reconstruction intervals were used. All of the machine surfaces were disinfected with ethanol and didecyldimethylammonium chloride (DDAC). After every CT, passive air ventilation was performed for at least 30 minutes.

DICOM data were transferred onto a picture archiving and communicating system (PACS) and two expert radiologists with 9 and 18 years of experience interpreted the images. Both radiologists were blinded to the lab data, clinical features, and patients' diagnosis. A final CT score was reached by consensus of the two radiologists. The opinion of a third radiologist was used to resolve dual-reader disagreements. All the CT scans were reviewed in axial, sagittal and coronal planes. In patients with more than one CT scan at admission, only the initial CT was evaluated. For classifying lung zone involvement, three zones were defined as follows: upper zone: above the carina region; middle zone: the area between the carina and inferior pulmonary vein; and lower zone: below the inferior pulmonary vein.[2] Predominant pattern of involvement was assessed and classified as GGO, consolidation, reticular or mixed. In addition, lesion distribution (peripheral, central or diffuse) and predominant zonal involvement (upper, middle, lower or diffuse) were recorded. In addition, the presence of other imaging features including crazy-paving, reverse halo sign, airway thickening, dilated vessels, airway dilatation, air bronchogram and lymphadenopathy (defined as a lymph node with a short-axis diameter > 10 mm) was assessed. The percentage of lung involvement was scored using the following system: 0: no involvement, 1: < 25%, 2: 26% to 50%, 3: 51% to 75%, and 4: > 75%.[26] The scores of each specific zone (upper, middle, and lower) of both lungs were summed up to calculate the zonal score (maximum score = 8) and the total score was calculated by summing scores of the upper, middle, and lower zones (maximum score = 24).

Laboratory Procedures

At admission, nasopharyngeal swab samples were taken from all patients with suspected SARS-CoV-2 infection and RT-PCR (DAAN gene Co Ltd device) was performed for every patient. Laboratory tests including biochemistry, complete blood count (CBC) and indices such as neutrophil/ lymphocyte ratio (NLR) and platelet/ lymphocyte ratio (PLR) ratios, and inflammatory markers such as C-reactive protein (CRP) were recorded. CRP levels were measured using the Rondox essay kit with immunoturbidimetric techniques. To evaluate CBC, NLR and PLR, venous blood samples were collected in potassiumethylene diamine tetraacetic acid tubes (dipotassium EDTA tubes) and the Sysmex-XE 2000i automated blood cell analyzer (Sysmex, Kobe, Japan) was used to for measurement within an hour. This is the standard duration time

for our laboratory, since it prevents EDTA-induced swelling.

Statistical Analysis

Continuous variables are reported as mean (± SD) and categorical variables are expressed as frequency (percentage). Variables were compared across outcome groups (death vs discharge) and also CKD stages. Normality assumptions were tested using the Shapiro-Wilk test. Student t-test was used for comparison of continuous data and Chi-square or Fischer's exact test was applied to compare categorical variables. All statistical analyses were performed by SPSS version 23 (IBM corp., Chicago, IL, USA). $P < .05$ was considered statistically significant.

RESULTS

Demographic Data

Table 1 shows demographic characteristics of patients at baseline. The mean age ± SD of patients was 60.65 ± 14.36 years (range: 27 to 87); 65.1% were male. Age and sex were equally distributed across the two groups of outcome ($P > .05$, $P > .05$; respectively). The most frequent CKD stage was stage IIIa and the least common was stage IV. Of the five patients with ESRD, three were already on dialysis and in the other two cases; dialysis was initiated for the first time after SARS-CoV-2 infection. Majority of patients (n = 32, 74.4%) had a positive history of cardiovascular diseases.

Clinical and Laboratory Findings

Table 2 shows clinical and laboratory data of patients at the time of admission. Of the total 43 patients, 5 (11.6%) died on follow-up; including four patients with an estimated GFR < 60 cc/min/ 1.73m^2 and one patient with stage II CKD. The rest of the cases (88.4%) were discharged. Disease outcome was not significantly different across different stages of CKD ($P > .05$). On admission, severe disease had developed in 58.1% of the patients. Mean duration of hospitalization was 11.65 ± 6.67 (range: 2 to 33), which was not significantly different across outcome groups ($P > .05$, $P > .05$; respectively, Table 2). Overall, the most common clinical presentation was dyspnea (65.1%), followed by cough (60.5%). Mean respiratory rate, temperature, and oxygen saturation did not vary significantly between those who died and those who were discharged (Table 2). Leukopenia, leukocytosis, and thrombocytopenia were observed in 7 (16.3%), 4 (9.3%), and 12 (27.9%) patients; respectively. The mean lymphocyte, neutrophil and eosinophil count was 1.29 ± 0.57 × 10^9 /L, 4.56 ± 2.81 × 10^9 /L, 0.083 ± 0.065 × 10^9 /L which did not display a significant difference between the two groups of outcome. Evaluation of serum biochemistry revealed that mean serum C-reactive protein and lactase dehydrogenase (LDH) level were higher

Table 1. Comparison of Patients' Baseline Characteristics Based on Final Disease Outcome.

Variables	Total Patients (n = 43)	Discharged (n = 38)	Death (n = 5)	*P*
Mean Age, years	60.65 ± 14.36 27 to 87	60.63 ± 14.50 27 to 87	60.8 ± 14.61 38 to 76	> .05
Sex				
Male	28 (65.1)	23 (60.5)	5 (100)	> .05
Female	15 (34.9)	15 (39.5)	-	
Comorbidities				
IHD	14 (32.6)	11 (28.9)	3 (60)	> .05
HTN	18 (41.9)	16 (42.1)	2 (40)	
Diabetes Mellitus	16 (37.2)	15 (39.5)	1 (20)	
Asthma	1 (2.3)	1 (2.6)	-	
CKD stage				
II	10 (23.3)	10 (26.6)	-	> .05
IIIa	19 (44.2)	17 (44.7)	2 (40)	
IIIb	7 (16.30)	5 (13.2)	2 (40)	
IV	2 (4.7)	2 (5.3)	-	
V	5 (11.6)	4 (10.5)	1 (20)	

Continuous variables are reported as mean ± SD and range. Categorical variables are reported as n (%). P values are calculated by χ^2 test, Fisher's exact test, or Student t-test.
Abbreviations: IHD, ischemic heart disease; HTN, hypertension; CKD, chronic kidney disease.

Table 2. Comparison of Patients' Baseline Clinical Presentation and Laboratory Findings Based on Final Disease Outcome

Variables	Total Patients (n = 43)	Discharged (n = 38)	Death (n = 5)	*P*
Clinical Presentation				
Dyspnea	28 (65.1)	25 (65.8)	3 (60)	
Fever	21 (48.8)	19 (50)	2 (40)	
Cough	26 (60.5)	23 (60.5)	3 (60)	
Sore Throat	5 (11.6)	4 (10.5)	1 (20)	
Chilling Sensation	9 (20.9)	9 (23.7)	-	
Headache	4 (9.3)	3 (7.8)	1 (20)	> .05
Myalgia	14 (32.6)	13 (34.2)	1 (20)	
Nausea	6 (14)	5 (13.1)	1 (20)	
Abdominal Pain	6 (14)	5 (13.1)	1 (20)	
Diarrhea	4 (9.3)	3 (7.8)	1 (20)	
Duration of Hospitalization, days	11.65 ± 6.67 2 to 33	11 ± 6.26 2 to 33	16.6 ± 8.38 7 to 29	> .05
Oxygen saturation, %	88.73 ± 6.52 68 to 98	89.31 ± 5.21 74 to 98	85.5 ± 12.15 68 to 96	> .05
Respiratory rate,/min	17.77 ± 3.80 12 to 30	17.73 ± 3.71 12 to 30	18 ± 4.9 12 to 24	> .05
Temperature, ºC	37.17 ± 0.90 35 to 39	37.13 ± 0.91 35.5 to 39	37.4 ± 0.88 35 to 38.3	> .05
Leukocyte Count				
< 4 × 10^9 /L	7 (16.3)	6 (15.8)	1 (20)	
× 10^9 /L	32 (74.4)	28 (73.6)	4 (80)	> .05
> 4 × 10^9 /L	4 (9.3)	4 (10.6)	-	
Platelet count				
< 150 × 10^9 /L	12 (27.9)	10 (26.3)	2 (40)	
150-450 × 10^9 /L	29 (67.4)	26 (68.2)	3 (60)	> .05
> 450 × 10^9 /L	2 (4.7)	2 (5.2)	-	
Hemoglobin Level, g/dL	13.56 ± 2.87 6.7 to 18.9	13.59 ± 2.54 6.7 to 18.9	13.26 ± 2.53 9 to 15.3	> .05
Differential Count				
Neutrophilia	4 (9.3)	4 (10.5)	-	
Lymphocytopenia	23 (53.5)	20 (52.6)	3 (60)	> .05
Eosinopenia	3 (7)	3 (7.9)	-	
NLR	4.03 ± 2.99	4.11 ± 3.15	3.36 ± 0.93	> .05
PLR	179.57 ± 73.52	184.5 ± 74.4	142.7 ± 60.44	> .05
NLR*CRP	174.8 ± 199.1	176.5 ± 210.6	160.1 ± 28.0	> .05
Serum Creatinine, mg/L	1.89 ± 1.59 0.8 to 7.3	1.80 ± 1.53 0.80 to 7.30	2.58 ± 2.06 1.26 to 6.24	> .05
Serum BUN, mg/L	51.2 ± 47.3 10 to 231	47.56 ± 45.05 10 to 231	90 ± 64.08 43 to 163	> .05
CRP, mg/dL	39.42 ± 20.08 1 to 73	38.56 ± 2.24 1 to 73	46.7 ± 17.58 33 to 69	> .05
Creatine Phosphokinase, IU/l	183.2 ± 140.59 15 to 1008	174.11 ± 201.3 15 to 1008	240.2 ± 210.1 82 to 531	> .05
Lactase Dehydrogenase, IU/l	408.4 ± 232.7 10.93 to 1413	355 ± 127.5 10.93 to 571	740.2 ± 452.9 430 to 1413	< .05
Serum Calcium, mmol/L	8.59 ± 0.68 6 to 9.9	8.6 ± 0.7 6 to 9.9	8.65 ± 0.65 7.8 to 9.3	> .05
Serum Phosphorus, mg/dL	3.55 ± 0.86 2.2 to 5.1	2.85 ± 1.61 2.2 to 4.7	3.7 ± 1.97 2.3 to 5.1	> .05
Serum Magnesium, mmol/L	2.06 ± 0.73 1.2 to 4.8	2.08 ± 0.77 1.2 to 4.8	1.86 ± 0.2 1.7 to 2.1	> .05
25 (OH) Vitamin D, ng/mL	37.93 ± 26.2 5 to 126	37.76 ± 26.75 5 to 126	39.33 ± 27.46 17 to 70	> .05

Continuous variables are reported as mean ± standard deviation and range. Categorical variables are reported as n (%). P values are calculated by χ^2 test, Fisher's exact test, or Mann-Whitney U test.
Abbreviations: NLR, Neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CRP, C-reactive protein; BUN, blood urea nitrogen.

than normal in all patients. Also, baseline LDH level was significantly higher in patients who had experienced death ($P < .05$). Blood urea nitrogen and serum creatinine showed borderline significance in regards to disease outcome.

Imaging Findings

Table 3 shows chest CT findings of patients

Table 3. Comparison of Patients' Initial Chest CT Findings Based on Final Disease Outcome

Variables	Total Patients (n = 43)	Discharged (n = 38)	Death (n = 5)	*P*
Upper Zone Score	2.63 ± 1.77 0 to 6	2.65 ± 1.79 0 to 6	2.44 ± 1.81 0 to 5	> .05
Middle Zone Score	3.98 ± 2.12 0 to 8	3.78 ± 2.15 0 to 8	4.4 ± 1.14 4 to 7	> .05
Lower Zone Score	4.3 ± 2.31 0 to 8	4.05 ± 2.28 0 to 8	6.2 ± 1.64 4 to 8	< .05
Total Score	10.91 ± 5.67 1 to 22	10.5 ± 5.75 1 to 22	14 ± 4.18 8 to 19	> .05
Pattern of Involvement				
Ground Glass Opacification	15 (34.9)	12 (31.5)	3 (60)	> .05
Consolidation	4 (9.3)	3 (7.9)	1 (20)	
Reticular	7 (16.3)	7 (18)	-	
Mixed	4 (9.3)	3 (7.9)	1 (20)	
Lesion Distribution				
Axial				
Central	2 (4.7)	2 (5.2)	-	> .05
Peripheral	35 (87.4)	32 (84.2)	3 (60)	
Diffuse	6 (14)	4 (10.5)	2 (40)	
Craniocaudal				
Upper	3 (7)	3 (7.8)	-	> .05
Middle	8 (18.6)	8 (21)	-	
Lower	20 (46.5)	18 (47.4)	2 (40)	
Diffuse	12 (27.9)	9 (23.7)	3 (60)	
Anteroposterior				
Anterior	2 (4.7)	2 (5.2)	2 (40)	> .05
Posterior	29 (67.4)	29 (76.3)	-	
Diffuse	12 (27.9)	9 (23.7)	3 (60)	
Lung Involvement				
Bilateral	40 (93)	35 (92.1)	5 (100)	> .05
Unilateral	3 (7)	3 (7.9)	-	
Other Imaging Features				
Pleural Effusion	9 (20.9)	8 (21)	1 (20)	> .05
Pericardial Effusion	6 (14)	6 (15.8)	-	
Emphysema	1 (2.3)	1 (2.6)	-	
Fibrosis	1 (2.3)	1 (2.6)	-	
Bronchiectasis	1 (2.3)	1 (2.6)	-	
Bronchial Wall Thickening	37 (86)	32 (84.2)	5 (100)	
Crazy-paving Pattern	7 (16.3)	6 (15.8)	1 (20)	
Reversed-halo Sign	-	-	-	
Dilated Vessel	32 (74.4)	27 (71)	5 (100)	
Airway Dilatation	18 (41.9)	17 (44.7)	1 (20)	
Air Bronchogram	13 (30.2)	12 (31.5)	1 (20)	
Cavitation	-	-	-	
Interseptal Thickening	4 (9.3)	4 (10.5)	-	
Cyst	3 (7)	3 (7.8)	-	
Lymphadenopathy	3 (7)	3 (7.8)	-	

Continuous variables are reported as mean ± standard deviation and range. Categorical variables are reported as n (%). P-values are calculated by χ^2 test, Fisher's exact test, or Student t-test.

in detail. As shown, the mean ± SD score of the upper zone, middle zone, and lower zone were 2.63 ± 1.77, 3.98 ± 2.12, and 4.3 ± 2.31; respectively. The total lung score was 10.91 ± 5.67, which was not different across outcome groups ($P > .05$); however, in patients who died, lower zone score was higher ($P < .05$). We observed bilateral involvement in 93% of patients. Interestingly, bilateral lung involvement was seen in all patients who eventually experienced COVID-19-related mortality. The most common pattern of involvement was GGO followed by reticular pattern. Lesions were mainly distributed in the posterior and lower parts of the lungs. Moreover, these lesions were commonly found in the periphery of lungs. Among other imaging features, vessel dilatation was a frequent finding, observed in approximately 75% of patients. Also, we observed that airway thickening and vessel dilatation existed in all patients who had expired. Pleural effusion was seen in approximately one-fifth of patients and pericardial effusion was seen in 14% of our patients (Figure 2).

Comparison of Clinical, Laboratory, and CT Findings Based on CKD Stage

As shown in Table 4, patients with ESRD experienced the longest duration of hospitalization, however; when comparing across groups, no statistically significant different was seen. Mean oxygen saturation also did not vary in patients with different stages of CKD. Evaluation of biochemical parameters revealed that leukocyte count is associated with borderline difference across CKD stages ($P > .05$); however, this difference was not observed in platelet count and level of serum hemoglobin.

As shown by the total lung score, the extent of lung involvement did not differ across patients with different stage of CKD ($P > .05$, Table 4). However, the presence of consolidation and GGO was significantly different across CKD groups ($P < .05$). Although lymphadenopathy was more commonly observed in patients with a higher GFR ($P < .05$), the presence of other imaging features did not vary significantly between patients with different CKD stages.

DISCUSSION

Many recent studies have emphasized the role of SARS-CoV-2 infection in inducing acute kidney damage but evidence regarding the characteristics of COVID-19 infection in patients with a history of chronic renal disease is sparse.[6,7] Besides, no study has specifically investigated disease outcome in these patients based on stage of CKD. The results of our study showed that more than half of patients with CKD developed severe form of COVID-19. However, lower GFR and subsequently, higher stage of CKD, was not associated with a poorer prognosis and outcome.

To date, several risk factors have been proposed to increase the chance of developing progressive COVID-19 disease, among them the presence of co-existing morbidities. Recent reports have stated that CKD is significantly associated with increased COVID-19 severity and mortality.[5,12] Our results

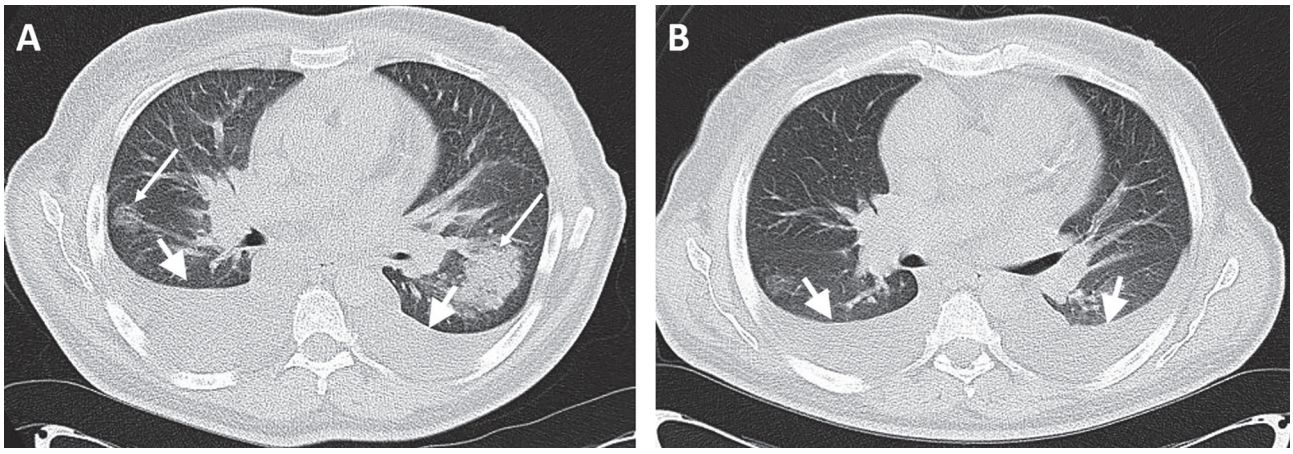

Figure 2. A) A 55-year-old male patient with a history of underlying chronic kidney disease (GFR = 9.1, stage V) presented with dry cough and dyspnea which had started since 5 days ago. Initial computed tomography (CT) imaging showed bilateral moderate pleural effusion predominantly in right side, ground glass opacity and area of consolidation in middle zones. B) CT imaging obtained 22 days later show bilateral mild pleural effusion and complete lesion absorption. The patient was discharged after 7 days.

Table 4. Comparison of Clinical and Laboratory Data and CT Scores Based on CKD Stage

Variables	Stage II (n = 10)	Stage IIIa (n = 19)	Stage IIIb (n = 7)	Stage IV (n = 2)	Stage V (n = 5)	*P*
Days of Hospitalization	13 ± 8.5	10.2 ± 6.2	10.6 ± 2.8	10.5 ± 2.1	15.4 ± 6.4	> .05
Oxygen Saturation, %	90.5 ± 5.1	88.6 ± 5.7	90.0 ± 4.7	92.0 ± 2.3	82.0 ± 12.7	> .05
Leukocyte Count, × 10^9 /L	5.32 ± 1.36	6.09 ± 3.64	5.25 ± 1.98	4.25 ± 0.07	9.06 ± 3.03	> .05
Platelet Count, × 10^9 /L	214.2 ± 78.6	206.3 ± 89.2	170.7 ± 96.7	134.5 ± 96.8	337.1 ± 181.2	> .05
Hemoglobin Level, g/dL	14.4 ± 2.6	13.7 ± 2.4	13.9 ± 3.93	12.0 ± 1.37	11.2 ± 3.3	> .05
Lymphopenia	7 (70)	8 (42.1)	2 (28.6)	2 (100)	4 (80)	> .05
Neutrophilia	-	2 (10.5)	-	-	2 (40)	> .05
Eosinopenia	-	1 (5.3)	1 (14.3)	-	1 (20)	> .05
NLR	3.07 ± 1.35	4.3 ± 3.9	4.3 ± 1.7	2.3 ± 0.1	5.2 ± 3.2	> .05
PLR	168.4 ± 64.5	175.9 ± 46.5	185.3 ± 94.3	147.4 ± 44.7	236.9 ± 128.1	> .05
NLR*CRP	138.5 ± 100.5	207.3 ± 274.1	181 ± 67.8	108.9 ± 73.1	114.1 ± 101.5	> .05
C-reactive Protein, mg/dL	38.4 ± 19.3	41.3 ± 22.8	39.3 ± 6.44	66.0 ± 15.3	29.0 ± 27.6	> .05
Lactase Dehydrogenase, IU/l	392.5 ± 75.5	330.3 ± 142.1	619.4 ± 484.5	450.0 ± 43.8	378.6 ± 78.3	> .05
Upper Zone Score	3.5 ± 1.9	2.8 ± 1.8	1.85 ± 0.89	2.0 ± 0.0	1.41 ± 1.67	> .05
Middle Zone Score	4.1 ± 2.6	4.6 ± 1.9	3.1 ± 2.1	2.5 ± 0.7	3.0 ± 2.0	> .05
Lower Zone Score	4.5 ± 2.75	5.1 ± 1.9	2.8 ± 2.4	4.5 ± 0.7	3 ± 2	> .05
Total Zone Score	12.1 ± 7.0	12.5 ± 5.0	7.8 ± 5.1	9 ± 1.4	7.9 ± 4.9	> .05

Continuous variables are reported as mean ± standard deviation and range. Categorical variables are reported as n (%). P values are calculated by χ^2 test, Fisher's exact test, or Student t-test.
Abbreviations: NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio; CRP, C-reactive protein.

approved this finding, showing that the risk of developing severe disease is twice as higher as compared with the general patient population.[13,14] Also, mortality rate was considerably higher (11.6%) in our patients than the rate reported for the general population.[13-5] The comorbidities associated with increased odds of COVID-19-related death are prevalent in patients with CKD. A large study in China estimated mortality rate of COVID-19 to be 10.5% in patients with cardiovascular diseases.[16] In our cohort of patients, more than 75% of cases had a positive history of cardiovascular diseases, possibly justifying the high mortality rate that was observed.

Our patients mostly manifested with dyspnea and cough, which is similar to that of non-CKD patients.[3,17] In contrast to other studies, we did not find a significantly worse outcome in the elderly.[17-9] A recent study on kidney transplant patients reported fever in 80% of cases, however; we observed fever in less than half of our patients. Furthermore, in the mentioned study, patients who required hospitalization were more likely to have reported dyspnea.[20] However, the result of our study failed to show any relationship between disease presentation and final outcome.

We observed a borderline significant difference in patients' outcome based on serum creatinine and BUN level. In a recent study, it was reported that elevated levels of BUN and serum creatinine are significantly associated with the death of patients with COVID-19.[6] In anothor study, these factors were found to be predictive of in-hospital death.[7] Despite this, our study did not display a difference in disease severity, outcome, or duration of hospitalization as the level of GFR decreased. In this study, the only biochemical factor which demonstrated a significant relationship with outcome was level of LDH. This finding had previously been reported by several studies.[3,21-3] CRP was elevated in 69.7% of our patients, which was very close to the rate (60.7%) reported by Guan and his colleagues,[3] however it was not predictive of disease outcome.

Normal white blood cell count was a more frequent finding in our series of patients compared with leukopenia, which is consistent with the results of another study conducted on kidney transpalnt patients.[24] Although we did not perform a subset analysis on lymphocyte count, a study on hemodyalis patients with COVID-19 pneumonia showed that T-cell count was significantly less as compared to non-hemodyalisis patients.[5]

Lymphocytopenia has been addressed as a marker of diseaese severity in COVID-19.[25] Despite the higher mortality rate obsereved in our study, lymphocytopenia existed in just a little more than half of our patients on admission, which is

lower than the rate reported for general patient population.[18,21,25] Moreover, unlike other studies reporting NLR and PLR as important indicators of predicting disease progression,[26-9] we did not observe such a finding in CKD patients.

The CT imaging features of COVID-19 pneumonia resemble various other conditions such as organizing pneumonia or inflammatory lung processes.[30,31] Trujillo *et al.* recently evaluated kidney transplant patients infected with SARS-CoV-2, reporting no significant difference between imaging features of survivors and non-survivors.[32] Our study also displayed the same results. However, we found that predominant radiologic patterns among CKD patients are slightly different to those of other patients. In this study, the most frequently observed patterns were GGO followed by reticular pattern, while in other studies, GGO and consolidation have been reported as the typical chest CT features of COVID-19 pneumonia.[19,33] It has been reported that reticular pattern is a late finding; however, even in late stages, reticular pattern has been observed in 3% to 6% of the general population,[34] which is considerably lower than the rate observed in our study. Another interesting finding was the high prevalence of vessel dilatation in the CT imaging of our patients, in particular those who died. Vascular enlargement has been reported to convey prognostic information, thus, this observation might be justified by the fact that our patients had presented with a more severe form of disease.[35,36] Also, of note, pleural effusion was seen in more than one-fifth of our patients. Generally, the observation of pleural effusion in a patient with acute respiratory distress, especially in early stages, is not in favor of COVID-19 pneumonia and leads away from its diagnosis.[37-9] However, based on the results of our study and also considering the fact that pleural effusion is a common complication in patients with impaired renal function, in particular in those with ESRD,[40,41] the presence of pleural effusion should not exclude the possibility of COVID-19 diagnosis in this specific patient population. Other imaging findings were similar to studies investigating the general population; for example, our study demonstrated bilateral lung involvement, mainly in the peripheral posterior lobes and with lower lung zone predilection, which is consistent with the majority of published studies.[42,43] Regarding CT score, lower zone score was found to be higher in patients who died, however, total CT score did not differ based on patients' CKD stage or disease outcome. Therefore, we suggest that the extent of lower zone involvement could be considered as a marker of disease burden.

Our study had some limitations. First, the time from symptom onset to presentation was not evaluated in this study. Second, the sample size in our study was relatively small, which could possibly affect the reults.

CONCLUSION

In conclusion, the results of this study showed that compared to the general population, patients with CKD are vulnerable to a more severe form of COVID-19 and experience a higher rate of death. Thus, the presence of CKD should be considered as an important factor in risk stratification of COVID-19 patients and imply the need for close monitoring and timely management of these patients. Nevertheless, higher stage of CKD is not related to worse prognosis or more extensive lung involvement .

ACKNOWLEDGEMENT

None.

DECLARATION OF INTEREST

The authors report no conflict of interest.

FUNDING

None.

REFERENCES

1. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. The New England Journal of Medicine. 2020; 382:727-33;10.
2. Haseli S, Khalili N, Bakhshayeshkaram M, Sanei-Taheri M, Moharramzad Y. Lobar Distribution of COVID-19 Pneumonia Based on Chest Computed Tomography Findings; A Retrospective Study. Archives of Academic Emergency Medicine. 2020; 8:55.
3. Guan W-j, Ni Z-y, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. New England journal of medicine. 2020; 382:1708-20.
4. Oyelade T, Alqahtani J, Canciani G. Prognosis of COVID-19 in Patients with Liver and Kidney Diseases: An Early Systematic Review and Meta-Analysis. Tropical Medicine and Infectious Disease. 2020; 5:80.
5. Ma Y, Diao B, Lv X, et al. 2019 novel coronavirus disease in hemodialysis (HD) patients: Report from one HD center in Wuhan, China: medRxiv. 2020; 10.1101/2020.02.24.20027201.

6. Li Z, Wu M, Yao J, et al. Caution on Kidney Dysfunctions of COVID-19 Patients. medRxiv. 2020; 10.1101/2020.02.08.20021212.
7. Cheng Y, Luo R, Wang K, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney International. 2020; 97:829-38.
8. KDIGO C. Work Group: Kidney disease: Improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. J Kidney Int Suppl. 2013; 3:1-150.
9. Samavat S, Nafar M, Firozan A, et al. COVID-19 Rapid Guideline in Kidney Transplant Recipients. Iranian journal of kidney diseases. 2020; 14:231-4.
10. Levey AS, Coresh J, Greene T, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. Annals of internal medicine. 2006; 145:247-54.
11. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected: interim guidance. 2020; 13 March. https://www.who.int/publications-detail/clinical-management-of-severe-acute-respiratory-infection-when-novel-coronavirus-(ncov)-infection-is-suspected.
12. Henry BM, Lippi G. Chronic kidney disease is associated with severe coronavirus disease 2019 (COVID-19) infection. Int Urol Nephrol. 2020; 52(6):1193-1194.
13. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020; 323:1239-42.
14. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. The Lancet Respiratory Medicine. 2020; 8:475-81.
15. Sun P, Lu X, Xu C, Sun W, Pan B. Understanding of COVID-19 based on current evidence. Journal of medical virology. 2020; 92:548-51.
16. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 2020; 395:497-506.
17. Bhatraju PK, Ghassemieh BJ, Nichols M, et al. Covid-19 in Critically Ill Patients in the Seattle Region - Case Series. The New England journal of medicine. 2020; 382(21):2012-2022.
18. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet (London, England). 2020; 395:1054-62..
19. Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. The Lancet Infectious Diseases. 2020; 20:425-34.
20. Husain SA, Dube G, Morris H, et al. Early Outcomes of Outpatient Management of Kidney Transplant Recipients with Coronavirus Disease 2019. Clinical Journal of the American Society of Nephrology. 2020; 05170420.
21. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA. 2020; 323:1061-9.
22. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Internal Medicine. 2020; e200994.
23. Fan BE, Chong VCL, Chan SSW, et al. Hematologic parameters in patients with COVID-19 infection. American journal of hematology. 2020; 95(6):E131-E134.
24. Abrishami A, Samavat S, Behnam B, Arab-Ahmadi M, Nafar M, Sanei Taheri M. Clinical Course, Imaging Features, and Outcomes of COVID-19 in Kidney Transplant Recipients. European Urology. 2020; 10.1016/j.eururo.2020.04.064.
25. Tan L, Wang Q, Zhang D, et al. Lymphopenia predicts disease severity of COVID-19: a descriptive and predictive study. Signal Transduction and Targeted Therapy. 2020; 5(1):33.
26. Moutchia J, Pokharel P, Kerri A, et al. Clinical Laboratory Parameters Associated with Severe or Critical Novel Coronavirus Disease 2019 (COVID-19): A Systematic Review and Meta-analysis. medRxiv. 2020; 10.1101/2020.04.24.20078782.
27. Yang A-P, Liu J-P, Tao W-Q, Li H-M. The diagnostic and predictive role of NLR, d-NLR and PLR in COVID-19 patients. International immunopharmacology. 2020; 84:106504.
28. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID-19 in Wuhan, China. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2020; ciaa248.
29. Liu Y, Du X, Chen J, et al. Neutrophil-to-lymphocyte ratio as an independent risk factor for mortality in hospitalized patients with COVID-19. Journal of Infection. 2020; 81(1):e6-e12.
30. Chung M, Bernheim A, Mei X, et al. CT Imaging Features of 2019 Novel Coronavirus (2019-nCoV). Radiology. 2020; 295:202-7.
31. Pan F, Ye T, Sun P, et al. Time Course of Lung Changes On Chest CT During Recovery From 2019 Novel Coronavirus (COVID-19) Pneumonia. Radiology. 2020; 295(3):715-721.
32. Trujillo H, Caravaca-Fontán F, Sevillano Á, et al. SARS-CoV-2 Infection in Hospitalized Patients with Kidney Disease. Kidney International Reports. 2020; 5(6):905-9.
33. Ng M-Y, Lee EYP, Yang J, et al. Imaging Profile of the COVID-19 Infection: Radiologic Findings and Literature Review. Radiology: Cardiothoracic Imaging. 2020; 2:e200034.
34. Wang Y, Dong C, Hu Y, et al. Temporal changes of CT findings in 90 patients with COVID-19 pneumonia: a longitudinal study. Radiology. 2020; 200843.
35. Bai HX, Hsieh B, Xiong Z, et al. Performance of radiologists in differentiating COVID-19 from viral pneumonia on chest CT. Radiology. 2020; 200823;10.1148/radiol.2020200823.
36. Qanadli SD, Beigelman-Aubry C, Rotzinger DC. Vascular Changes Detected With Thoracic CT in Coronavirus Disease (COVID-19) Might Be Significant Determinants for Accurate Diagnosis and Optimal Patient Management.

American Journal of Roentgenology. 2020; W1-W10.

37. Bernheim A, Mei X, Huang M, et al. Chest CT findings in coronavirus disease-19 (COVID-19): relationship to duration of infection. Radiology. 2020.
38. Mahdavi A, Khalili N, Davarpanah AH, et al. Radiologic Management of COVID-19: Preliminary Experience of the Iranian Society of Radiology COVID-19 Consultant Group (ISRCC). 2020; 17:e102324.
39. Liu K-C, Xu P, Lv W-F, et al. CT manifestations of coronavirus disease-2019: A retrospective analysis of 73 cases by disease severity. European Journal of Radiology. 2020; 126:108941.
40. Ahluwalia G. Exudative pleural effusion in chronic kidney disease: An aetiological dilemma. The Indian journal of medical research. 2015; 141:269-70.
41. Ray S, Mukherjee S, Ganguly J, Abhishek K, Mitras S, Kundu S. A cross-sectional prospective study of pleural effusion among cases of chronic kidney disease. Indian J Chest Dis Allied Sci. 2013; 55:209-13.
42. Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. American Journal of Roentgenology. 2020.
43. Tabatabaei SMH, Talari H, Moghaddas F, Rajebi H. Computed Tomographic Features and Short-term Prognosis of Coronavirus Disease 2019 (COVID-19) Pneumonia: A Single-Center Study from Kashan, Iran. Radiology: Cardiothoracic Imaging. 2020; 2:e200130.

Correspondence to:
Nooshin Dalili, MD
Assistant Professor of Nephrology, Chronic Kidney Disease Research Center, Shahid Labbafinejad Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Fax: 0098 2240 9288
E-mail: drn.dalili@sbmu.ac.ir

Received June 2020
Revised June 2020
Accepted June 2020