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

Jun Wu,1 Jushuang Li,1 Geli Zhu,1 Yanxia Zhang,1 Zhimin Bi,1 Yean Yu,1 Bo Huang,2 Shouzhi Fu,3 Yiqing Tan,4 Jianbin Sun,5 and Xiangyou Li1

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.

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 2 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...
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 with COVID-19 pneumonia 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 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.
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 and 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, CO2, 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
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 the hospital. A total of 40 patients on hemodialysis (82%) had been discharged, and seven 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 (controls) had been discharged, and two patients (4%) had died. The percentage of patients being transferred to the intensive care unit and requiring invasive ventilation was 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.
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...
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 has 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 applied. 
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 multi-

center cohort study would help to define the clinical 
manifestation, risk factors, and clinical outcomes. Second, 
we did not investigate the effect of extracorporeal mem-
brane oxygenation as rescue therapy on the clinical out-
comes in severe patients on hemodialysis due to some 
objective reasons.

In summary, the main symptoms of COVID-19 pneu-
monia, 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 prom-
inent 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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<th>Hemodialysis, n=49</th>
<th>Control, n=52</th>
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</thead>
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<tr>
<td>Shock</td>
<td>8 (16)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>ARDS</td>
<td>10 (20)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>9 (18)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Acute cardiac injury</td>
<td>14 (29)</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Treatments</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxygen inhalation</td>
<td>41 (84)</td>
<td>43 (83)</td>
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<tr>
<td>Antiviral therapy</td>
<td>47 (96)</td>
<td>51 (98)</td>
</tr>
<tr>
<td>Antibiotic therapy</td>
<td>29 (59)</td>
<td>35 (67)</td>
</tr>
<tr>
<td>Glucocorticoid therapy</td>
<td>8 (16)</td>
<td>14 (27)</td>
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<tr>
<td>Intermittent</td>
<td>49 (100)</td>
<td>0 (0)</td>
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<tr>
<td>hemodialysis</td>
<td></td>
<td></td>
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<tr>
<td>Continuous KRT</td>
<td>17 (35)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Noninvasive ventilation</td>
<td>12 (25)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Invasive mechanical ventilation</td>
<td>3 (6)</td>
<td>1 (2)</td>
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ARDS, acute respiratory distress syndrome.


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J.W., J.L., and G.Z. contributed equally to this work.


**AFFILIATIONS**

1Department of Nephrology, Tongren Hospital of Wuhan University (Wuhan Third Hospital), Wuhan University, Wuhan, Hubei, People’s Republic of China
2Department of Respiratory Medicine, Tongren Hospital of Wuhan University (Wuhan Third Hospital), Wuhan University, Wuhan, Hubei, People’s Republic of China
3Department of Critical Care Medicine, Tongren Hospital of Wuhan University (Wuhan Third Hospital), Wuhan University, Wuhan, Hubei, People’s Republic of China
4Department of Radiology, Tongren Hospital of Wuhan University (Wuhan Third Hospital), Wuhan University, Wuhan, Hubei, People’s Republic of China
5Department of Laboratory Medicine, Tongren Hospital of Wuhan University (Wuhan Third Hospital), Wuhan University, Wuhan, Hubei, People’s Republic of China