RESEARCH LETTER

The clinical course and short-term outcomes of coronavirus disease 2019 in a cohort of hemodialysis patients

Anna Petrulewicz[1*], Alicja Rydzewska-Rosołowska[2*], Bartosz Fiderkiewicz[1,3], Anna Wasińska-Krawczyk[1,3], Szymon Brzósko[4,5], Jerzy Walecki[6], Andrzej Rydzewski[1,3]

1 Department of Internal Medicine, Nephrology and Transplantation Medicine, Centre of Postgraduate Medical Education, Central Clinical Hospital of the Ministry of the Interior and Administration, Warsaw, Poland
2 2nd Department of Nephrology and Hypertension with Dialysis Unit, Medical University of Bialystok, Białystok, Poland
3 Centre of Postgraduate Medical Education, Warsaw, Poland
4 1st Department of Nephrology and Transplantation with Dialysis Unit, Medical University of Bialystok, Białystok, Poland
5 DaVita Poland, Wrocław, Poland
6 Department of Radiology, Centre of Postgraduate Medical Education, Central Clinical Hospital of the Ministry of the Interior and Administration, Warsaw, Poland

Correspondence to:
Alicja Rydzewska-Rosołowska, MD, PhD, 2nd Department of Nephrology and Hypertension with Dialysis Unit, Medical University of Bialystok, ul. Skłodowskiej-Curie 24A, 15-276 Białystok, Poland, phone: +48 85 831 78 72, email: alicja.rosolowska@umb.edu.pl
Received: April 24, 2020.
Revision accepted: June 9, 2020.
Published online: July 4, 2020.
Pol Arch Intern Med. 2020; 130 (9): 809-812
doi:10.20452/pamw.15479

* AP and ARR contributed equally to this work.

Introduction Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a novel coronavirus causing coronavirus disease 2019 (COVID-19). Its spread started when multiple cases of pneumonia of unknown origin occurred in Wuhan, China, and were first reported to the World Health Organization Country Office in China on December 31, 2019. The infection spread rapidly to other parts of the world and was declared a pandemic on March 11, 2020, when the number of cases hit 118 000 in 114 countries of the world.[1]

The first case in Poland was reported on March 4, 2020. Local transmission of SARS-CoV-2 was reported to the World Health Organization on March 10, 2020.[2] On March 13, 2020, the Central Clinical Hospital of the Ministry of the Interior and Administration in Warsaw was one of the 19 hospitals in Poland repurposed into a designated hospital adapted to take care of patients with COVID-19 only. The hemodialysis facility was also turned into a dialysis clinic for COVID-19-positive patients in order to serve hemodialysis patients from Warsaw and the Masovian region (5.403 million people and 2713 chronic hemodialysis patients). Between March 20 and April 18, 2020, 23 maintenance hemodialysis patients and a single patient on hemodialysis due to acute kidney injury, all with confirmed COVID-19, were under our care.

Reports on hemodialysis patients with SARS-CoV-2 infection are limited, with conflicting data on mortality: 15.2% mortality in the United Kingdom Renal Registry,[3] 24% mortality in Lombardy, Italy,[4] versus no COVID-19-related mortality in Wuhan, China.[5,6] That is why we aimed to describe demographic characteristics, the clinical course of COVID-19, laboratory and imaging findings, and outcomes in this unique patient population.

Patients and methods **Study population and data collection** We included only the dialyzed patients transferred to our Dialysis Unit who had a confirmed diagnosis of COVID-19. A confirmed diagnosis was defined as a positive result of reverse transcriptase–polymerase chain reaction assay test (gene targets: RdRp, E, and N) for SARS-CoV-2 performed using the patient's nasopharyngeal swab.

Twenty-three adults (at the age of 18 years or older) were identified from 6 different hemodialysis clinics in the Masovian region. We included 19 maintenance hemodialysis patients in the analysis (for a follow-up longer than 14 days and / or until an endpoint in treatment was reached, ie, virus elimination or the patient's death). Three patients in whom the follow-up was shorter than 14 days and a single dialysis-dependent patient with acute kidney injury due to ethylene glycol ingestion were excluded.

Medical records were obtained from each institution and included information on patients' demographics and comorbidities. Laboratory and radiologic data were retrieved from patients' electronic records. Additional tests and imaging were left at the discretion of the treating physician.

Ethics The Bioethics Committee of the Central Clinical Hospital of the Ministry of the Interior and Administration approved the study. To reduce the risk of SARS-CoV-2 transmission on paper, informed consent was waived and anonymized data were analyzed.

Statistical analysis Descriptive statistics were used for data summary. Study results were reported as mean (SD) or median and interquartile range, whereas categorical variables were presented as number and percentage. The Shapiro–Wilk test for normality was used. Two-sample *t* test and the Mann–Whitney test were used to compare the 2 study groups with regard to continuous variables (depending on normal or skewed distribution), and the χ^2 test was applied to the nominal ones. A *P* value less than 0.05 was considered significant. No missing data imputation procedure was applied. The analysis was performed using the Stata software, version 9.2 (College Station, Texas, United States).

Results **Demographic and clinical characteristics of the study patients** The identified hemodialysis patients with COVID-19 comprised 0.7% of the entire hemodialysis-dependent population in the Masovian region. The demographic and clinical characteristics of the 19 study patients are shown in TABLE 1. None of the patients had recently traveled and all except 1 had presumed close contact with an infected person (based on an epidemiological investigation conducted at each facility). All individuals were hospitalized on the day of COVID-19 diagnosis.

Cough (9 patients [47.4%]) and body temperature exceeding 37.5 °C (9 patients [47.4%]) were the most common symptoms observed in our cohort. Two patients were asymptomatic at presentation, but they had typical, bilateral, peripheral ground-glass opacities in the lower lobes on computed tomography (CT). Comorbidities were common (TABLE 1).

Diagnostic workup The laboratory and radiologic findings of the study patients reported on admission are also shown in TABLE 1. Only 3 patients (15.8%) had a low white blood cell count (below 4.4×10^3/μl), and 11 patients (57.9%) presented with lymphocytopenia (lymphocyte count below 1×10^3/μl). Of note, 17 patients (89.5%) had an elevated procalcitonin level (higher than 0.25 ng/ml). Chest radiography was performed in all patients, and CT in 8 (42.1%).

Therapeutic intervention According to the standard hospital protocol (based on the recommendations of the Polish Society of Epidemiology and Infectious Diseases), all patients were treated in the same manner. Every SARS-CoV-2-positive patient received chloroquine 250 mg twice a day (started at day 1 and continued for 7 to 10 days), and if the Modified Early Warning Score[7] was higher than or equal to 3, lopinavir / ritonavir 400 mg + 100 mg twice a day (compassionate use, after approval of the local bioethics committee) was additionally prescribed. Most patients received antibiotics (16 [84.2%]), most commonly azithromycin (13 [68.4%]). No formal analysis of chloroquine adverse effects was conducted. No patient required discontinuation or dose reduction due to adverse effects, but the QTc interval was assessed based on cardiac monitoring only; serial electrocardiograms were not available. Concomitant treatment was left at the discretion of the treating physician. Supplemental low-oxygen therapy was required in 8 patients (42.1%).

Follow-up and outcomes All patients were followed up for a mean (SD; range) time of 16 (6; 5–29) days. During that time, 4 patients required intubation and invasive mechanical ventilation because of acute respiratory distress syndrome (21.1%), and 5 patients died (mortality, 26.3%; 4 individuals died in the intensive care unit, and a single patient in the nephrology department). The patients who died were all male, at a mean (SD) age of 70.6 (12.9) years and had a mean (SD) Charlson Comorbidity Index of 7.8 (3.1). Two of them had a history of a recent (less than 3 months before COVID-19 diagnosis) cardiovascular event (myocardial infarction or stroke). They had a significantly higher median (interquartile range) Modified Early Warning Score score (2 [0–2] versus 0; $P = 0.002$) and a lower mean (SD) lymphocyte count (0.63 [0.09] $\times 10^3$/μl versus 1.1 (0.4) $\times 10^3$/μl; $P = 0.04$). As of April 18, 2020, 7 study patients (36.8%) were able to eliminate the virus (repeat testing was performed in clinically stable patients: if positive, a retest was ordered after 7 days; 2 negative tests one day apart were required to confirm elimination). The mean (SD) elimination time was 15.1 (1.95) days.

Discussion In this research letter, we reported on 19 hemodialysis patients diagnosed with COVID-19, accounting for roughly 0.7% of the entire hemodialysis population in the analyzed region. The percentage is relatively small compared with unpublished data from Lombardy, Italy, showing that 8% of hemodialysis patients were infected.[4] Of note, the current strategy in Poland is that only patients with a body temperature exceeding 37.5 °C and / or respiratory symptoms, and / or proven contact with an infected person are tested. Other possible explanations might be that either the social distancing strategy is working well in Poland or that the epidemic peak has not been reached yet (much more probable).

The mean (SD) age of our study patients was 65.7 (12.2) years, which is similar to that of the entire hemodialysis population from the Masovian region ($P \leq 0.05$) and in line with previous reports on hemodialysis patients[5,6]; the mean age of all hospitalized patients in Wuhan, China, was lower.[8] Similar to other authors, we observed a predominance of men among study

TABLE 1 Demographic, clinical, laboratory, and imaging characteristics of the study patients on admission

Characteristic		Patients (n = 19)
Age, y, mean (SD; range)		65.7 (12.2; 34–85)
Male sex		13 (68.4)
BMI, kg/m^2, mean (SD; range)		23.2 (3.8; 15.2–31.1)
Dialysis vintage, y, mean (SD; range)		5.1 (4.4; 0–16)
Cause of kidney failure	Diabetic kidney disease	2 (10.5)
	Glomerulonephritis	4 (21.1)
	Other	11 (57.9)
	Unknown	2 (10.5)
Comorbidities	Diabetes	3 (15.8)
	Hypertension	18 (94.7)
	Coronary artery disease	5 (26.3)
	Chronic heart failure	8 (42.1)
	Cerebrovascular disease	6 (31.6)
	Chronic pulmonary disease	2 (10.5)
	Connective tissue disease	1 (5.3)
	Liver disease	2 (10.5)
	History of neoplasm	6 (31.6)
Charlson Comorbidity Index, mean (SD; range)		6.8 (2.6; 3–12)
Symptoms	Temperature >37.5 °C	9 (47.4)
	Cough	9 (47.7)
	Dyspnea	7 (36.8)
	Fatigue	6 (31.6)
	Diarrhea	4 (21.1)
	Abdominal pain	1 (5.2)
Past or current smoking status		12 (63.2)
SpO_2, %, median (IQR)		96 (92–98)
MEWS on admission, median (IQR)		0 (0–2)
White blood cell count	Total, $\times 10^3$/µl, mean (SD; range)	5.344 (1.378; 2–7.85)
	$\geq 10 \times 10^3$/µl	0
	$\leq 4.4 \times 10^3$/µl	3 (15.8)
Lymphocyte count	Total, $\times 10^3$/µl, mean (SD; range)	0.95 (0.4; 0.34–0.168)
	$\leq 1 \times 10^3$/µl	11 (57.9)
AST >40 U/l		1 (5.2)
ALT >40 U/l		0
CRP	Total, mg/l, median (IQR)	54.5 (13.5–109.9)
	>10 mg/l	15 (78.9)
Procalcitonin	Total, ng/ml, median (IQR)	0.88 (0.33–1.6)
	≥0.25 ng/ml	17 (89.5)
Infection, positive n/total n (%)	Influenza A and B	0/12
	Legionella	0/3
	Chlamydia	0/7
Chest X-ray findings, n/total n (%)	Clear	8/19 (42.1)
	Bilateral infiltrates	9/19 (47.4)
	Pleural effusion	3/19 (15.8)
CT findings, n/total n (%)	Bilateral ground-glass opacity	5/8 (62.5)
	Nodules	1/8 (12.5)
	Pleural effusion	2/8 (25)

Data are presented as number (percentage) unless otherwise indicated.

Abbreviations: ALT, alanine transaminase; AST, aspartate aminotransferase; BMI, body mass index; CRP, C-reactive protein, CT, computed tomography; IQR, interquartile range; MEWS, Modified Early Warning Score

patients. Contrary to reports from Wuhan, China, where diarrhea was the most common clinical presentation reported[5] or patients were largely asymptomatic,[6] cough and body temperature above 37.5 °C were predominant in our cohort. This is in agreement with symptoms reported by numerous authors in patients not requiring hemodialysis.[8] Most patients had multiple comorbidities, with the dominant one being hypertension, which may reflect a higher risk of the severe COVID-19 course.[9]

Similar to other reports, more than half of our study patients had lymphocytopenia. However, interestingly, almost 90% of them exhibited an elevated procalcitonin level (higher than 0.25 ng/ml), which might be indicative of a concomitant bacterial infection and is also a predictive factor for mortality in COVID-19.[10] Although it is difficult to draw firm conclusions, a notable finding is that pleural effusion was observed in 15.8% of patients on chest X-ray and in 25% on CT. In this specific population of patients, pleural effusion, which is usually not seen in COVID-19,[11] might be present owing to volume overload and concomitant heart failure.

The course and outcomes of COVID-19 in our cohort of hemodialysis patients are significantly different than those reported before. Two papers demonstrated no need for intubation and invasive mechanical ventilation and no mortality associated with COVID-19 in this population.[5,6] The reason for the presumed milder disease course is the compromise of the immune system and the inability to trigger the deadly cytokine storm.[12] Unfortunately, in our study, over 20% of patients required invasive mechanical ventilation and over 26% of patients died until April 18, 2020. This number is closer to the unpublished data from the United Kingdom Renal Registry and Lombardy, Italy, where mortality rates in hemodialysis patients with COVID-19 were approximately 15% and 24%, respectively.[3,4]

Limitations We are aware of the limitations of our report. In some of the study patients, data were missing, follow-up was incomplete, and the sample size was small. However, considering the need to disseminate objective clinical data and the urgent timeline, we found it essential to share the data gathered until now. On the other hand, we collected clinical data on all confirmed cases of COVID-19 among hemodialysis patients in a single region of Poland. Furthermore, all patients received care of the same standard (an identical approach was used, as the patients were treated in one center) and reached an endpoint in treatment (virus elimination or death) or were followed up for at least 14 days.

Conclusions In conclusion, our study provided data on the clinical course of COVID-19 in a cohort of hemodialysis patients, which, contrary to previous Chinese experience, were not always favorable.[5,6]

ARTICLE INFORMATION

ACKNOWLEDGMENTS The authors would like to thank all the physicians who transferred patients to the Department of Internal Medicine, Nephrology and Transplantation Medicine in Central Clinical Hospital of the Ministry of the Interior and Administration, Warsaw, Poland.

CONFLICT OF INTEREST None declared.

HOW TO CITE Petrulewicz A, Rydzewska-Rosołowska A, Fiderkiewicz B, et al. The clinical course and short-term outcomes of coronavirus disease 2019 in a cohort of hemodialysis patients. Pol Arch Intern Med. 2020; 130: 809-812. doi:10.20452/pamw.15479

REFERENCES

1 World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media--briefing-on-covid-19--11-march-2020. Accessed April 7, 2020.

2 World Health Organization. Coronavirus disease 2019 (COVID-19) situation report – 49. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200310-sitrep-50-covid-19.pdf. Accessed April 7, 2020.

3 UK Renal Registry. https://renal.org/renal-association-statement-ppe--use-masks-dialysis-patients/. Accessed April 14, 2020.

4 LVRiella. RGR Dr Brunori. COVID-19 and dialysis in Italy. https://twitter.com/LVRiella/status/1244964797927612416. Posted March 31, 2020. Accessed April 14, 2020.

5 Wang R, Liao C, He H, et al. COVID-19 in hemodialysis patients: a report of 5 cases. Am J Kidney Dis. 2020; 76: 141-143.

6 Ma Y, Diao B, Lv X, et al. 2019 novel coronavirus disease in hemodialysis (HD) patients: report from one HD center in Wuhan, China. medRxiv. 2020. https://www.medrxiv.org/content/10.1101/2020.02.24.20027201v2. Accessed April 7, 2020.

7 Subbe CP, Kruger M, Rutherford P, et al. Validation of a modified Early Warning Score in medical admissions. QJM. 2001; 94: 521-526.

8 Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020; 382; 1708-1720.

9 Lippi G, Wong J, Henry BM. Hypertension in patients with coronavirus disease 2019 (COVID-19): a pooled analysis. Pol Arch Intern Med. 2020; 130: 304-309..

10 Shi S, Qin M, Shen B, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. JAMA Cardiol. 2020; 5: 802-810.

11 Li X, Zeng W, Li X, et al. CT imaging changes of corona virus disease 2019 (COVID-19): a multi-center study in Southwest China. J Transl Med. 2020; 18: 154.

12 Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020; 395: 1033-1034.