Clinical Characteristics of and Medical Interventions for COVID-19 in Hemodialysis Patients in Wuhan, China

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ABSTRACT

Background Reports indicate that those most vulnerable to developing severe coronavirus disease 2019 (COVID-19) are older adults and those with underlying illnesses, such as diabetes mellitus, hypertension, or cardiovascular disease, which are common comorbidities among patients undergoing maintenance hemodialysis. However, there is limited information about the clinical characteristics of hemodialysis patients with COVID-19 or about interventions to control COVID-19 in hemodialysis centers.

Methods We collected data retrospectively through an online registration system that includes all patients receiving maintenance hemodialysis at 65 centers in Wuhan, China. We reviewed epidemiologic and clinical data of patients with laboratory-confirmed COVID-19 between January 1, 2020 and March 10, 2020.

Results Of 7154 patients undergoing hemodialysis, 154 had laboratory-confirmed COVID-19. The mean age of the 131 patients in our analysis was 63.2 years; 57.3% were men. Many had underlying comorbidities, with cardiovascular disease (including hypertension) being the most common (68.7%). Only 51.9% of patients manifested fever; 21.4% of infected patients were asymptomatic. The most common finding on chest computed tomography (CT) was ground-grass or patchy opacity (82.1%). After initiating comprehensive interventions—including entrance screening of body temperature and symptoms, universal chest CT and blood tests, and other measures—new patients presenting with COVID-19 peaked at 10 per day on January 30, decreasing to 4 per day on February 11. No new cases occurred between February 26 and March 10, 2020.

Conclusions We found that patients receiving maintenance hemodialysis were susceptible to COVID-19 and that hemodialysis centers were high-risk settings during the epidemic. Increasing prevention efforts, instituting universal screening, and isolating patients with COVID-19 and directing them to designated hemodialysis centers were effective in preventing the spread of COVID-19 in hemodialysis centers.

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A novel coronavirus named severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2) emerged in late 2019 in Wuhan, China, and is now rapidly spreading throughout the world.[1] The disease caused by this coronavirus, named coronavirus disease 2019 (COVID-19) by the World Health Organization, is characterized by symptoms of viral pneumonia but also causes damage to other organs including the kidneys.[2–4] According to the published literature, older patients with underlying illness such as diabetes mellitus, hypertension, and cardiovascular disease tend to be susceptible to COVID-19 and become severely ill,[5] but the effect of COVID-19 on hemodialysis patients has not yet been reported.

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Patients undergoing maintenance hemodialysis (MHD) have abnormal immune systems because of the uremic state,[6] which is often accompanied by significant comorbidities like cardiovascular disease, diabetes, and cerebrovascular disease.[7,8] It would be interesting to know whether the clinical course of patients undergoing MHD having COVID-19 is different from that of other COVID-19 patients. Moreover, patients undergoing MHD in outpatient department must routinely visit the hospital and stay with dozens of patients undergoing MHD in a dialysis unit for 3–4 hours at a time, which may lead to widespread crosscontamination. Therefore, epidemic control of COVID-19 in dialysis centers may present a big challenge. However, to date, limited information is available regarding the epidemiologic and clinical characteristics of COVID-19 in dialysis centers and patients undergoing MHD, which is of great importance to prevent the spread of the epidemic in dialysis centers and patients undergoing MHD.

In this study, we retrospectively collected and analyzed detailed clinical data from all patients undergoing MHD identified as having laboratory-confirmed COVID-19 distributed across 65 medical institutions throughout Wuhan, China. The morbidity data and clinical features of COVID-19 in patients undergoing MHD are presented, and the effectiveness of intervention measures for epidemic control of COVID-19 in MHD centers is examined.

Significance Statement

Although reports indicate that patients receiving maintenance hemodialysis are at risk for severe illness with coronavirus disease 2019 (COVID-19), information about this population of patients is limited. Using data retrospectively collected from a registration system that included 7154 patients undergoing hemodialysis at 65 hospitals in Wuhan, China, the authors found that 154 patients had laboratory-confirmed COVID-19. In a detailed analysis of epidemiologic and clinical characteristics for 131 COVID-19 patients who provided oral consent, they showed that hemodialysis centers are high-risk settings for COVID-19, and described interventions that effectively prevented COVID-19 spread among patients at such centers. These measures included requiring patients to wear a medical mask during dialysis and in public, conducting universal screening for the infection, and isolating infected patients and directing them to designated hemodialysis centers.

CONCISE METHODS

Study Design and Participants

Data for this multicenter, retrospective, observational study were obtained from the online registration system of the Wuhan Hemodialysis Quality Control Center (WHQCC), which includes all patients undergoing MHD in Wuhan, a mega-city in China with a population of 10 million people. This registration system updates the information of confirmed and suspected COVID-19 patients *via* the liaison of 65 medical institutions. Since late January 2020, these 65 centers have been performing strict entrance screening of patients for body temperature and respiratory or digestive tract symptoms, as well as universal screening of chest computed tomography (CT) scans and blood tests, including C-reactive protein and blood cell testing. Patients who have fever or related symptoms, or radiologic findings of viral pneumonia, have throat swabs taken for immediate nucleic acid testing and are double-checked 24 hours later. In total, between January 1 and March 10, 2020, 131 of 7154 patients undergoing MHD throughout Wuhan, China were identified as having laboratory-confirmed COVID-19 and were enrolled. Patients on continuous RRT, hemoperfusion, and hemofiltration were also included if they had ESKD and maintenance RRT was needed. The data cutoff for the study was March 10, 2020. This study was approved by the institutional ethics board of Wuhan No. 1 Hospital (W202003–2).

Diagnostic Criteria

COVID-19 was diagnosed according to the New Coronavirus Pneumonia Prevention and Control Program (seventh edition) published by the National Health Commission of China. Briefly, people with residence history in Wuhan in the 14 days before onset with any two of the following clinical manifestations were diagnosed as suspected cases: (*1*) fever and/or respiratory symptoms; (*2*) pneumonia manifestations of COVID-19 in radiologic imaging; and (*3*) the total number of white blood cells was normal or decreased, and the lymphocyte count was normal or decreased in the early stage of onset. Suspected cases with positive results of nucleic acid testing for SARS-CoV-2 were diagnosed as confirmed cases. Quantitative real-time RT-PCR assays of throat swab specimens were utilized for SARS-CoV-2 RNA detection, and performed by the local health authority as previously described.[3,9] Because the SARS-CoV-2 serum-specific antibody test was not popular before March 10, 2020 and yields a proportion of false positives, only patients with infection confirmed by quantitative real-time RT-PCR were included in this study.

Clinical Classification

We defined the degree of severity of COVID-19 (mild versus moderate versus severe versus critical) according to the New Coronavirus Pneumonia Prevention and Control Program (seventh edition). Briefly, mild refers to patients who had mild clinical symptoms without manifestation of viral pneumonia on chest CT scans. Moderate refers to patients who had symptoms such as fever and respiratory tract symptoms, *etc*., with manifestation of viral pneumonia on chest CT scans. Severe refers to adults who met any of the following criteria: (*1*) respiratory rate $\geq$30 breaths/min; (*2*) oxygen saturation $\leq$93% at rest state; and (*3*) arterial PO_2/oxygen concentration $\leq$300 mm Hg. Patients with pulmonary lesion progression $>$50% within 24–48 hours on radiologic imaging were treated as severe cases. Critical refers to patients that met any of the following criteria: (*1*) occurrence of respiratory failure requiring mechanical ventilation; (*2*) presence of shock; and (*3*) other organ failure that requires monitoring and treatment in the intensive care unit.

Data Collection

We extracted from the registration system exposure history, demographic data, clinical features, laboratory findings, chest CT scans, and treatment details for all patients with laboratory-confirmed COVID-19 between January 1 and March 10, 2020, and retrospectively reviewed the data. We conducted direct communication with patients or their families as much as possible. Written informed consent was waived because of the rapid emergence of this infectious disease, and verbal consent obtained. The date of disease onset was defined as the date when the symptoms were noticed. We obtained data by direct communication with patients or their families, attending doctors, and other health care providers if data were missing from the records or clarification was needed.

All laboratory testing was performed according to the clinical care needs of the patient. Laboratory assessments consisted of a complete blood count, blood chemical analysis, coagulation testing, assessment of liver function, and measurement of electrolytes, C-reactive protein, lactate dehydrogenase, and creatine kinase. The presence of a radiologic abnormality was determined on the basis of description on medical charts or in documentation; if imaging scans were available, they were reviewed by attending physicians in respiratory medicine or an imaging specialist.

Treatment measures included antiviral or antibiotic therapy, corticosteroid therapy, traditional Chinese medicine, respiratory support, extracorporeal membrane oxygenation. Acute Respiratory Distress Syndrome (ARDS) was defined according to the Berlin definition.[10] Cardiac injury was defined as the serum levels of cardiac biomarkers (*e.g.*, troponin I) being above the 99th percentile upper reference limit, or if new abnormalities were shown *via* electrocardiography and echocardiography. A trained team of physicians reviewed and abstracted the data. All data were entered into a computerized database and crosschecked by two physicians (HT and CT).

Statistical Analyses

We aimed to report the overall situation of SARS-CoV-2 infection in all patients undergoing MHD in Wuhan city during the study period. Therefore, we included the maximum number of patients who met the inclusion criteria. Continuous variables were expressed as mean (SD) or median [interquartile range (IQR)], and categorical variables as number (%). No imputation was made for missing data. We assessed differences between disease severities of mild/moderate and severe/critical using a two-sample *t* test or Wilcoxon rank-sum test depending on parametric or nonparametric data for continuous variables, and the chi-squared test for categorical variables; otherwise, Fisher's exact test was used when the data were limited. A two-sided P value <0.05 was considered statistically significant. All analyses were performed with using SAS software (version 9.4).

RESULTS

From January 1 to March 10, 2020, of 7154 patients undergoing MHD who were in the outpatient MHD center or had been hospitalized in different medical institutions, 154 patients were reported to the WHQCC as having laboratory-confirmed COVID-19. According to the diagnostic criteria in this study, the incidence of COVID-19 in patients undergoing MHD in Wuhan was 2.15%. In total, 23 of 154 patients without verbal consent were excluded. A total number of 131 patients were included in the final analysis (Figure 1). By

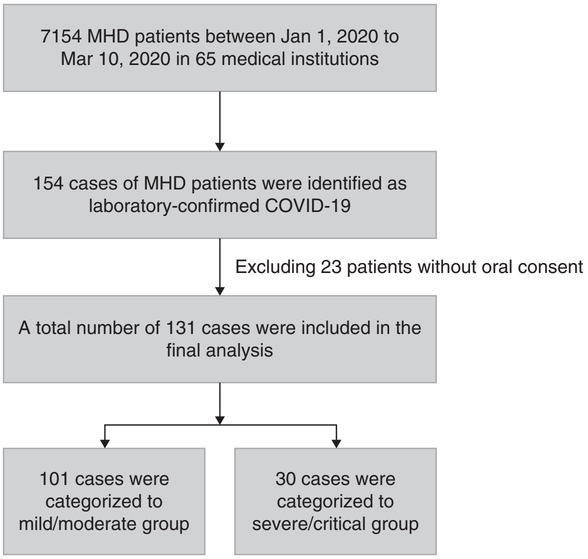

Figure 1. Flow chart illustrating study population selection. Jan, January; Mar, March.

March 1010, 2020, 47 patients were alive and had been discharged from hospital, 43 patients were alive but remained hospital, and 41 patients were deceased.

Baseline Characteristics

The baseline characteristics of the patients are shown in Table 1. The mean age of the patients was 63.2 years (SD 13.1), ranging from 31 years to 92 years. In total, 75 (57.3%) patients were men. The mean body mass index of the patients was 23.1 (SD 4.0). In total, 29.8% of patients were current smokers. All patients were residents of Wuhan or had contact with residents of Wuhan; 62 (47.7%) patients had a history of exposure to patients with confirmed COVID-19, whereas 34 (26%) patients had one or more family members who had been infected by SARS-COV-2.

The most common primary causes of ESKD in these patients were diabetic nephropathy (26.7%) and hypertensive kidney disease (26%), followed by GN (19.1%), polycystic kidney disease (3.1%), lupus nephritis (3.1%), and other causes (22.1%) like failure of kidney transplantation or obstructive kidney disease. Among the overall population, 95.4% had at least one coexisting disorder, with cardiovascular disease (including hypertension) being the most common comorbidity (68.7%), followed by diabetes (22.9%). Other coexisting illnesses included chronic obstructive pulmonary disease (3.8%), hepatitis B virus infection (8.4%), hepatitis C virus infection (2.3%), and cancer (1.5%).

The hemodialysis modalities of these patients before the epidemic included hemodialysis (93.9%), hemodiafiltration (28.2%), and hemoperfusion (2.3%). Over one half of the patients (61.8%) used arteriovenous fistula as hemodialysis access, and 35.1% of them used central venous catheter. The majority of these patient underwent dialysis three times per

Table 1. Baseline characteristics of patients with COVID-19 according to the severity of disease

Characteristics	Total (n=131)	Mild/Moderate (n=101)	Severe/Critical (n=30)	P Value
Age (yr), mean (SD)	63.3 (13.2)	63.1 (13.4)	64.3 (12.4)	0.66
Sex, n (%)				0.94
Male	75 (57.3)	58 (57.4)	17 (56.7)	
Female	56 (42.7)	43 (42.6)	13 (43.3)	
BMI (kg/m^2), mean (SD)	23.1 (4.0)	23.3 (4.1)	22.6 (3.7)	0.44
Current smoker, n (%)	39 (29.8)	32 (31.7)	7 (23.3)	0.38
Contact with COVID-19 patients, n (%)	62 (47.7)	51 (50.5)	11 (37.9)	0.23
COVID-19 patients in the family, n (%)	34 (26.0)	25 (24.8)	9 (30.0)	0.56
Primary causes of ESKD, n (%)				
Diabetic nephropathy	35 (26.7)	25 (24.8)	10 (33.3)	0.35
Hypertensive kidney disease	34 (26.0)	24 (23.8)	10 (33.3)	0.29
GN	25 (19.1)	19 (18.8)	6 (20.0)	0.88
Polycystic kidney disease	4 (3.1)	1 (1.0)	3 (10.0)	0.04[a]
Lupus nephritis	4 (3.1)	4 (4.0)	0 (0.0)	0.57
Others	29 (22.1)	28 (27.7)	1 (3.3)	0.005
Coexisting disorder, n (%)				
Cardiovascular disease	90 (68.7)	65 (64.4)	25 (83.3)	0.049
Diabetes mellitus	30 (22.9)	25 (24.8)	5 (16.7)	0.35
Chronic obstructive pulmonary disease	5 (3.8)	4 (4.0)	1 (3.3)	0.99[a]
Cancer	2 (1.5)	1 (1.0)	1 (3.3)	0.41[a]
Hepatitis B infection	11 (8.4)	7 (6.9)	4 (13.3)	0.27[a]
Hepatitis C infection	3 (2.3)	3 (3.0)	0 (0.0)	0.99[a]
Previous hemodialysis modality, n (%)				
Hemodialysis	123 (93.9)	94 (93.1)	29 (96.7)	0.68[a]
Hemodiafiltration	37 (28.2)	26 (25.7)	11 (36.7)	0.24
Hemoperfusion	3 (2.3)	3 (3.0)	0 (0.0)	0.99[a]
Previous hemodialysis access, n (%)				0.10[a]
AVF	81 (61.8)	64 (63.4)	17 (56.7)	
CVC	46 (35.1)	36 (35.6)	10 (33.3)	
CVC/AVF	2 (1.5)	1 (1.0)	1 (3.3)	
AVG	1 (0.8)	0 (0.0)	1 (3.3)	
Others	1 (0.8)	0 (0.0)	1 (3.3)	
Previous hemodialysis frequency (times/wk), n (%)				0.11
<3	37 (28.2)	32 (31.7)	5 (16.7)	
≥ 3	94 (71.8)	68 (68.3)	25 (83.3)	
Dialysis yr, median (IQR)	2.6 (0.8–6.0)	2.7 (0.8–6.0)	2.2 (0.8–5.9)	0.83[b]
Previous medication, n (%)				
ACEI/ARB	45 (34.6)	29 (28.7)	16 (55.2)	0.01
Immunosuppressant	7 (5.4)	7 (6.9)	0 (0.0)	0.35[a]

P values were calculated by the *t* test or Wilcoxon test for continuous variables, and the chi-squared test for categorical variables, otherwise Fisher's exact test was used when the data were limited. BMI, body mass index; AVF, arteriovenous fistula; CVC, central venous catheter; AVG, arteriovenous graft; ACEI/ARB, angiotensin converting enzyme inhibitor/angiotensin receptor blocker.
[a] *P* values from Fisher's exact test.
[b] *P* values from the Wilcoxon test.

week before the epidemic and the median number of years of dialysis was 2.6 (IQR 0.8–6.0).

There were 101 mild/moderate patients and 30 severe/critical patients. The primary causes of ESKD in patients with severe/critical disease were similar to those with mild/moderate disease, except that polycystic kidney disease was more common in the severe/critical group. Moreover, the presence of cardiovascular disease was more frequent in patients with severe/critical disease than among those with mild/moderate disease (83.3% versus 64.4%). However, age, gender, smoking status, dialysis access, dialysis frequency, and dialysis years between the two groups of disease severity were similar. We also inspected the medication history of these patients and found that administration of renin-angiotensin-aldosterone system (RAAS) inhibitors was more common in severe/critical patients. Although no statistically significant differences were obtained in this small sample comparison, no signals for more severe or critical disease were found in patients undergoing immunosuppression.

Clinical Characteristics and Laboratory Findings

The clinical characteristics of the patients and the laboratory findings at the time of diagnosis are presented in Table 2. The most common symptoms were fever (51.9%), fatigue (45%), cough (37.4%), sputum production (29%), dyspnea (26%), nausea/vomiting (13.7%), diarrhea (13.7%), and sore throat (7.7%). The mean systolic BP and diastolic BP were 147.5 mm Hg (SD 22.0) and 82.1 mm Hg (SD 13.1), respectively. Data from laboratory tests showed that the median levels of hemoglobin and lymphocytes of these patient were 105×10^9 cells/L (IQR 91.0–118.0) and 0.7×10^9 cells/L (IQR 0.5–1.1). Most of the patients had normal white cell and platelet counts. Levels of albumin were also within the normal range for the majority of the patients. In total, 40 (30.5%) patients had at least one organ with organ function damage, including 24 (28.2%) with cardiac injury, 16 (15.5%) with liver dysfunction, 16 (13.8%) with ARDS, and 9 (9.6%) with a cerebrovascular event.

Symptoms like fever, fatigue, cough, expectoration, dyspnea, and nausea or vomiting were more frequent in the severe/critical group, which was reasonable. Liver dysfunction and ARDS was also more frequent in the severe/critical group. No significant differences were found in hematology tests.

Radiologic Findings

Of all pulmonary CT scans that were performed, the most common abnormities revealed were ground-glass or patchy opacity (82.1%). The lesions often involved bilateral lungs (86.7%). Consolidation in lungs was uncommon (4.3%). Representative chest CT scan images from patients with different severities of the disease are presented in Figure 2. The time-dependent change in a radiologic abnormity of an asymptomatic patient is also presented.

Treatment

As shown in Table 3, some of the patients switched from normal hemodialysis to continuous RRT, which may have been because of the severity of the disease or having been transferred to a medical institution without a dialysis center. The median time from COVID-19 diagnosis to first dialysis received was 3.5 (IQR 2.0–6.0) days. In total, 92 (80%) patients received antivirals, 92 (84.4%) received antibiotics, and 66 (73.3%) received traditional Chinese medicine. Only 19 (17.3%) patients received a systemic corticosteroid. Noninvasive ventilation and mechanical ventilation were administered to 20.9% and 1.8% patients, respectively. No patient received extracorporeal membrane oxygenation or convalescent plasma therapy.

Effectiveness of Medical Intervention Measures

Daily numbers of patients undergoing MHD with confirmed COVID-19, counted by date of onset, over the course of the epidemic are shown in Figure 3, and the weekly average incidence rates of COVID-19 in the MHD population are shown in Supplemental Figure 1. Among the 131 patients undergoing MHD with COVID-19, the earliest date of illness onset was January 6, 2019. Diagnoses of COVID-19 continuously increased by two patients per day from January 23, 2020 and peaked at ten per day on January 30, 2020. Around the January 28, 2020, comprehensive intervention measures were implemented by dialysis centers, like strict entrance screening of temperatures and symptoms, and universal screening of pulmonary CT scans and blood tests for patients undergoing MHD. In addition, all patients began wearing medical masks during dialysis and in public places in line with local policies. Patients undergoing MHD who were suspected to have COVID-19 were quickly isolated and transferred to a fever clinic for further examination, and reported to the WHQCC in the meantime. The WHQCC collected all of the information for these patients and the situations in the 65 dialysis centers in Wuhan city, and quickly requisitioned two hospitals as designated dialysis centers for patients undergoing MHD with COVID-19. After February 1, 2020, disease onset began to decline after epidemic response actions were implemented. The WHQCC started a COVID-19 daily reporting system on February 3, 2020, and expanded the number of designated dialysis centers to six on February 5, 2020. After that date, disease onset continued to decrease and was maintained at a relatively low level, and at our study end date of March 10, 2020, no new patients with infection had been reported since February 26, 2020.

Characteristics of Asymptomatic Patients

For the 28 (21.4%) patients who were asymptomatic over the whole course of the disease and were diagnosed by universal screening, there were no significant differences between them and the symptomatic group regarding age and gender (Table 4). Interestingly, diabetes, as a primary cause of ESKD or a coexisting disorder, was much more common in symptomatic patients and lymphocytopenia was also more severe. On the other hand, patients using RAAS inhibitors were likely to develop symptoms when infected.

DISCUSSION

To the best of our knowledge, this is the first multicenter study to focus on patients undergoing MHD who have had COVID-19. We retrospectively collected epidemiologic and clinical data for 131 patients undergoing MHD with laboratory-confirmed COVID-19, and reviewed the effectiveness of epidemic response actions and intervention measures for controlling the spread of the epidemic. Notably, according to our findings, the MHD population is highly susceptible to COVID-19 and there is a high risk of outbreaks in MHD centers.

Our data showed that these patients are more likely to be of older age and smokers than patients in the general population. Cardiovascular disease was the predominant comorbidity, which was related to the degree of severity of the disease. Patients using RAAS inhibitors tended to become critically ill or develop obvious symptoms. The disease symptoms of our patients were similar to those of the general population, but only one half of them had a fever and nearly one quarter were

Table 2. Clinical characteristics of patients with COVID-19 according to the severity of disease

Characteristics	Total (n=131)	Mild/Moderate (n=101)	Severe/Critical (n=30)	P Value
Symptoms, n (%)				
Fever	68 (51.9)	46 (45.5)	22 (73.3)	0.008
Fatigue	59 (45.0)	41 (40.6)	18 (60.0)	0.06
Cough	49 (37.4)	29 (28.7)	20 (66.7)	<0.001
Sputum production	38 (29.0)	23 (22.8)	15 (50.0)	0.004
Dyspnea	34 (26.0)	19 (18.8)	15 (50.0)	<0.001
Nausea/vomiting	18 (13.7)	10 (9.9)	8 (26.7)	0.03[a]
Diarrhea	17 (13.0)	11 (10.9)	6 (20.0)	0.22[a]
Sore throat	10 (7.7)	6 (5.9)	4 (13.8)	0.23[a]
BP (mm Hg), mean (SD)				
Systolic BP	147.5 (22.0)	147.0 (23.5)	148.8 (17.9)	0.71
Diastolic BP	82.1 (13.1)	82.9 (12.3)	80.3 (15.0)	0.36
Radiologic findings				
CT scan image features, n (%)				0.01[a]
Ground-glass/patchy opacity	96 (82.1)	72 (81.8)	24 (82.8)	
Cord shadow	9 (7.7)	8 (9.1)	1 (3.5)	
Consolidation	5 (4.3)	1 (1.1)	4 (13.8)	
Other	7 (6.0)	7 (8.0)	0 (0.0)	
Lesion region, n (%)				0.71[a]
Bilateral lung	98 (86.7)	71 (84.5)	27 (93.1)	
Left lung	7 (6.2)	6 (7.1)	1 (3.5)	
Right lung	8 (7.1)	7 (8.3)	1 (3.5)	
Laboratory findings, median (IQR)				
Hemoglobin (g/L)	105.0 (91.0–118.0)	106.0 (91.0–119.0)	99.9 (82.0–116.0)	0.28[b]
PLT (10^9/L)	144.2 (107–186)	142.0 (108.0–184.5)	147.5 (100.0–213.0)	0.68[b]
White blood cells (10^9/L)	5.0 (3.8–7.3)	4.8 (3.7–7.2)	5.7 (4.5–7.7)	0.18[b]
Lymphocytes (10^9/L)	0.7 (0.5–1.1)	0.8 (0.5–1.1)	0.5 (0.3–1.2)	0.19[b]
Neutrophils (10^9/L)	3.9 (3.0–6.1)	3.7 (2.6–5.6)	5.3 (3.4–6.6)	0.09[b]
Albumin (g/L)	37.7 (34.0–40.7)	38.0 (34.2–40.8)	36.8 (33.4–39.7)	0.31[b]
Complications, n (%)				
Cardiac injury (n=85)	24 (28.2)	16 (25.8)	8 (34.8)	0.41
Liver dysfunction (n=103)	16 (15.5)	7 (9.1)	9 (34.6)	0.004[a]
Cerebrovascular event (n=94)	9 (9.6)	7 (10.1)	2 (8.0)	0.99[a]
ARDS (n=116)	16 (13.8)	4 (4.5)	12 (44.4)	<0.001[a]

P values were calculated by the *t* test or Wilcoxon test for continuous variables, and the chi-squared test for categorical variables, otherwise Fisher's exact test was used when the data were limited. PLT, platelet.
[a]*P* values from Fisher's exact test.
[b]*P* values from the Wilcoxon test.

asymptomatic. Therefore, universal screening of pulmonary CT scans and etiologic testing for the virus are necessary to control the epidemic in patients undergoing MHD, and should be done at the earliest opportunity.

Patients undergoing MHD have impaired immune systems and are at high risk of infectious disease, including significantly increased risk of serious complications from infection and increased mortality rates.[6,11] Infection has risen to become the second most common cause of mortality in patients with ESKD after cardiovascular diseases.[12] In addition to bacterial infections, ESKD patients undergoing MHD are also susceptible to viral infections like hepatitis B virus, hepatitis C virus, HIV, and influenza.[13] A major outbreak of SARS that affecting >300 patients in Hong Kong was triggered by a patient on dialysis. It has been speculated that a patient having renal failure might carry an extraordinarily high viral load of SARS, which could lead to a large outbreak.[14] Kwan *et al.*[15] reported that dialysis patients have a higher rate of contracting SARS (1.72%) compared with the general population (0.003% in Hong Kong), but the degree of disease severity, and the mortality rate of the dialysis group was similar to the control group. Given the fact that SARS-CoV-2 has up to 85% sequence similarity with SARS,[16] we should be alert to the possibility that the epidemiologic and clinical characteristics of COVID-19 could follow the same trend as SARS in patients undergoing MHD. On the other hand, there are additional difficulties in the management of patients undergoing MHD who have COVID-19. For example, there are additional infection control issues in preventing crosscontamination within the dialysis unit and dealing with the disposal of spent dialysate.

In this study, we found that the morbidity of COVID-19 in patients undergoing MHD was around 2%, which is much higher than that of the general population in Wuhan (about

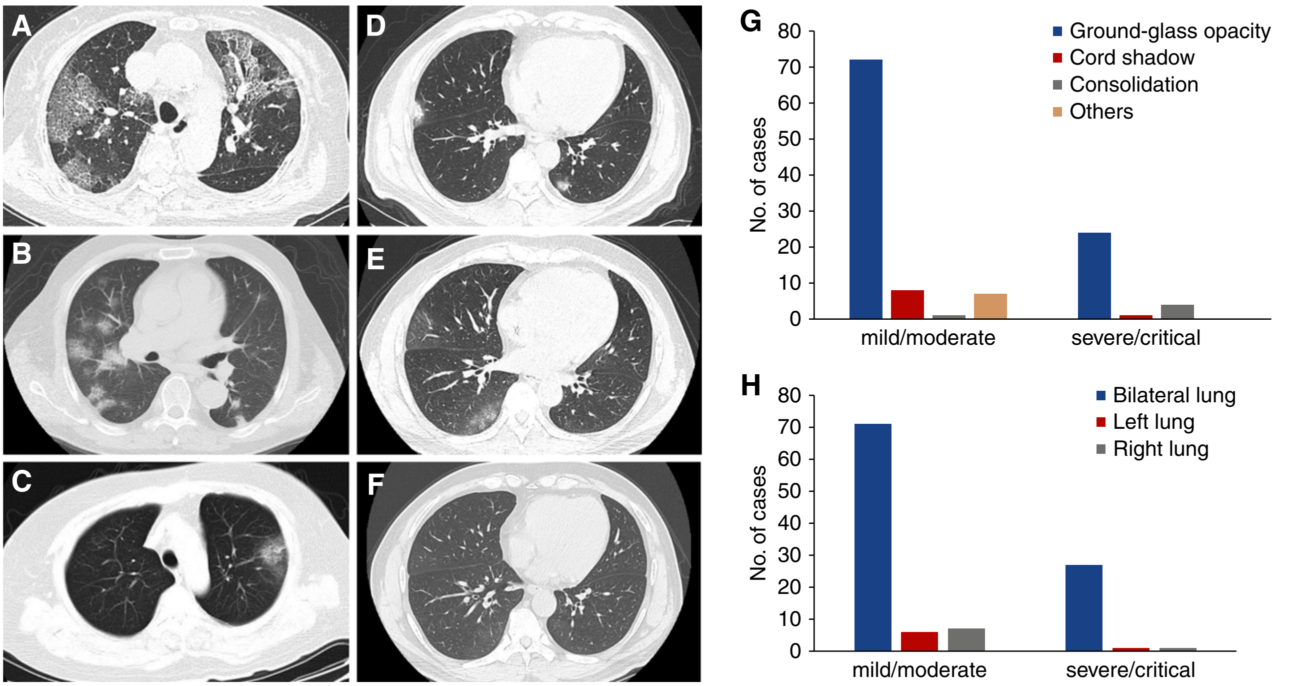

Figure 2. Chest CT scan images of representative patients. (A) Transverse chest CT scan images from an 82-year-old woman who was critically ill showing bilateral ground-glass opacity and consolidation with interlobular septal thickening on day 5 after symptom onset. (B) Transverse chest CT scan image from a 63-year-old man with severe pneumonia showing bilateral multiple ground-glass opacity on day 5 after symptom onset. (C) Transverse chest CT scan image from a 58-year-old woman with only cough showing unilateral ground-glass opacity on day 3 after symptom onset. (D–F) Transverse chest CT scan images from an asymptomatic 53-year-old man showing (D) unilateral ground-glass opacity and consolidation on day 0, (E) decreased density of ground-glass opacity on day 8, and (F) a roughly normal image on day 17 after a positive nucleic acid result. (G and H) Summarized data of (G) CT scan image features and (H) lesion regions of mild/moderate and severe/critical patients.

0.5% until March 10, 2020), indicating a high incidence of COVID-19 in patients undergoing MHD. This may be partly attributed to the advanced age of the dialysis population, the high frequency of visit hemodialysis units, and the gathering of people during the hemodialysis process. There were more men than women in the group of patients infected by SARS-CoV-2, which is in accordance with previous studies.[3,4,9] Notably, the smoking rate was strikingly higher in our group (29.8% versus 12.6% reported by Guan *et al.*[4]). It has been reported that patients with COVID-19 of older age, with underlying

Table 3. Treatments used for patients with COVID-19 according to the severity of disease

Characteristics	Total (*n*=131)	Mild/Moderate (*n*=101)	Severe/Critical (*n*=30)	*P* Value[a]
Present hemodialysis modality, *n* (%)				
Hemodialysis	77 (58.8)	64 (63.4)	13 (43.3)	0.05
CRRT	36 (27.5)	24 (23.8)	12 (40.0)	0.08
Hemodiafiltration	5 (3.8)	2 (2.0)	3 (10.0)	0.08[a]
Days from COVID-19 diagnosis to first dialysis, median (IQR)	3.5 (2.0–6.0)	4.0 (2.0–6.0)	2.6 (2.0–9.0)	0.64[b]
Drugs, *n* (%)				
Antivirals (*n*=115)	92 (80.0)	66 (75.9)	26 (92.9)	0.05
Antibiotics (*n*=109)	92 (84.4)	65 (80.3)	27 (96.4)	0.07[a]
Glucocorticoids (*n*=110)	19 (17.3)	9 (10.7)	10 (38.5)	0.002[a]
Chinese medicine (*n*=90)	66 (73.3)	52 (80.0)	14 (56.0)	0.02
Mechanical ventilation, *n* (%)				
Noninvasive (*n*=110)	23 (20.9)	16 (19.3)	7 (25.9)	0.46
Invasive (*n*=109)	2 (1.8)	0 (0.0)	2 (7.4)	0.06[a]

P values were calculated by the *t* test or Wilcoxon test for continuous variables, and the chi-squared test for categorical variables, otherwise Fisher's exact test was used when the data were limited. CRRT, continuous RRT.
[a]*P* values from Fisher's exact test.
[b]*P* values from the Wilcoxon test.

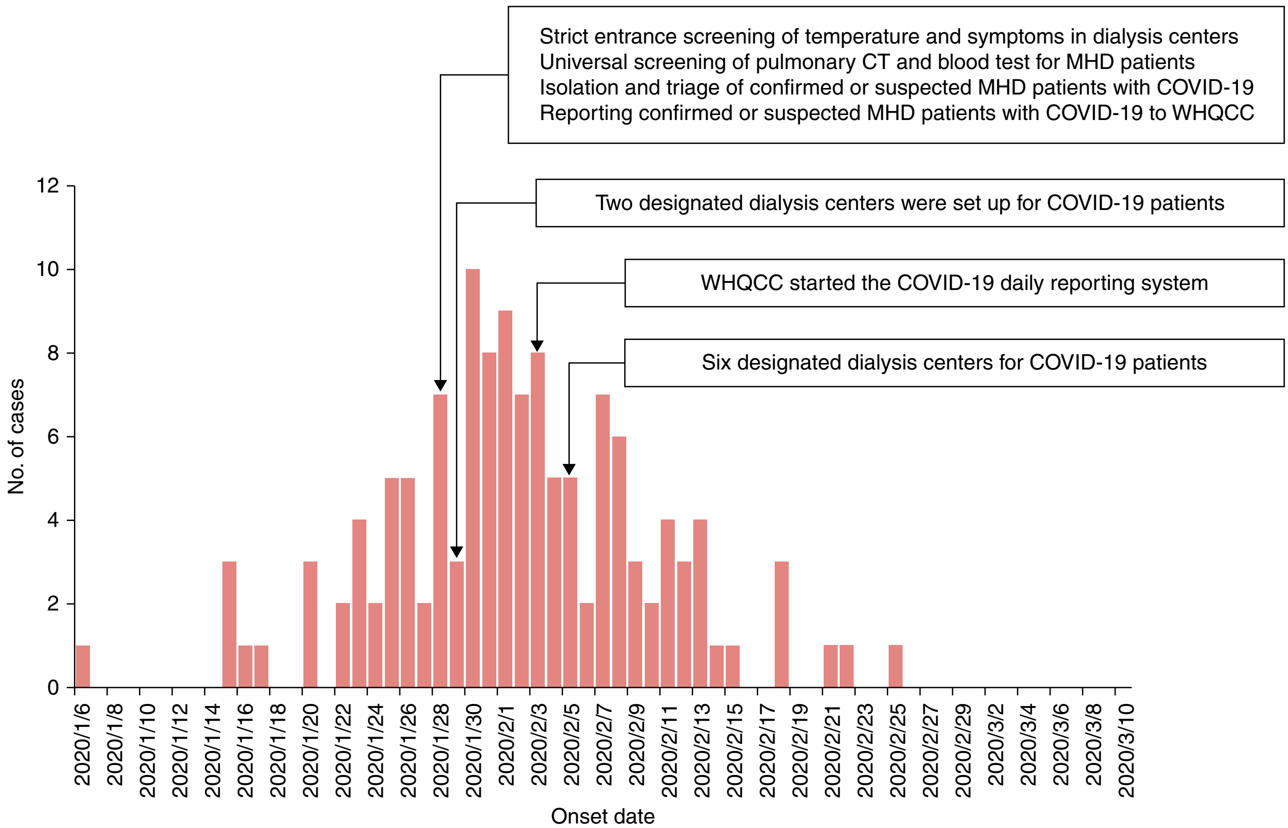

Figure 3. The onset of, and medical interventions implemented to prevent the spread of, COVID-19 among hemodialysis patients in Wuhan up until March 10, 2020.

diseases, elevated d-dimer levels, and high-sensitivity cardiac troponin I levels tend to become more critically ill.[5,17] We also found that patients with cardiovascular disease were more likely to develop severe illness, but there were no significant differences between severe/critical and mild/moderate patients regarding age, gender, smoking status, and complications like diabetes, chronic obstructive pulmonary disease, and cancer. The dialysis model, access, frequency of dialysis and age had no significant effect on the degree of disease severity.

Considering the high risk of crosscontamination in a dialysis unit, strict policies regarding entrance screening of temperatures and symptoms, and the requirement for all the patients to wear medical masks, are necessary and reasonable. The disease symptoms of our patients were similar to those of the general population.[3,9] However, these symptoms may difficult to be distinguished from uremic symptoms. Diabetic patients were more likely to have symptoms when infected, which may be because of abnormal immune responses and chronic inflammation in these patients. Only 51.9% of patients experienced fever, compared with 88.7% in the general population,[3] and many patients were asymptomatic over the whole clinical course. The representative changes in the chest CT scans of patients undergoing MHD with COVID-19 were similar to those in the general population,[3,18] but sometimes it was difficult to distinguish them from lung changes caused by their uremia or inadequate dialysis.

Lymphocytopenia was common in our patients, and there was a trend of decline in the severe/critical group, which is consistent with the results of recent reports.[5,17] Previous studies have suggested that the severity of lymphocytopenia reflects the severity of SARS-CoV-2 infection, but this feature was not prominent enough in our study. The uremic state is associated with a wide range of impairments in lymphocyte and granulocyte functions, and lymphocytopenia is common in dialysis patients.[6,19] Therefore, whether or not lymphocytopenia helps to identify SARS-CoV-2 in the early phase of infection needs further investigation. The tissue damage observed in patients with COVID-19 is thought to be caused mainly by an unchecked cytokine storm occurring during the second phase; it is plausible that abnormalities in their immune systems could predispose patients undergoing MHD to a modified response to SARS-CoV-2 infection, and particular attention needs to be paid to the virus shedding period.

Temporal distribution of patients undergoing MHD who had COVID-19 shows that, in the early stage of the epidemic in Wuhan, there was also a trend of a rapid increase of disease onset in patients undergoing MHD. After February 1, 2020, the numbers of patients undergoing MHD diagnosed with COVID-19 gradually decreased and diminished. This

Table 4. The characteristics of patients with COVID-19 according to their disease symptoms

Characteristics	Asymptomatic (*n*=28)	Symptomatic (*n*=103)	*P* Value
Age (yr), mean (SD)	62.1 (15.4)	63.7 (12.6)	0.58
Sex (*n*, %)			0.66
Male	15 (53.6)	60 (58.3)	
Female	13 (46.4)	43 (41.8)	
Primary causes of ESKD, *n* (%)			
Diabetic nephropathy	3 (10.7)	32 (31.1)	0.03
Hypertensive kidney disease	4 (14.30)	30 (29.1)	0.11
GN	4 (14.3)	21 (20.4)	0.47
Polycystic kidney disease	1 (3.6)	3 (2.9)	0.99[a]
Lupus nephritis	2 (7.1)	2 (1.9)	0.20[a]
Others	14 (50.0)	15 (14.6)	<0.001
Coexisting disorder, *n* (%)			
Cardiovascular disease	17 (60.7)	73 (70.9)	0.30
Diabetes mellitus	1 (3.6)	29 (28.2)	0.006
Chronic obstructive pulmonary disease	1 (3.6)	4 (3.9)	0.99[a]
Cancer	1 (3.6)	1 (1.0)	0.38[a]
Hepatitis B infection	2 (7.1)	9 (8.7)	0.99[a]
Hepatitis C infection	1 (3.6)	2 (1.9)	0.52[a]
Laboratory findings, median (IQR)			
Hemoglobin (g/L)	110.0 (91.0–121.0)	104 (90.0–117.4)	0.24[b]
PLT (10^9/L)	151.5 (108.9–191.0)	138.5 (105.0–185.5)	0.80[b]
White blood cells (10^9/L)	5.3 (3.5–7.9)	5.0 (4.0–7.3)	0.82[b]
Lymphocytes (10^9/L)	1.0 (0.8–1.3)	0.7 (0.4–1.0)	0.008[b]
Neutrophils (10^9/L)	4.0 (2.6–6.4)	3.9 (3.0–6.1)	0.93[b]
Previous medication, *n* (%)			
ACEI/ARB	4 (14.3)	41 (40.2)	0.01
Immunosuppressant	3 (10.7)	4 (3.9)	0.17[a]

P values were calculated by the *t* test or Wilcoxon test for continuous variables, and the chi-squared test for categorical variables, otherwise Fisher's exact test was used when the data were limited. ACEI/ARB, angiotensin converting enzyme inhibitor/angiotensin receptor blocker.
[a]*P* values from Fisher's exact test.
[b]*P* values from the Wilcoxon test.

indicates that the epidemic response actions taken by the WHQCC and the intervention measures taken by MHD centers effectively curbed the spread of the epidemic, and included upgrading the level of prevention for staff, the requirement for all patients to wear masks during dialysis, strict monitoring of suspected patients, universal screening of pulmonary CT scans, blood tests, and selected nucleic acid testing, quickly isolating and distributing patients with the infection, and, last but not least, setting up an online reporting system and establishing designated dialysis centers for patients undergoing MHD with COVID-19. It should be noted that the universal screening of pulmonary CT scans combined with detection was critically important in helping the differentiation and identification of asymptomatic COVID-19 patients in dialysis centers, especially during the early phase of the pandemic.

This study has several strengths. First, this is the first multicenter study to date with a major focus on the epidemiologic and clinical characteristics of patients undergoing MHD with COVID-19 in China. Second, we included all confirmed patients undergoing MHD with COVID-19 in Wuhan, which may reveal a comprehensive picture relating to patients undergoing MHD with COVID-19 in China. The large number of patients undergoing MHD with COVID-19 enabled us to conduct detailed stratified analyses regarding their clinical course. Finally, we have verified the effectiveness of comprehensive medical intervention measures in controlling the development of the epidemic in patients undergoing MHD, which may provide helpful information for the control of the epidemic in patients undergoing MHD in other regions of the world.

This study also has a number of limitations. First, because of the retrospective study design, many patients were diagnosed in outpatient settings where medical information was only briefly documented and incomplete laboratory testing was performed. Second, because many patients remained in the hospital or lost contact, their outcomes were unknown at the time of data cutoff, which is not shown here. Third, some of the patients were asymptomatic and were identified by screening, there was a limited frequency of quantitative viral RNA detection, and rates of positive RNA detection from throat swabs are low, which may affect estimates of morbidity. We may also have missed patients whose pulmonary CT scans were negative. To gain a better understanding of patients undergoing MHD withCOVID-19, more detailed patient information should be collected and long-term follow-up is needed in future studies.

In summary, this is the first multicenter retrospective study to provide information about epidemiologic and clinical characteristics of patients undergoing MHD with COVID-19. Importantly, we have provided effective intervention measures for controlling the development of the epidemic. Considering the significance of this ongoing global public health emergency, although our conclusions are limited by the retrospective nature of the study, we believe that the findings reported here are important for understanding the clinical characteristics of COVID-19 and will help to control the development of the epidemic in patients undergoing MHD worldwide.

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Dr. Miao and Dr. Zhang conceived and designed the study. Dr. Liu, Dr. Tang, and Dr. Xiong drafted the manuscript. Dr. Liu and Dr. Tang analyzed the data. Dr. Lei, Dr. Liu, Dr. Tang, Dr. Tian, and Dr. Tu, collected the data. Dr. Chen, Dr. Dong, Dr. Luo, Dr. Shi, and Dr. Wang provided additional guidance for data collection and analysis. All authors critically revised the manuscript for important intellectual content and approved the final version for publication.

DISCLOSURES

All authors have nothing to disclose.

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SUPPLEMENTAL MATERIAL

This article contains the following supplemental material online at http://jasn.asnjournals.org/lookup/suppl/doi:10.1681/ASN.2020030354/-/DCSupplemental.

Supplemental Figure 1. The weekly average incidence rate of COVID-19 among patients undergoing MHD in Wuhan from January 6, 2020 to March 10, 2020.

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