

Characteristics and outcomes of hemodialysis patients with COVID-19

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Background Since December, 2019, with the outbreak of coronavirus disease 2019 (COVID-19) it has now spread throughout the world, COVID-19 is now considered a globally pandemic. Previous studies mostly focus on general population with COVID-19 infection. Currently, clinical information about COVID-19 in hemodialysis patients is lacking.

Methods In this retrospective, single-centre study, we included 16 hemodialysis patients with COVID-19 from Feb. 5th to Mar. 20th, 2020, in Wuhan Fourth Hospital. Moreover, 62 general patients with COVID-19 were included as control group. Clinical characteristics, treatments, and clinical outcomes were analyzed. **Results** Compared with general patients with COVID-19 infection, hemodialysis patients presented lower incidence of fever ($p=0.001$) and relatively higher incidence of preadmission comorbidities and shortness of breath (75%vs 61%; 50% vs 33.87%). hemodialysis patients had a lower level of hemoglobin ($p<0.001$), white blood cell count ($p=0.015$), neutrophil ($p=0.016$), AST ($p=0.037$), ALT ($p<0.001$) and procalcitonin ($p<0.001$), and higher level of D-dimer ($p<0.001$) and TT ($p<0.001$). higher incidence of pulmonary effusion, cord high density shadows, pleural thickening, atelectasis were observed in hemolysis patients ($p<0.05$). As clinical outcomes, hemodialysis patients showed relatively higher mortality and prolonged hospital stay. **Conclusion** Hemodialysis patients were a high-risk group of COVID-19 infections, as hemodialysis patients often had multiple comorbidities, worse physical condition, patients with COVID-19 may have prolonged hospital stay unfavorable prognosis, COVID-19 infection should be monitored intensively for hemodialysis patients.

17 **Abstract**

18 **Background** with the outbreak of coronavirus disease 2019 (COVID-19) in December, 2019, it
19 has spread throughout the world. COVID-19 is now considered a global pandemic. Currently,
20 clinical information about hemodialysis patients with COVID-19 is scarce.

21 **Methods** In this retrospective, single-center study, we recruited 16 hemodialysis patients with
22 COVID-19 from Feb. 5th to Mar. 20th, 2020, in Wuhan Fourth Hospital. Moreover, 62 nondialysis
23 patients with COVID-19 were included as control group. The clinical characteristics, laboratory
24 finding, treatment, and clinical outcomes were collected for the assessment.

25 **Results** Compared with nondialysis patients with COVID-19 infection, hemodialysis patients
26 presented lower incidence of fever($p=0.001$) and relatively higher incidence of preadmission
27 comorbidities and shortness of breath (75%vs 61%; 50% vs 33.87%). hemodialysis patients had a
28 lower level of hemoglobin ($p<0.001$), white blood cell count ($p=0.015$), neutrophil ($p=0.016$), AST
29 ($p=0.037$), ALT ($p<0.001$) and procalcitonin ($p<0.001$), and higher level of D-dimer($p<0.001$) and
30 TT ($p<0.001$). higher incidence of pulmonary effusion, cord high density shadows, pleural
31 thickening, atelectasis were observed in hemolysis patients($p<0.05$). As clinical outcomes,
32 hemodialysis patients showed relatively higher mortality and prolonged hospital stay.

33 **Conclusion** Hemodialysis patients were a high-risk group of COVID-19 infections, as
34 hemodialysis patients often had multiple comorbidities, worse physical condition, patients with
35 COVID-19 may have prolonged hospital stay unfavorable prognosis, COVID-19 infection should
36 be monitored intensively for hemodialysis patients.

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38 Since December 2019, with the outbreak of coronavirus disease 2019 (COVID-19), it has now
39 spread throughout the world [1], COVID-19 is now considered a globally pandemic by the World
40 Health Organization. As of April 5, 2020, a total of 1133758 cases have been confirmed and 62784
41 deaths have been reported across 209 countries or regions [2]. Previous studies have showed that
42 the elderly are susceptible to COVID-19 infection, particularly those with chronic comorbidities [3,
43 4]. The initial COVID-19 cases indicated that 41.3% are due to hospital-related transmission [5].
44 As hemodialysis patients need admit to hospital for dialysis two to three times per week, most
45 patients were immunocompromised due to uremia and physical proximity of patients during
46 hemodialysis. These factors increase the risk of disease transmission and lead to hemodialysis
47 patients being more susceptible to COVID-19 infection than the general population. Most
48 hemodialysis patients are older age and have certain comorbidities, such as coronary disease,
49 hypertension, diabetes, and lung disease, that are associated with unfavorable outcomes in patients
50 with COVID-19[6]. Previous COVID-19 infection studies mostly focus on general population [7,
51 8]. Currently clinical information regarding the clinical features and outcome of COVID-19 in
52 hemodialysis patients is lacking. So, according to describing clinical characteristics, laboratory
53 finding, radiological characteristics, treatment, and outcomes of 16 hemodialysis patients
54 confirmed to have COVID-19 infection, we aimed to provide an insight for the clinical assessment
55 and management of hemodialysis patients with COVID-19.

56

57 **Patients and methods**

58 **Study design and participants**

59 For this retrospective, single-center study, we recruited hemodialysis patients with confirmed
60 COVID-19 infection from Feb. 5th to Mar. 20th, 2020. in Wuhan Fourth Hospital, Tongji Medical
61 College, Huazhong University of Science and Technology, Wuhan, China. Wuhan Fourth Hospital
62 is one famous comprehensive hospital with long history of 150-years. During a major outbreak of
63 COVID-19 in Wuhan, Chinese government arranged Wuhan Fourth Hospital as designated
64 hospital for hemodialysis patients with COVID-19 infection. Hemodialysis patients with
65 confirmed and suspected COVID-19 infection were admitted centrally to Wuhan Fourth Hospital.
66 All enrolled hemodialysis patients with confirmed COVID-19 infection were diagnosed according
67 to WHO interim guidance in this study [9]. The results were further compared with a control group
68 of 62 nondialysis COVID-19 patients from the same hospital that were matched for sex and age.
69 This study was approved by institutional review board (IRB) at Wuhan Fourth Hospital (IRB
70 approval number: KY 2020-032-01). Informed consent was waived as part of a public health
71 outbreak investigation.

72 **Data Collection**

73 Two doctors in our team collected and checked clinical information from electronic medical
74 records in Wuhan Fourth Hospital. Patient information including epidemiology, demographics,
75 medical history, laboratory findings, comorbidities, treatment regimens (antiviral, antibiotic,
76 corticosteroid therapies, immune glucocorticoid therapy, and respiratory support), length of

77 hospital stay, and clinical outcomes were collected and analyzed. If data were missing from the
78 medical records, we obtained data by communication with attending doctors or patients directly.

79 **Definitions**

80 The discharge criteria were defined as: body temperature has returned to normal for more than
81 three days, the respiratory symptoms have improved significantly, and the chest CT imaging
82 showed obvious inflammation absorption. Two consecutive nucleic acid tests for throat swabs
83 were negative and the time interval was at least one day. Finally, after an evaluation by the expert
84 team, a comprehensive evaluation was made whether the patient can be discharged.

85 **Statistical analysis**

86 In the descriptive statistical analysis, categorical variables were expressed as numerical values
87 (%). Continuous variables were directly presented as median with interquartile ranges. All
88 statistical analysis was performed using SPSS software (version 21.0).

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91 **Results**

92 **Clinical characteristics**

93 A total of 16 hemodialysis patients with COVID-19 were included in this study. All patients were
94 hospitalized. Clinical characteristics of 16 hemodialysis patients were showed in Table 1. The
95 median age of all hemodialysis patients was 61 years (interquartile range 54-78 years), 8 of 16
96 patients were female. No case had exposure to Huanan seafood market that appeared to be the
97 epicenter of COVID-19 infection. All patients had contact history of epidemic area and contact
98 history of fever patients. 12 cases (75%) had comorbidities, with coronary disease, hypertension
99 and diabetes being the most common. The most common initial symptoms at admission were
100 cough (75%) and shortness of breath (50%), followed by fatigue (50%) and fever (43.75%). The
101 median incubation period was 9 days (interquartile range 4.3-12 days), (Table 1). Compared with
102 nondialysis patients, hemodialysis patients presented lower incidence of fever($p=0.001$). Although
103 there is no statistical difference, hemodialysis patients had higher incidence of preadmission
104 comorbidities and shortness of breath.

105 **Radiological and laboratory findings**

106 Abnormal chest CT scan were observed in 16 patients (100%) at admission, the chest CT imaging
107 showed typical signs of viral infection in hemodialysis (Figure 1), such as bilateral patchy
108 shadowing (100%) and ground-glass opacities (62.5%), (Table S1). But compared with
109 nondialysis patients, hemodialysis patients presented higher incidence of pulmonary effusion
110 ($p<0.001$), cord high density shadows ($p<0.001$), pleural thickening ($p=0.0046$), atelectasis
111 ($p=0.0046$) and consolidation of lung($p=0.053$). Almost all hemodialysis patients had anemia

112 (15[93.75%] patients), hypoproteinemia (16[100%] patients), lymphopenia (16[100%] patients)
113 and coagulopathy with elevated D-dimer (14[92.86%] patients) at admission. Infection-related
114 biomarkers including procalcitonin and C-reactive protein, were also abnormal in almost all
115 patients (Table S1). Compared with nondialysis patients, hemodialysis patients had a lower level
116 of hemoglobin ($p<0.001$), white blood cell count ($p=0.015$), neutrophil ($p=0.016$), AST ($p=0.037$),
117 ALT ($p<0.001$) and procalcitonin ($p<0.001$), and higher level of D-dimer($p<0.001$) and TT
118 ($p<0.001$).

119 **Treatment and outcomes**

120 After hospital admission, all patients received treatment according to the Chinese Diagnosis and
121 Treatment Protocol for Novel Coronavirus Pneumonia (6th version) [10]. 15 of 16 patients received
122 oxygen therapy in isolation. 14 of 16 patients received antiviral treatment, including Arbidol (0.2g
123 three times daily, orally), Lopinavir and Ritonavir Tablets (0.5mg two times daily, orally), and
124 Oseltamivir (75mg two times daily, orally) and Ribavirin (500 mg once per day, intravenously).
125 Traditional Chinese medicines, such as Lianhuaqingwen capsules and Toujiequwen Keli, were
126 also given. 14 (87.5%) patients were treated with antibiotic, including Amoxicillin clavulanate
127 potassium, Levofloxacin, Moxifloxacin, Cephalosporin, Ceftriaxone, Cefoxitin, Cefoperazone
128 sulbactam. 9 (56.25%) patients received a single antibiotic treatment and 5 (31.25%) patients
129 received combination treatment. Two (12.5%) patients also received corticosteroids treatment, and
130 1(6.25%) patients received intravenous immunoglobulin therapy (Table S2). Compared with
131 nondialysis patients, there was no difference in treatment between dialysis patients and general
132 patients. Moreover, hemodialysis was performed according to the previous frequency in isolation

133 room designated for COVID-19 patients. At the end of follow-up (April 5, 2020), all clinical
134 outcomes of patients have been observed. The median hospitalization days was 21 days
135 (interquartile range, 15.5-30.25 days), 13 patients had recovered and been discharged from the
136 hospital, 3 patients were dead, mortality was 18.75%. Although there is no statistical difference,
137 hemodialysis patients showed higher mortality and prolonged hospital stay ($p=0.427$ and $p=0.077$).

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140 **Discussion**

141 This study represents the clinical characteristics and outcomes of hemodialysis patients infected
142 with COVID-19. Currently, the research about hemodialysis patients with COVID-19 is scarce.
143 This study is one of the first to report clinical characteristics and outcomes exhaustively.
144 We found most of the hemodialysis patients with COVID-19 were middle age and senile patients,
145 12 cases (75%) had comorbidities, including coronary disease, hypertension and diabetes. As most
146 hemodialysis patients were immunocompromised due to uremia [11-13]. These factors may lead
147 to longer hospital stay and higher mortality in hemodialysis patients than general population.
148 Hemodialysis patients presented similar clinical symptoms as general patients with COVID-19,
149 including fever, cough, sore throat, shortness of breath, myalgia, headache, fatigue and diarrhoea
150 [3, 7]. The length of the incubation period was almost the same, about 1-14 days. As previous
151 study reported, only 18.7% patients had shortness of breath in nondialysis population [7], but the
152 percent rate of shortness of breath was 50% in hemodialysis patients. We suggested it is
153 attributable to several factors, firstly, most of hemodialysis patients (50%) had pulmonary effusion
154 caused by hypoproteinemia due to chronic kidney disease and inadequate hemodialysis. Secondly,
155 some hemodialysis patients had lung inflammation and pleural thickening for a long time due to
156 long-term accumulation of fluid in the lungs. Moreover, hemodialysis patients had lower incidence
157 of fever, this is probably related to the relatively suppressed immunity caused by uremia.
158 In this study, almost all hemodialysis patients had anemia, hypoproteinemia and lymphopenia
159 coagulopathy with elevated D-dimer at admission. These factors increased the risk of unfavorable
160 prognosis. Previous study revealed severe lymphopenia and elevated D-dimer were risk factors for

161 prognosis of patients with COVID-19[6]. But in hemodialysis patients, elevated D-dimer may be
162 partly caused by uremia and hemodialysis. Hence, we could not simply assess D-dimer levels as
163 risk factors for mortality in hemodialysis patients with COVID-19, as did in general population.
164 All hemodialysis patients had all typical signs of viral infection in chest CT imaging, including
165 ground-glass opacities and bilateral patchy shadowing. But many maintenance hemodialysis
166 patients had pulmonary effusion due to inadequate hemodialysis, and chronic lung inflammation
167 caused by uremia and pulmonary effusion may lead to CT imaging features such as cord high
168 density shadows, pleural thickening, atelectasis and pulmonary fibrosis. Moreover, Healthcare-
169 associated pneumonia (HDAP) is the common infectious problems encountered in hemodialysis
170 patients [14, 15]. Therefore, these CT features may make the diagnosis of COVID-19 infection
171 more difficult in hemodialysis patients, compared with nondialysis population.

172 Respiratory syndrome coronavirus 2 (SARS-CoV-2), which cause the COVID-19 disease, belongs
173 to the β -type coronavirus, which has an envelope, the particles are round or oval, often
174 polymorphic, and the diameter is 60-140nm [16]. Current research showed SARS-CoV-2 has more
175 than 79% homology with severe acute respiratory syndrome (SARS) coronavirus, and the S
176 proteins of SARS-CoV-2 and SARS-CoV, have an sequence similarity of around 77%[17, 18],
177 However, clinical studies demonstrated there were many differences between SARS-CoV-2 and
178 SARS coronavirus, SARS-CoV-2 has higher infectivity and lower lethality compared with SARS
179 coronavirus[7, 8, 19, 20]. A study about severe acute respiratory syndrome in dialysis patients
180 showed dialysis patients had similar clinical features and mortality rates as the nondialysis patients,
181 but dialysis patients tend to have less pronounced symptoms and had a much longer hospital stay

182 compared with nonuremic patients [21]. In our study, dialysis patients tend to have lower incidence
183 of fever but higher incidence of shortness of breath and unfavorable clinical prognosis. We
184 suggested it may be attributable to great differences in the pathogenic mechanisms of the two
185 viruses, and further research is needed to demonstrate the differences.

186 The limitations of this study include the small number of patients from a single center, and a
187 systematic and comprehensive study including large number of samples across multiple centres
188 are needed to search COVID-19 infections in hemodialysis patients. Then as our hospital are
189 designated hospital for only hemodialysis patients with COVID-19 infection, so we can only
190 collect information of hemodialysis patients without COVID-19, and we cannot describe the
191 epidemiology of COVID-19 infections in hemodialysis patients. However, this study provides
192 some initial experiences about the characteristics of COVID-19 in hemodialysis patients.

193 In summary, we describe clinical characteristics and outcomes of hemodialysis patients with
194 COVID-19 infection. Overall, hemodialysis patients were a high-risk group of COVID-19
195 infections, hemodialysis patients had similar clinical characteristics, with multiple comorbidities
196 and worse physical condition, hemodialysis patients had prolonged hospital stay and unfavorable
197 clinical prognosis. COVID-19 infection should be monitored intensively for hemodialysis patients.

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205 **Author contributions**

206 Dr. Luo had full access to all of the data in the study and takes responsibility for the integrity of
207 the data and the accuracy of the data analysis.

208 **Study concept and design:** C.A. Cao, Y.Y. Luo.

209 **Acquisition, analysis, or interpretation of data:** Y.Y. Luo, Z.F. Liu, J.L. Li, X. Peng.

210 **Drafting of the manuscript:** Y.Y. Luo, Z.F. Liu.

211 **Critical revision of the manuscript for important intellectual content:** C.A. Cao, X. Peng.

212 **Statistical analysis:** Y.Y. Luo.

213 **Administrative, technical, or material support:** J.L. Li, X. Peng.

214 **Study supervision:** C.A. Cao.

215

216 **Data sharing Statement**

217 With the permission of the corresponding author, we can provide participant data, statistical

218 analysis.

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233 **Conflict of interest**

234 The authors have nothing to disclose.

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237 **Reference**

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242 [covid-19.pdf?sfvrsn=ca96eb84_2](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200410-sitrep-81-covid-19.pdf?sfvrsn=ca96eb84_2) (accessed Apr. 11, 2020).
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288 **Figure legend**

289 Figure 1: Chest CT imaging of four hemodialysis patients. Patient 4 (A), patient 9 (B), patient 13
290 (C), and patient 16 (D). The brightness of patients' lungs is diffusely decreased, presenting typical
291 signs of viral infection (large area of multiple ground-glass opacities or patchy shadow with an
292 uneven density), pulmonary effusion and cord high density shadows due to uremia and inadequate
293 hemodialysis.

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Table 1 (on next page)

Table 1

Clinical characteristics of hemodialysis patients with COVID-19

1 **Table 1 Clinical characteristics of hemodialysis patients with COVID-19**

characteristics	No. (%)		p value
	Hemodialysis Patients	General Patients	
Age (years), median (IQR)	61(54-78)	62(50-70)	0.439
Male	8(50)	33(53.2)	0.755
Contact history of epidemic area	16(100)	62(100)	>0.99
Preadmission comorbidities	12(0.75)	38(0.61)	0.467
Hypertension	11(68.75)	19(30.65)	0.012
Diabetes	3(18.75)	11(17.74)	>0.99
Cardiovascular diseases	4(25)	4(6.45)	0.086
Cerebrovascular diseases	0(0)	2(3.23)	>0.99
Malignancy	1(6.25)	2(3.23)	>0.99
COPD	0(0)	2(6.45)	>0.99
Tuberculosis	0(0)	2(3.23)	>0.99
Pneumonia related manifestations			
Cough	12(75)	45(72.58)	0.699
shortness of breath	8(50)	19(33.87)	0.248
Fatigue	8(50)	42(67.74)	0.305
Fever	7(43.75)	54(87.10)	0.001
Diarrhoea	2(12.5)	11(17.74)	0.90
Myalgia	2(12.5)	23(37.10)	0.275
Headache	1(6.25)	2(3.22)	>0.99
Sore throat	1(6.25)	3(4.84)	>0.99
Incubation period (days)	9 (4.3-12)	8(5-12)	0.674

2

Figure 1

Figure 1

Chest CT imaging of four hemodialysis patients

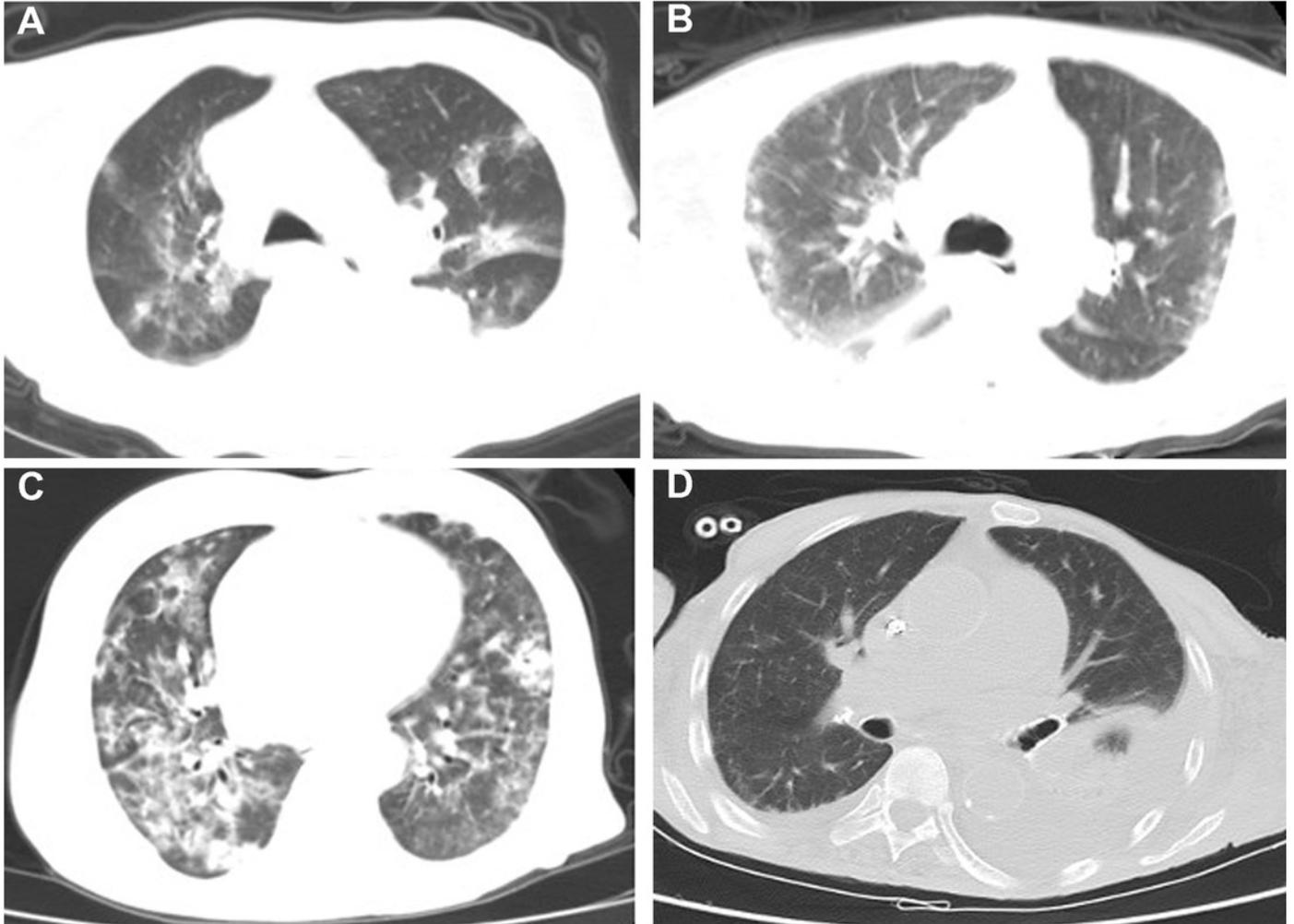


Table 2 (on next page)

Table 2

Laboratory results of Hemodialysis patients with COVID-19

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Table 2 Laboratory results of Hemodialysis patients with COVID-19

characteristics	No. (%)		p value
	Hemodialysis Patients	General Patients	
Admission radiologic findings (chest CT)			
Bilateral patchy shadowing	16(100)	58(93.5)	0.683
Ground-glass opacities	10(62.5)	47(75.8)	0.451
Pulmonary effusion	8(50)	2(3.23)	<0.001
Cord high density shadows	7(43.75)	4(6.45)	<0.001
Pleural thickening	4(25)	1(1.6)	0.0046
Atelectasis	4(25)	1(1.6)	0.0046
Consolidation of lung	2(12.5)	0(0)	0.053
Blood routine			
Hemoglobin (g/L)	91.5(79.25-102.5)	127.5(115-141.75)	<0.001
White blood cell count ($\times 10^9/L$)	4.29(3.56-6.69)	6.22(4.66-8.38)	0.015
Neutrophil($\times 10^9/L$)	3.19(2.47-5.3)	5.18 (3.27-7.44)	0.016
Lymphocyte count ($\times 10^9/L$)	0.65(0.51-0.91)	0.74(0.40-1.17)	0.656
Coagulation function			
APTT	31.5(26.6-43.3)	35.5(32.13-38.32)	0.29
Prothrombin time (s)	12.2(11.05-14.13)	12.9(12.3-13.33)	0.133
TT	19.5(18.9-20.98)	15.7(14.7-16.5)	<0.001
D-dimer (mg/L)	1.84(0.88-4.55)	0.49(0.24-1.27)	<0.001
Blood biochemistry			
AST (U/L)	20(13-24)	25.5(17-42.25)	0.037
ALT (U/L)	10(6.25-13.5)	28(16-42.25)	<0.001
Serum creatinine ($\mu\text{mol/L}$)	1067.5(855.08-1392.23)	70.5(55.75-82.25)	<0.001

Infection-related biomarkers			
C-reactive protein (mg/L)	39.3(23.85-87.53)	44.74(20.73-74.20)	0.782
Procalcitonin (ng/mL)	0.85(0.44-2.79)	0.04(0.04-0.06)	<0.001

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Table 3 (on next page)

Table 3

Treatment and clinical outcome of Hemodialysis patients with COVID-19

1 **Table 3 Treatment and clinical outcome of Hemodialysis patients with COVID-19**

characteristics	No. (%)		p value
	Hemodialysis Patients	General Patients	
Oxygen therapy	15(93.75)	52(83.9)	0.542
Mechanical ventilation	2(12.5)	6(9.68)	>0.99
Antibiotic treatment	14(87.5)	47(75.8)	0.503
Antiviral treatment	14(87.5)	60(96.8)	0.388
Traditional chinese medicine	14(87.5)	56(90.3)	1
Glucocorticoids	2(12.5)	15(24.2)	0.503
Intravenous immunoglobulin therapy	1(6.25)	9(14.5)	0.644
Length of stay (d)	21 (15.5-30.25)	14 (11-20)	0.077
Outcomes (death	3(18.75)	5(8.06)	0.427

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