Original Article

An Analysis on the Clinical Features of Maintenance Hemodialysis Patients with Coronavirus Disease 2019: A Single Center Study

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Abstract

Background and Objectives: Patients on maintenance hemodialysis (MHD) are at high risk for coronavirus disease 2019 (COVID-19). However, patients undergoing MHD who are infected with COVID-19 are not fully studied. The objective of this study is to describe the characteristics of patients with COVID-19 undergoing MHD and provide a basis for the recognition and prevention of COVID-19 infection. **Materials and Methods:** Patients undergoing MHD were assigned into the normal group (537 cases), diagnosed group (66 cases), and suspected group (24 cases). General data, clinical symptoms, hemodialysis indicators, and laboratory indicators were collected and compared. **Results:** A total of 627 patients undergoing MHD were evaluated. The prevalence of COVID-19 was 10.53% (66/627), mortality was 18.18% (12/66), and death rate was 1.91% (12/627). In addition, 26% of patients were asymptomatic. Cough was the most common symptom (36%), followed by fatigue (16%), dyspnea (16%), and fever (13%). Ultrafiltration volume, ultrafiltration rate, and the duration of weekly dialysis in the diagnosed group were significantly lower than those in the other two groups. Moreover, neutrophil ratio and neutrophil, monocyte, and total carbon dioxide levels in the diagnosed group were significantly higher than those in the normal group, and the lymphocyte ratio was considerably lower than in the normal group. Sixty-five of the suspected and diagnosed patients had positive pulmonary CT findings. **Conclusion:** Compared with the general population, patients on hemodialysis have a significantly higher risk of contracting COVID-19 and postinfection mortality. Moreover, most patients undergoing hemodialysis have no obvious clinical symptoms after infection with COVID-19 but only have pulmonary changes which make it particularly important to screen and manage patients undergoing hemodialysis on outpatient basis.

Key words: Clinical characteristics, hemodialysis, novel coronavirus

INTRODUCTION

In early December 2019, the first case of pneumonia of unknown source occurred in Wuhan, Hubei Province.[1] Soon after, it was identified that the infection was caused by the novel coronavirus (2019-nCoV).[2,3] As of April 1, 2020, the virus has infected more than 877,000 people and caused the death of more than 43,000 people across six continents. Its primary routes of transmission are respiratory droplets and contact transmission. The clinical manifestations include fever, fatigue, and dry cough, which gradually develop into dyspnea.

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Submitted: 23-Nov-2021 **Revised:** 23-Jan-2022
Accepted: 30-Mar-2022 **Published:** 28-Jun-2022

Access this article online

Quick Response Code:

Website: www.journal-imna.com

DOI: 10.4103/imna.imna_6_22

How to cite this article: Cheng L, Min Y, Tu C, Mao D, Yang Y, Song Y, *et al*. An analysis on the clinical features of maintenance hemodialysis patients with coronavirus disease 2019: A single center study. Integr Med Nephrol Androl 2022;9:6.

Most patients have a good prognosis, yet, in certain cases, especially in the elderly population, the virus may cause acute respiratory distress syndrome, septic shock, or even death.

Patients undergoing hemodialysis generally have hypoimmunity. Their frequent visits to and from hospitals may increase their exposure to infections. Even though they remain in hemodialysis rooms with a relatively closed environment and concentrated staff, their condition is often accompanied by various complications, such as cardiovascular and cerebrovascular diseases and diabetes, making them a high-risk group for infection. The purpose of this study is to describe the characteristics of coronavirus disease 2019 (COVID-19) infection in patients undergoing maintenance hemodialysis (MHD) and to provide evidence for the recognition and prevention of COVID-19 infection.

MATERIALS AND METHODS

Study participants

Patients undergoing MHD in the Blood Purification Center of Wuhan No. 1 Hospital from December 30, 2019, to February 20, 2020, were enrolled in this study. This study was approved by the Ethics Committee of Wuhan First Hospital ([2020] No. 8) (Trial Registration: ChiCTR, ChiCTR2000030719). On March 12, 2020, registered, http://www. chictr. org. cn/showproj aspx? Proj = 50,867). This study followed the guidelines of the Declaration of Helsinki and the consent was obtained from all parents.

Data collection

General data, including sex, age, clinical symptoms, primary disease, hemodialysis indicators (including hemodialysis years, duration of hemodialysis, vascular access type, dry weight, ultrafiltration volume, ultrafiltration rate, dehydration ratio, systolic blood pressure, and diastolic blood pressure) and laboratory indicators (white blood cell [WBC] count, red blood cell [RBC] count, hemoglobin [Hb] level, platelet [PLT] count, neutrophil ratio [N%], neutrophil count [N#], lymphocyte ratio [L%], lymphocyte count [L#], monocyte percentage [M%], monocyte count [M#], erythrocyte sedimentation rate [ESR], and glutamic pyruvic transaminase [GPT], glutamic oxaloacetic transaminase [GOT], total protein [TP], albumin [ALB], γ-glutamyl transpeptidase [γ-GT], urea nitrogen [BUN], creatinine [Cr], total carbon dioxide [TCO_2], uric acid [UA], kalium [K], calcium [Ca], phosphorus [P], serum ferritin [SF], parathyroid hormone [PTH], C-reactive protein [CRP], procalcitonin [PCT], and lactate dehydrogenase [LDH] levels) were collected and compared.

Diagnostic criteria

Patients undergoing MHD were defined as patients who have undergone hemodialysis for at least 3 months. Suspected and confirmed COVID-19 patients were diagnosed according to COVID-19 Diagnosis and Treatment Protocol (Trial Version 6) jointly released by the NHC and the National Administration of Traditional Chinese Medicine.[4] In short, the suspected cases of COVID-19 were defined as ones with epidemiological history and clinical symptoms, including fever, respiratory symptoms, radiological features of viral pneumonia, normal or reduced total WBC count, and reduced L#. The confirmed COVID-19 cases were defined as having positive results from high-throughput sequencing or real-time reverse transcriptase chain reaction (RT-PCR).

Statistical analysis

SPSS 22.0 software (IBM, Armonk, NY, USA) was used for the data analysis. Measurement data with normal distribution were expressed as mean ± standard deviation and those with skewed distribution were expressed as median and interquartile spacing, i.e., M (P25, P75). Enumeration data were expressed as n (%). The measurement data with normal distribution were compared by ANOVA, and those with skewed distribution were analyzed by Mann–Whitney U-test. Kruskal–Wallis test was used between multiple groups, and enumeration data were analyzed by the χ^2 test. $P < 0.05$ was considered to be statistically significant.

RESULTS

General characteristics

Up to February 20, 2020, there were 627 patients undergoing MHD in the hemodialysis center of the Wuhan No. 1 Hospital; 66 were diagnosed with COVID-19, 24 were suspected with COVID-19 infection, and 12 died due to COVID-19 infection. The mortality rate after infection with COVID-19 was 18.18%, and the overall mortality rate for single-center dialysis patients was 1.91%. The residence of COVID-19 patients was mainly concentrated in Qiaokou District (29.89%), Jianghan District (16.67%), and Hanyang District (15.56%), as illustrated in Figure 1.

Of the patients with COVID-19 (suspected + diagnosed), 40 (44.44%) were men and 50 (55.56%) were women, with an average age of 61.34 + 12.59 years. There were 34 cases (37.78%) with primary glomerulonephritis, 16 cases (17.78%) with diabetic nephropathy, 24 cases (26.67%) with hypertensive renal damage, four cases (4.44%) with lupus nephritis, and 12 cases (13.33%) with other diseases [Table 1].

Among the primar y clinical manifestations of COVID-19 cases, asymptomatic ones accounted for 26%. Cough was

the most common (36%) complaint in symptomatic patients, followed by fatigue (16%), dyspnea (16%), fever (13%), anorexia (4%), diarrhea (2%), and vomiting (1%). Of the patients undergoing MHD infected with COVID-19, most were classified into the common type, followed by the severe type, and the critical type [Figure 2].

Hemodialysis characteristics

A comparison of hemodialysis-related characteristics between the three groups showed that ultrafiltration volume, ultrafiltration rate, and duration of weekly hemodialysis in the diagnosed group were significantly lower than those in the other two groups ($P < 0.05$) [Table 2].

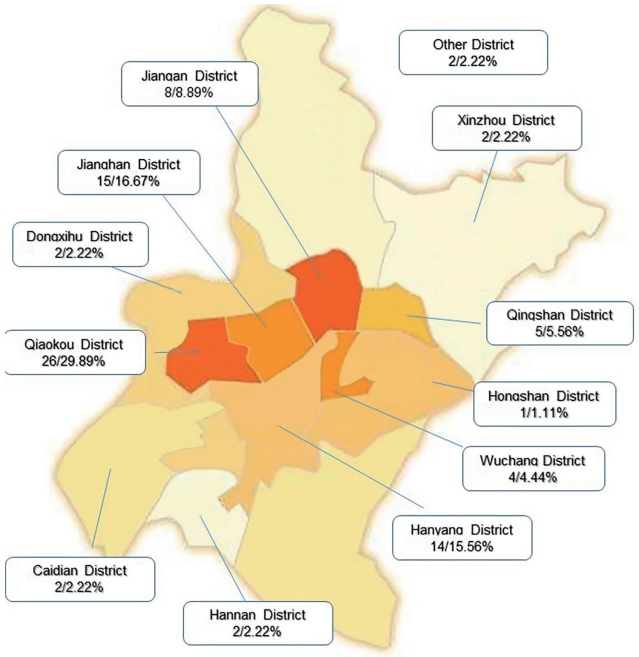

Figure 1: Distribution of patients according to residence (people/%)

Laboratory results

The comparison in laboratory results between the three groups indicated that N%, N#, M#, and TCO_2 levels in the diagnosed group was significantly higher than those in the normal group but L% was significantly lower [Table 3].

Imaging examination

Of all suspected and diagnosed patients, 65 had positive pulmonary CT findings, including 12 (18.46%) patients with single lung involvement, 53 (81.54%) patients with both lung involvement, 10 (15.38%) with a single lesion, 55 (84.62%) with multiple lesions, 40 (61.54%) with patchy lesions, 23 (35.38%) with ground-glass opacities, and 2 (3.08%) patients with patchy ground-glass opacities [Figure 3].

DISCUSSION

This study was performed in a single center, focusing on all patients undergoing dialysis and patients with COVID-19

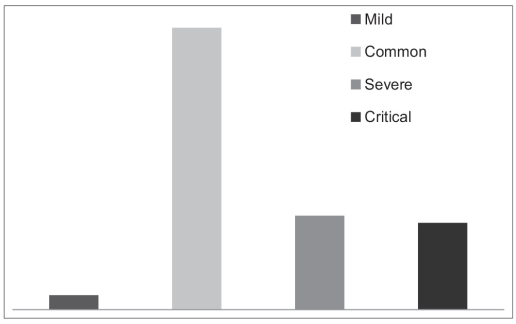

Figure 2: The clinical classification of confirmed patients was according to Diagnosis and Treatment Protocols for COVID-19 (trial version 6). Mild refers to mild clinical symptoms and no pneumonia manifestations on imaging. Common refers to symptoms such as fever and respiratory tract, and pneumonia can be seen on imaging. Severe refers to shortness of breath, pulse oxygen saturation ≤93%, PaO_2 (arterial partial pressure of oxygen)/FiO_2 (inhaled oxygen concentration) ≤300 mmHg, or lung imaging indicates that the lesion has progressed significantly (>50%) within 24–48 h. Critical refers to respiratory failure, shock, or other organ failure that requires intensive care unit monitoring and treatment

Table 1: Comparison of general characteristics among normal, suspected, and coronavirus disease 2019 diagnosed patients undergoing maintenance hemodialysis

Characteristics	Normal group (n=537)	Suspected group (n=24)	Diagnosed group (n=66)	$F/Z/\chi^2$	P
Sex (male)	305 (56.80)	11 (45.83)	29 (43.94)	4.778	0.092
Age	60.35±12.61	58.33±12.54	62.44±12. 14	1.176	0.309
Hemodialysis (months)	62 (39.94)	68 (36.98)	57 (36.71)	0.605	0.739
Primary disease					
Primary glomerulonephritis	294 (54.75)	13 (4.0)	21 (31.82)	19.675	0.007
Diabetic nephropathy	72 (13.41)	2 (8.33)	14 (21.21)		
Hypertensive renal damage	91 (16.95)	4 (16.67)	20 (30.30)		
Lupus nephritis	11 (2.05)	0	4 (6.06)		
Other diseases	69 (12.85)	5 (20.83)	7 (10.61)		

Table 2: Comparison of hemodialysis-related characteristics among normal, suspected, and coronavirus disease 2019 diagnosed patients undergoing maintenance hemodialysis

Characteristics	Normal group (*n*=537)	Suspected group (*n*=24)	Diagnosed group (*n*=66)	*F*/*Z*/χ^2	*P*
Duration of weekly hemodialysis (h/week)	10.12±2.57	10.52±2.08	9.22±2.09	4.186	0.016
Vascular access type					
AVF	424 (79.0)	18 (75.0)	46 (69.7)	3.037	0.219
Non-AVF	113 (21.0)	6 (25.0)	20 (30.3)		
Dry weight (kg)	59.58±12.61	62.74±17.07	59.03±11.20	0.744	0.476
Ultrafiltration volume (kg)	2.16±0.82	2.33±0.89	1.64±0.76 △,▲	10.610	<0.001
Ultrafiltration rate	0.79±0.27	0.83±0.33	0.61±0.28 △,▲	8.648	<0.001
Dehydration ratio	1.37±0.11	1.38±0.10	1.35±0.07	1.070	0.344
SBP (mmHg)	147.4±21.88	151.26±23.46	145.46±29.57	0.508	0.620
DBP (mmHg)	79.80±12.71	80.39±16.29	76.71±14.52	1.276	0.280

△*Represents P < 0.05 compared with the normal group,* ▲*P < 0.05 compared with the suspected group. AVF: Arteriovenous fistula, SBP: Systolic blood pressure, DBP: Diastolic blood pressure*

Table 3: Comparison in laboratory indices between the three groups

Index	Normal group (*n*=537)	Suspected group (*n*=24)	Diagnosed group (*n*=66)	*F*/*Z*/χ^2	*P*
WBC (10^9/L)	6.06±2.69	6.37±1.81	6.50±3.35	0.751	0.472
RBC (10^{12}/L)	3.53±0.66	3.82±1.14	3.50±0.66	1.897	0.151
Hemoglobin (g/L)	103.02±17.41	99.08±18.95	101.29±17.54	0.812	0.445
PLT (10^9/L)	166.10±61.65	192.33±61.08	160.43±79.02	2.283	0.103
N% (%)	69.63±9.29	72.10±8.02	72.81±9.73△	3.997	0.019
N# (10^9/L)	4.19±1.94	4.66±1.35	4.82±3.11△	3.139	0.044
L% (%)	18.80±6.87	17.17±5.83	16.56±7.28△	3.554	0.029
L# (10^9/L)	1.05±0.42	1.13±0.50	0.95±0.41	2.293	0.102
M% (%)	6.96±2.69	6.72±2.88	7.76±3.19	2.635	0.073
M# (10^9/L)	0.40±0.18	0.43±0.20	0.46±0.20△	3.728	0.025
CRP (mg/L)	5.28 (3.23-21.75)	6.52 (3.23-82.65)	6.98 (3.23-34.80)	0.735	0.693
ESR (mm/h)	25.00 (46.00-75.00)	81.00 (55.50-102.00)	53.50 (22.50-85.75)	3.434	0.180
GPT (U/L)	9.00 (6.00-13.00)	8.00 (6.00-14.00)	10.00 (6.00-13.00)	0.092	0.955
GOT (U/L)	14.00 (11.00-18.00)	13.00 (10.0-17.00)	13.00 (11.50-20.00)	0.276	0.871
TP (g/L)	64.63±6.10	64.73±4.91	65.06±6.09	0.146	0.864
ALB (g/L)	38.71±3.87	37.32±6.72	38.54±4.38	1.304	0.272
γ-GT (U/L)	16.00 (12.00-29.00)	19.00 (13.00-52.00)	20.00 (14.00-32.00)	4.248	0.120
PCT (μg/L)	0.40 (0.19-1.27)	0.77 (0.26-5.43)	0.59 (0.31-1.24)	2.684	0.261
LDH (U/L)	183.17±59.12	169.92±40.45	184.60±51.96	0.344	0.709
BUN (mmol/L)	17.43±8.83	18.05±10.18	16.33±8.70	0.524	0.592
Creatinine (μmol/L)	710.17±337.12	667.83±355.32	694.65±321.22	0.223	0.800
TCO_2 (mmol/L)	22.91±3.48	23.01±3.61	24.10±3.145△	3.375	0.035
UA (mmol/L)	313.87±160.92	348.35±182.54	300.15±156.80	0.760	0.468
Kalium (mmol/L)	4.54±0.87	4.47±1.11	4.52±0.89	0.094	0.910
Calcium (mmol/L)	2.15±0.27	2.10±0.20	2.16±0.28	0.503	0.605
Phosphorus (mmol/L)	1.67±0.55	1.78±0.79	1.66±0.59	0.461	0.631
PTH (pg/mL)	322.65 (159.05-322.65)	295.80 (108.25-500.88)	242.60 (117.83-465.35)	5.841	0.054
SF (μmol/L)	12.55±7.84	11.17±3.82	8.16±4.29	1.622	0.201

△*Indicates comparison with the normal group, P < 0.05. WBC: White blood cells, RBC: Red blood cells, PLT: Platelets, N%: Neutrophil ratio, N#: Neutrophil, L%: Lymphocyte ratio, L#: Lymphocyte, M%: Monocyte percentage, M#: Monocyte, GPT: Glutamic pyruvic transaminase, GOT: Glutamic oxalacetic transaminase, TP: Total protein, ALB: Albumin, γ-GT: γ-glutamyl transpeptidase, PCT: Procalcitonin, LDH: Lactate dehydrogenase, BUN: Blood urea nitrogen, TCO_2: Total carbon dioxide, UA: Uric acid, PTH: Parathyroid hormone, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, SF: Serum ferritin*

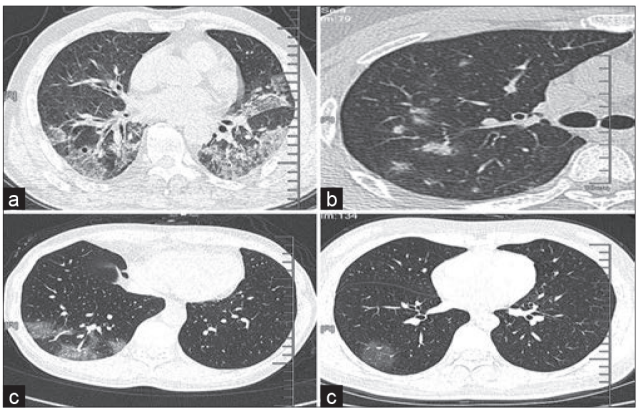

Figure 3: CT scan result. (a) Patchy ground-glass shadows in both lungs (b) Multiple small patchy ground-glass shadows in the right lung (c) Multiple patchy ground-glass shadows in the lower lobe of the right lung (d) Single ground-glass shadow in the lower lobe of the right lung

undergoing MHD. The epidemiological and clinical data of 627 patients undergoing MHD were collected retrospectively. The results suggest that the COVID-19 infection rate and mortality rate of patients undergoing MHD are high, which deserves great attention.

The results of this study showed that the overall morbidity in our center was 10.53%, while the death rate was 18.18%, which was similar to some foreign research results.[5-7] However, the mortality was higher than that of the single-center study in Jinyintan Hospital of Wuhan (11%)[8] and significantly higher than the overall domestic case-fatality rate (2.3%).[9] Reports indicated that the prevalence of COVID-19 in patients undergoing dialysis (1.72%) was significantly higher than in the general population (0.003%).[10] The immune system of patients undergoing dialysis is impaired to varying degrees, which leads to a higher risk of infection and death from COVID-19.[11] The average age of patients was greater than that of the patients not undergoing maintenance dialysis in the same study.[5] Evidence demonstrated that older patients are more vulnerable to COVID-19 and tend to become more critically ill.[12] Patients undergoing dialysis need to share the room with others, which increases the risk of additional infections.[13] As a result, the prevalence and mortality of patients with COVID-19 undergoing MHD are higher.

Cough was the most common (36%) symptom in our study, followed by fatigue (16%) and dyspnea (16%), which were slightly different from the fever symptoms reported in other studies.[1-4,8] However, it is hard to distinguish the symptoms of COVID-19 from uremia symptoms in patients undergoing dialysis. Besides, most of the patients undergoing MHD had no clinical manifestations, which was consistent with some previous reports,[14] thus significantly increasing the difficulty of screening. The result also suggests that the common type was dominant in the patients undergoing MHD infected with COVID-19, followed by the severe and critical types. This is consistent with previous studies.[1,15] Therefore, screening of patients in the hemodialysis room should be clinically strengthened.

This study showed that the duration of weekly hemodialysis, ultrafiltration rate, and ultrafiltration volume of patients in the diagnosed group were significantly lower than those in the other two groups, and thus might not guarantee adequate hemodialysis and may prevent timely removal of excess toxins and water from the body. This, in turn, may cause a series of complications such as water-sodium retention, electrolyte disorder, malnutrition, and increased death risk of patients. Therefore, during the epidemic, hemodialysis must be performed for as long as possible, and the ultrafiltration rate should be improved to ensure adequate hemodialysis and reduce carbon dioxide accumulation, so as to reduce the risk of infection.

Laboratory indicators in this study showed that L% in the diagnosed group was significantly lower than that in the normal group, which was consistent with similar studies.[1,9,14] However, due to long-term dialysis, the immune system function is widely damaged; therefore, lymphocytopenia is common in patients undergoing dialysis, regardless of whether they are infected with COVID-19. Therefore, whether or not lymphocytopenia helps to identify COVID-19 in the early phase of infection needs further investigation. This study also revealed that N%, N#, and M# in the diagnosed group were significantly higher than those in the normal group. Studies have shown that[15,16] mortality in patients with COVID-19 is associated with decreased lymphocytes and increased neutrophils; this may be one of the reasons for the high mortality rate of patients with COVID-19 in our center. The typical radiological pattern showed multifocal patchy peripheral consolidations in bilateral lungs.[17] In the present study, lung CT of patients with COVID-19 more commonly showed multiple patchy shadows in both lungs. Chest CT scan has been suggested as a useful tool to screen the suspected cases of COVID-19 infection and discard false-negative cases.[18,19] Thus, screening of lung CT should be performed for patients undergoing MHD in a timely manner, as well as early detection, isolation, and treatment.

This study has some limitations. First, this was a cross-sectional study, and thus further longitudinal investigations on the changes of the disease patterns are required. Second, the patients undergoing MHD who are diagnosed with COVID-19 must be transferred to designated hospitals for treatment under the government's regulations; thus, the examination results were not complete. Besides, this was a single-center study with a relatively

small sample size; therefore, the results need to be confirmed by future multi-center studies with a large sample size.

Financial support and sponsorship

This study was supported by the Scientific Research Project of Wuhan Municipal Health and Family Planning Commission (WG18C01).

Conflicts of interest

Fei Xiong is an Editorial Board Member of the journal. The article was subject to the journal's standard procedures, with peer review handled independently of this member and his research group.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Wuhan First Hospital ([2020] No. 8). This study followed the guidelines of the Declaration of Helsinki and the consent was obtained from all parents.

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