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Article

Clinical Features of Maintenance Hemodialysis Patients with 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China

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Abstract

Background and objectives Previous reports on the outbreak of coronavirus disease 2019 were on the basis of data from the general population. Our study aimed to investigate the clinical features of patients on maintenance hemodialysis.

Design, setting, participants, & measurements In this retrospective, single-center study, we included 49 hospitalized patients on maintenance hemodialysis and 52 hospitalized patients without kidney failure (controls) with confirmed coronavirus disease 2019 at Tongren Hospital of Wuhan University from January 30, 2020 to March 10, 2020. Demographic, clinical, laboratory, and radiologic characteristics and treatment and outcomes data were analyzed. The final date of follow-up was March 19, 2020.

Results The median age of 101 patients was 62 years (interquartile range, 49–72). All patients were local residents of Wuhan. In terms of common symptoms, there were differences between patients on hemodialysis and controls (fatigue [59% versus 83%], dry cough [49% versus 71%], and fever [47% versus 90%]). Lymphocyte counts were decreased (0.8×10^9/L [patients on hemodialysis] versus 0.9×10^9/L [controls], $P=0.02$). Comparing patients on hemodialysis with controls, creatine kinase–muscle and brain type, myoglobin, hypersensitive troponin I, B-type natriuretic peptide, and procalcitonin were increased, and the percentage of abnormalities in bilateral lung was higher in computed tomographic scan (82% versus 69%, $P=0.15$) and unilateral lung was lower (10% versus 27%, $P=0.03$). Common complications including shock, acute respiratory distress syndrome, arrhythmia, and acute cardiac injury in patients on hemodialysis were significantly higher. Compared with controls, more patients on hemodialysis received noninvasive ventilation (25% versus 6%, $P=0.008$). As of March 19, 2020, three patients on hemodialysis (6%) were transferred to the intensive care unit and received invasive ventilation. Seven patients on hemodialysis (14%) had died.

Conclusions The main symptoms of coronavirus disease 2019 pneumonia, including fever and cough, were less common in patients on hemodialysis. Patients on hemodialysis with coronavirus disease 2019 were at higher risk of death.

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Introduction

Since December 2019, a type of pneumonia caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan city. The disease has rapidly spread from Wuhan to other areas, and the World Health Organization has recently declared the coronavirus disease 2019 (COVID-19) a global public health emergency (1,2). It has been found that SARS-CoV-2 belongs to the group of β-coronaviruses related to human severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome, which have led to >10,000 cases in the past two decades, with mortality rates of 10% for SARS and 37% for Middle East respiratory syndrome (3,4).

Many studies have established the clinical features of patients with COVID-19 including epidemiologic, clinical, laboratory, and radiologic characteristics, treatment, and clinical outcomes (2,5,6). However, these findings mainly focused on the general population. The clinical characteristics of patients on maintenance hemodialysis are less known. Because of the relative suppressed immunity and the frequent hospital admissions of patients on dialysis, this special population is particularly vulnerable to respiratory pathogens and severe pneumonia.

During the outbreak of COVID-19, patients on maintenance hemodialysis were considered at higher risk of SARS-CoV-2 infection. Therefore, urgent questions need to be addressed including, when compared with the general population, whether the symptoms of patients on hemodialysis with COVID-19 are typical, whether patients on hemodialysis with COVID-19 will

Table 1. Demographics and baseline characteristics of patients infected with severe acute respiratory syndrome coronavirus 2

Demographics and Baseline Characteristics	No. (%)	
	Hemodialysis, $n=49$	Control, $n=52$
Age, median (IQR), yr	62 (54–71)	62 (47–73)
Sex, men	31 (63)	24 (46)
Hypertension	45 (92)	23 (44)
Diabetes	10 (20)	10 (19)
Cardiovascular disease	10 (20)	5 (10)
Malignancy	4 (8)	1 (2)
Cerebrovascular disease	1 (2)	2 (4)
COPD	1 (2)	0 (0)
Chronic liver disease	3 (6)	1 (2)
Signs and symptoms		
Fever	23 (47)	47 (90)
Fatigue	29 (59)	43 (83)
Dry cough	24 (49)	37 (71)
Anorexia	28 (57)	34 (65)
Dyspnea	22 (45)	12 (23)
Expectoration	16 (33)	23 (44)
Myalgia	2 (4)	10 (19)
Diarrhea	6 (12)	8 (15)
Dizziness	7 (14)	7 (14)
Nausea	4 (8)	6 (12)
Sore throat	3 (6)	2 (4)
Vomiting	2 (4)	5 (10)
Headache	1 (2)	3 (6)
Onset of symptom to hospital admission, median (IQR), d	9.0 (6.0–13.0)	7.0 (3.3–10.0)

IQR, interquartile range; COPD, chronic obstructive pulmonary disease.

have prominent laboratory and radiologic abnormalities, and whether patients on hemodialysis with COVID-19 will have poor clinical outcomes. Answers to these questions will be very helpful for taking timely and effective measures to deal with COVID-19 pneumonia in patients on hemodialysis.

In this study, we aimed to investigate the clinical characteristics of patients on maintenance hemodialysis with COVID-19 pneumonia.

Materials and Methods

Patients

At the end of January 2020, Tongren Hospital of Wuhan University was designated by the government as one of the hospitals for the hospitalization of patients with COVID-19 who were living in the Hongshan District and East Lake High-Tech Development Zone in Wuhan city. All patients were assigned by the government to be hospitalized according to their current residential address. The isolation wards of department of nephrology were used for hospitalization of all patients on hemodialysis with COVID-19. In this study, we included all patients on hemodialysis with confirmed COVID-19 from January 30, 2020 to March 10, 2020. In addition, we included all patients with confirmed COVID-19 without kidney failure (controls) from other isolation wards from January 30, 2020 to March 10, 2020. Patients diagnosed as COVID-19 suspected cases were excluded from this study. The study was approved by the Medical Ethical Committee of Tongren Hospital of Wuhan University (approval no. KY2020–012). Diagnosis of COVID-19 pneumonia was on the basis of World Health Organization interim guidance (7) and the New Coronavirus Pneumonia Prevention and Control Program (fifth edition) published by the National Health Commission of China (8). Oral consent was obtained from patients. All patients enrolled in this study were living in Wuhan during the outbreak period of COVID-19. The clinical outcomes were monitored up to March 19, 2020, the final date of follow-up.

Data Collection

Data, including demographic information, medical history, exposure history, comorbidities, symptoms, signs, laboratory examinations, chest computed tomographic (CT) scans, and treatment measures, were obtained from the electronic medical record system of Tongren Hospital of Wuhan University. Two independent trained physicians in the research team collected and double checked the data from the electronic medical record system. If the data were missing, they would directly communicate with attending doctors or other medical workers to ascertain the epidemiologic and symptom data. All clinical data were analyzed by the research team of the Departments of Nephrology, Respiratory Medicine, Critical Care Medicine, Radiology, and Laboratory Medicine. The onset date was defined as the day when the symptom was noticed by the patients. Acute cardiac injury was defined as an elevated serum cardiac biomarker (troponin I) value of >99% of the upper reference limit or new abnormalities shown in electrocardiogram (2). Arrhythmia refers to any change from the normal sequence of electrical impulses, which may happen too fast, too slowly, or erratically. Here, arrhythmia was defined as new abnormalities on the basis of electrocardiogram compared with the baseline on admission.

Real-Time RT-PCR Assay for SARS-CoV-2

All patients' throat swab samples were collected for SARS-CoV-2 nucleic acid detection using real-time RT-PCR assay. The nucleic acid testing was conducted in the clinical laboratory of Tongren Hospital of Wuhan University by using fluorescent RT-PCR kits for SARS-CoV-2 produced by The Beijing Genomics Institute, which has provided >50,000 samples for testing in Wuhan. RT-PCR assay was performed according to the manufacturer's protocol.

Statistical Analyses

Continuous variables were expressed as mean, median, and interquartile range (IQR) values, and categorical variables were described as frequency rates and percentages in each category. To compare the continuous variables, independent group t tests (data were normally distributed) and the Mann–Whitney test (data were not normally distributed) were used. Proportions for categorical variables were compared using the chi-squared or Fisher exact test. No patients were lost to follow-up. There were no missing data. Statistical analyses were done with SPSS version 20.0 software (SPSS Inc.). The P values of 0.05 were considered statistically significant.

Table 2. Laboratory findings of patients infected with severe acute respiratory syndrome coronavirus 2 on admission to hospital

Laboratory Parameters	Normal Range	Median (IQR)	
		Hemodialysis, n=49	Control, n=52
White blood cell count, $\times10^9$/L	3.5–9.5	5.6 (4.7–7.6)	5.6 (4.2–7.3)
Neutrophil count, $\times10^9$/L	1.8–6.3	4.0 (3.1–5.6)	3.8 (2.7–4.9)
Lymphocyte count, $\times10^9$/L	1.1–3.2	0.8 (0.5–1.0)	0.9 (0.7–1.3)
Hemoglobin, g/dl	11.5–15.0	10.4 (8.2–12.2)	12.7 (11.4–13.4)
Platelet count, $\times10^9$/L	125–350	169 (120–234)	227 (172–314)
CRP, mg/L	0–5	13 (5–39)	11 (4–67)
Procalcitonin ≥0.05, ng/ml, no. (%)	<0.05	45 (96)	16 (31)
D-dimer, mg/L	0–0.5	1.6 (0.6–4.6)	0.9 (0.3–3.2)
Albumin, g/dl	4.0–5.5	3.9 (3.5–4.2)	3.7 (3.3–4.1)
Creatinine, mg/dl	0.5–1.2	11.8 (8.2–15.9)	0.8 (0.6–1.0)
BUN, mg/dl	9–20	70 (48–106)	12 (9–16)
Alanine aminotransferase, IU/L	7–40	14 (11–22)	24 (15–44)
Aspartate aminotransferase, IU/L	0–45	17 (14–24)	27 (23–38)
Total bilirubin, mg/dl	0.02–0.24	0.06 (0.03–0.08)	0.11 (0.08–0.15)
Creatine kinase, IU/L	30–180	82 (46–159)	67 (38–109)
Creatine kinase–MB, IU/L	0–25	10 (8–18)	9 (6–11)
Lactic dehydrogenase, IU/L	114–240	193 (160–298)	218 (171–304)
Cystatin C, mg/L	0–1.26	6.4 (5.1–7.1)	1.0 (0.8–1.3)
CO_2, meq/L	20–29	19 (15–21)	23 (22–26)
Serum calcium, mg/dl	8.4–10.4	8.8 (8.0–9.2)	8.8 (8.4–9.2)
Serum phosphate, mg/dl	2.5–4.6	6.2 (5.0–8.4)	3.4 (3.1–4.0)
Serum potassium, meq/L	3.5–5.3	4.9 (4.2–5.6)	4.1 (3.7–4.4)
BNP, pg/ml	2–121	522 (157–1206)	17 (6–50)
Hypersensitive troponin I, ng/ml	0–0.040	0.070 (0.024–0.141)	0.003 (0.000–0.007)
Myoglobin, ng/ml	0–110	363 (187–620)	44 (38–76)
IgG, mg/dl	860–1740	1504 (1192–1829)	1355 (1189–1538)
IgA, mg/dl	100–420	261 (220–314)	276 (204–379)
IgM, mg/dl	50–280	135 (80–205)	140 (90–205)
C3, mg/dl	70–140	87 (75–102)	111 (104–123)
C4, mg/dl	10–40	32 (27–43)	33 (21–42)

IQR, interquartile range; CRP, C-reactive protein; MB, muscle and brain type; BNP, B-type natriuretic peptide.

Results

Demographics Characteristics

A total of 101 hospitalized patients with confirmed COVID-19 were included in this study, including 49 patients on hemodialysis and 52 patients without kidney failure (controls). The median age for patients on hemodialysis and controls was 62 years (IQR, 54–71) and 62 years (IQR, 47–73), respectively. The percentages of men were 63% and 46% in hemodialysis and control groups, respectively. In hemodialysis group, 92% of patients had at least one underlying disorder. Demographics characteristics of all patients are shown in Table 1. There were no patients who had a history of direct contact with wildlife.

Clinical Manifestation

Symptoms of the patients on admission are shown in Table 1. The time intervals from the onset of symptoms to hospital admission for patients on hemodialysis tended to be longer compared with the controls, although this was not statistically significant. In the hemodialysis group, the most common symptoms were fatigue (59%), anorexia (57%), dry cough (49%), fever (47%), and dyspnea (45%). In the control group, the most common symptoms were fever (90%), fatigue (83%), dry cough (71%), anorexia (65%), and expectoration (44%).

Laboratory Parameters and Chest CT Scans

Extensive laboratory testing of patients was performed on admission (Table 2). Except for parameters related to kidney failure (creatinine, BUN, cystatin C, hemoglobin, CO_2, serum phosphate, and potassium), there were few differences between patients on hemodialysis and controls that were clinically significant. Important difference might be associated with cellular immune deficiency: lymphocyte counts were decreased in patients on hemodialysis. In addition, important differences were related to markers of cardiovascular disease in patients on hemodialysis: creatine kinase–muscle and brain type, myoglobin, hypersensitive troponin I, and B-type natriuretic peptide were increased in patients on hemodialysis. The mean procalcitonin level was also higher in patients on hemodialysis, although this marker may be less reliable in patients with ESKD.

All patients had a chest CT scan before or during hospitalization. The typical findings of chest CT images were multiple patchy ground-glass opacities or consolidation in lungs (Figures 1–3). In the hemodialysis group, the pattern of abnormality observed was bilateral (40, 82%) and unilateral (5, 10%). Also, four patients (8%) who had no abnormal radiologic findings were diagnosed by symptoms plus laboratory RT-PCR results. However, in control group, the pattern of abnormality observed was bilateral (36, 69%) and unilateral (14, 27%). Also, there were two patients (4%) who had no abnormal radiologic findings.

Complications and Treatment

Patients on hemodialysis were more likely than the controls to have shock (16% versus 4%, respectively), acute respiratory

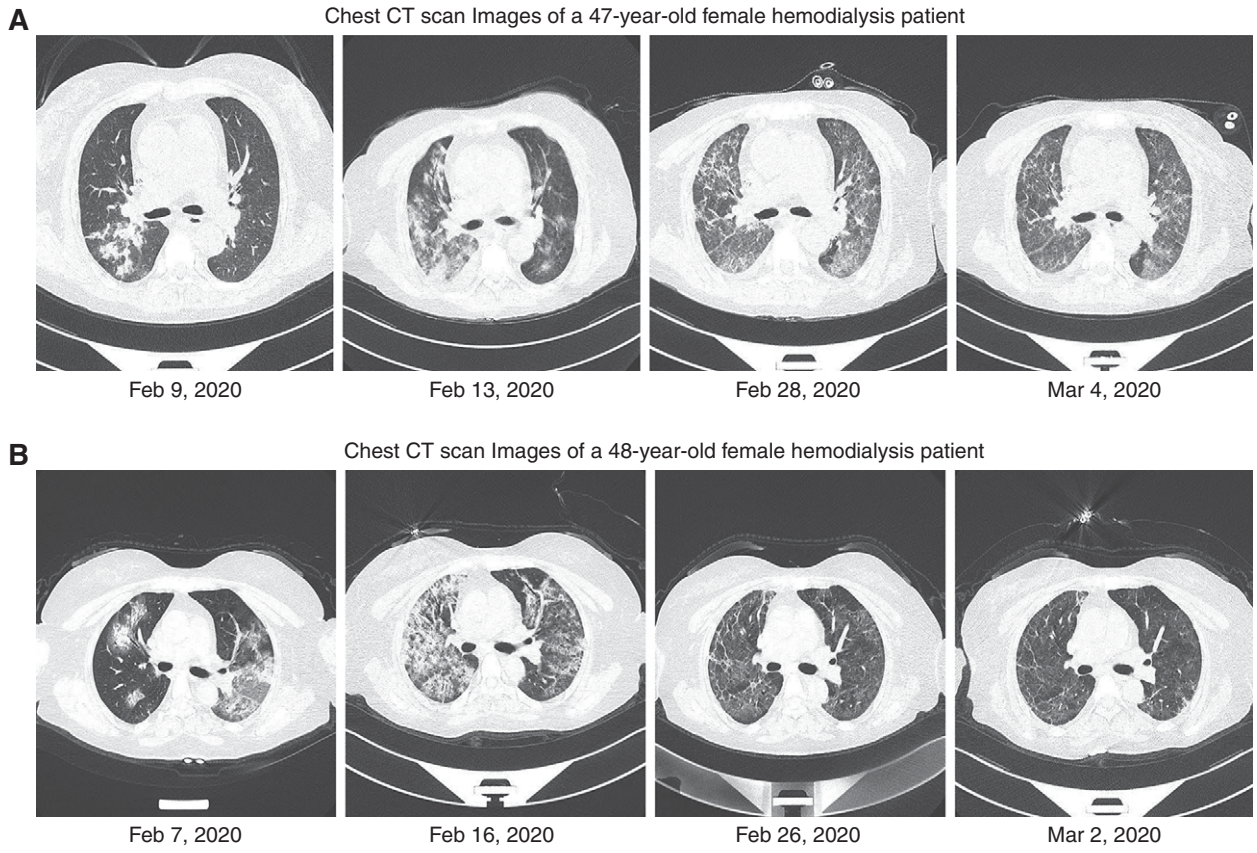

Figure 1. | Chest computed tomographic (CT) scan images of two patients on hemodialysis infected with severe acute respiratory syndrome coronavirus 2. (A) Right-sided pathy consolidation and ground-glass opacities on admission. Expansion of pulmonary lesions, with enlargement of consolidations in right lung and appearance of ground-glass opacities in left lung after 4 days. Parts of consolidations being dissipated into ground-glass opacities in right lung, with enlargement of ground-glass opacities in left lung after 15 days. Resolution of the lesions in left and right lungs after 5 days. (B) Bilateral ground-glass opacities and consolidations on admission. Expansion of pulmonary lesions, with enlargement of bilateral ground-glass opacities and consolidations after 9 days. Bilateral consolidations being resolved in left and right lungs after 10 days. Further resolution of the lesions after 5 days. Two patients were discharged.

distress syndrome (20% versus 6%, respectively), arrhythmia (18% versus 2%, respectively), and acute cardiac injury (29% versus 8%, respectively).

Both groups of patients received oxygen therapy, antiviral therapy, antibiotics, corticosteroid therapy, and respiratory support. Compared with controls, more patients on hemodialysis need mechanical ventilation (noninvasive: 25% versus 6%, $P=0.008$; invasive: 6% versus 2%, $P=0.28$) (Table 3).

Clinical Outcomes

As of March 19, 2020, the final date of follow-up, two patients on hemodialysis (4%) were still in hospital. A total of 40 patients on hemodialysis (82%) had been discharged, and 7 patients on hemodialysis (14%) had died. The percentage of patients being transferred to the intensive care unit and requiring invasive ventilation was 6%. On the other hand, a total of 50 patients without kidney failure (96%) had been discharged, and 2 patients (4%) had died. The percentages of patients being transferred to the intensive care unit and requiring invasive ventilation were 2%.

Discussion

Our study investigated the clinical features of 49 hospitalized patients on hemodialysis and 52 hospitalized patients without kidney failure (controls) infected by SARS-CoV-2. We found that there were some differences between patients on hemodialysis and controls. Fever, fatigue, and dry cough were the dominant symptoms in controls, which was consistent with recent publications (2,5,6). In patients on hemodialysis, the most common symptoms were fatigue and anorexia which were just like uremic symptoms. Fever and cough were less common. Therefore, absence of fever might be difficult for early diagnosis in some patients on hemodialysis, and these patients might be missed in the process of differentiation and screening (7). Previous studies observed that patients on dialysis with SARS tended to have less obvious symptoms (9,10) that might be difficult to distinguish from uremic symptoms. In addition, the atypical symptoms in such patients infected with SARS-CoV-2 probably were related to the rapid spread (11).

Recent reports have suggested that lymphopenia was more common in patients with severe cases or patients in the intensive care unit than in patients with nonsevere cases

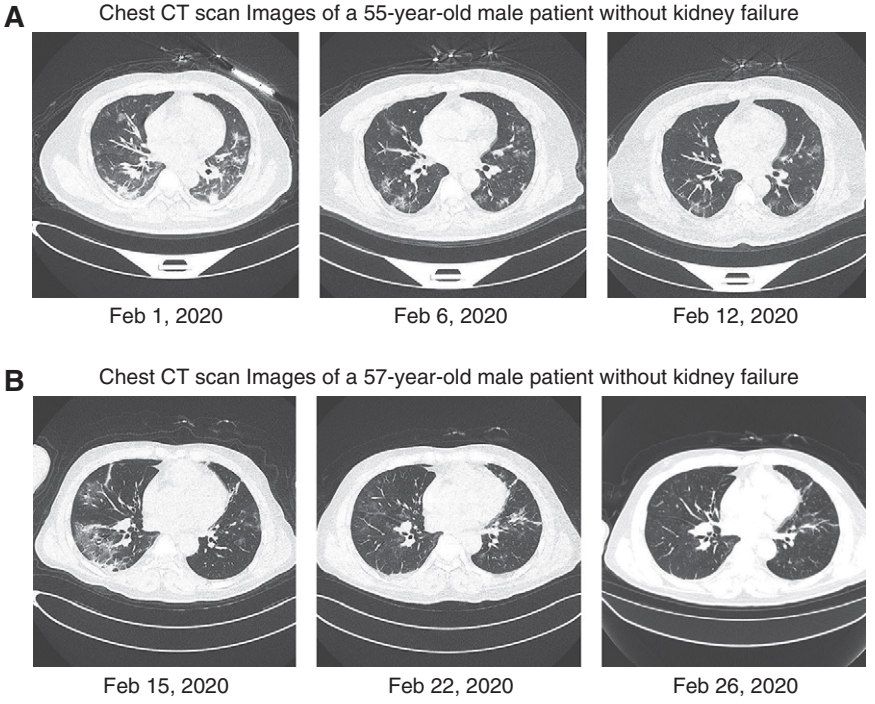

Figure 2. | **Chest CT scan images of two patients without kidney failure infected with severe acute respiratory syndrome coronavirus 2.** (A) Bilateral consolidations and ground-glass opacities on admission. Bilateral consolidations being resolved in left and right lungs after 5 days. Further resolution of the lesions after 6 days. (B) Right-sided ground-glass opacities and consolidation and slight ground-glass opacities in left lung on admission. Resolution of the lesions in right lung and slight consolidation in left lung after 7 days. Further resolution of the lesions in right and left lungs after 4 days. Two patients were discharged.

or patients not in the intensive care unit (6,12). Our study got similar results as two recent reports. That is, lymphopenia was more common in the hemodialysis group than in the control group. The typical findings of chest CT images were multiple patchy ground-glass opacities or consolidation in lungs. Although statistically insignificant, the percentage of abnormalities in bilateral lung was higher when comparing the hemodialysis group with the control group. However, on the basis of a larger sample size or more cases, we might find the differences. Of course, we cannot exclude the possibility that CT scans were done in different times of symptom onset (13). Among patients on hemodialysis with clinical deterioration, chest CT radiographs showed expansion of pulmonary lesions after admission (Figures 1 and 3). The absorption of ground-glass opacities or consolidation was slower in patients on hemodialysis compared with

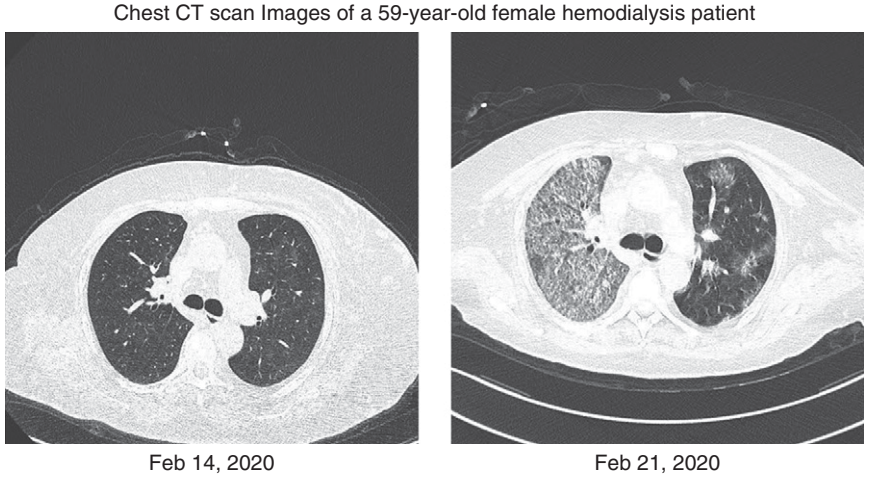

Figure 3. | **Chest CT scan images of a patient on hemodialysis infected with severe acute respiratory syndrome coronavirus 2.** There were no obvious abnormal radiologic findings on admission. Extensive ground-glass opacities can be seen in right lung after 7 days. The patient was dead.

Table 3. Complications and treatments of patients infected with severe acute respiratory syndrome coronavirus 2

Complications and Treatments	No. (%)	
	Hemodialysis, $n=49$	Control, $n=52$
Complications		
Shock	8 (16)	2 (4)
ARDS	10 (20)	3 (6)
Arrhythmia	9 (18)	1 (2)
Acute cardiac injury	14 (29)	4 (8)
Treatments		
Oxygen inhalation	41 (84)	43 (83)
Antiviral therapy	47 (96)	51 (98)
Antibiotic therapy	29 (59)	35 (67)
Glucocorticoid therapy	8 (16)	14 (27)
Intermittent hemodialysis	49 (100)	0 (0)
Continuous KRT	17 (35)	0 (0)
Noninvasive ventilation	12 (25)	3 (6)
Invasive mechanical ventilation	3 (6)	1 (2)

ARDS, acute respiratory distress syndrome.

controls (Figure 1 versus Figure 2). We assumed that long-term anemia, malnutrition, and underlying comorbidities contributed to decreased healing capacity.

As of March 19, 2020, the final date of follow-up, seven patients on hemodialysis had died, including three patients who were dead due to COVID-19 pneumonia and four patients who were dead due to cardiovascular disease or gastrointestinal hemorrhage. The overall mortality was higher than those in previous studies (6,12). Nevertheless, infection of SARS-CoV-2 was an important factor leading to death of patients on hemodialysis.

At present, no effective drugs or specific treatment have been recommended for COVID-19 pneumonia. For patients on hemodialysis in our study, oxygen therapy, antiviral drugs, antibacterial agents, corticosteroid, intermittent hemodialysis or continuous KRT, and respiratory support were applicated. Among 49 patients on hemodialysis, 16% of them received corticosteroid, 35% of them received continuous KRT, and 31% of them received mechanical ventilation.

There were some limitations in this study. First, because of the limited number of cases from one single center, it is hard to evaluate risk factors for disease severity and mortality with multivariable adjusted methods. A multicenter cohort study would help to define the clinical manifestation, risk factors, and clinical outcomes. Second, we did not investigate the effect of extracorporeal membrane oxygenation as rescue therapy on the clinical outcomes in severe patients on hemodialysis due to some objective reasons.

In summary, the main symptoms of COVID-19 pneumonia, including fever and cough, were less common in patients on hemodialysis, which might cause difficulty for early diagnosis. When compared with patients without kidney failure, patients on hemodialysis had more prominent laboratory abnormalities, chest CT manifestation, and poor clinical outcomes. Considering the significance of this ongoing global public health emergency, although our study does have some limitations, we believe that these findings are important for understanding the clinical features of COVID-19 infection in patients on hemodialysis so that we can take timely and effective measures for early diagnosis, early isolation, and early management.

Disclosures

The authors have nothing to disclose.

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