The 2019 novel coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) epidemic was first reported in December 2019 in Wuhan, China, and has been declared a public health emergency of international concern by the World Health Organization (WHO). It may progress to a pandemic associated with substantial morbidity and mortality.\(^1\) In the WHO European Region, coronavirus disease 2019 (COVID-19) screening was implemented on January 27, 2020, linked to 2 clusters in Germany and France.\(^2\) Although primarily a respiratory disease, COVID-19 can cause damage to tissues and organs other than the lung, leading to multiorgan dysfunction in patients at high risk.\(^3\)

Maintenance hemodialysis (HD) patients are at increased risk for COVID-19 and its complications due to a high burden of comorbid conditions and the mandatory congregate nature of HD facilities.\(^4\) Furthermore, logistical aspects of HD may further increase the risk for disease transmission.\(^5\) These include frequent encounters at health care facilities with other patients and staff, the physical proximity of patients during HD, and transportation to and from HD sessions.\(^6\) The dialysis community, recognizing the risk faced by HD patients, has published guidance and suggestions on risk mitigation of COVID-19 in this vulnerable patient population.\(^9\)\(^12\)

There is limited information regarding the epidemiology of COVID-19 in maintenance HD patients. In this report, we describe our experience with COVID-19 in our center, in which 38 maintenance dialysis patients developed COVID-19.

**METHODS**

**Study Participants and Data Collection**

This study was conducted in a center located in the 11th district of Paris. Our center includes 2 maintenance HD units (1 in-center HD facility [medical dialysis unit] and 1 self-care HD facility [AD: auto-dialysis]). All patients return home after HD sessions. Dialysis procedures, protective measures, and medical staff are similar in the 2 units.

On March 13, 2020, we had 2 COVID-19–positive patients. Following recognition of these cases, we implemented barrier measures including mask wearing for all patients and caregivers and a systematic screening procedure using a real-time reverse transcription-polymerase chain reaction (RT-PCR) assay. Figure 1 summarizes the
management flow and outcomes of the cluster followed up throughout the epidemic. Following infection identification, COVID-19–positive patients were grouped in a confined unit. The medical team participated in discussions with the corporate clinical team of Diaverum, as well as in webinars for patients receiving HD, and created awareness posters for dialysis facilities. From March 31 to April 4, 2020, a total of 38 moderately to severely ill or critically ill patients with confirmed COVID-19 were identified.

We obtained epidemiologic, clinical, laboratory, and radiologic characteristics, as well as treatment and outcome data, from electronic medical records for patients by using data collection forms. All data were collected in the context of care in accordance with the French law and included the Général Data Protection Régulation (GPD). We collected data for demographic characteristics, medical history, exposure history, underlying chronic diseases, symptoms and signs, laboratory findings, computed tomography (CT) of the chest, and treatment (including antiviral therapy, antibiotics, corticosteroid therapy, and oxygen support).

We monitored clinical data until April 15, 2020. A trained team of physicians and researchers analyzed patient medical records and independently entered and cross-checked data in a computerized database.

**Laboratory Measurements**

**Real-Time RT-PCR Assay for SARS-CoV-2**

Nasopharyngeal swab samples of patients were collected for SARS-CoV-2 testing. Testing was done locally in the center by experienced nurses. The ORF1ab gene and the E gene were used for real-time RT-PCR according to the manufacturer’s instructions (Roche Molecular Systems).

**Clinical Laboratory Measurements**

The initial clinical laboratory investigation included a complete blood cell count, serum biochemical tests (including liver function, creatine kinase, lactate dehydrogenase, and electrolytes), and a coagulation profile.
patients, nurses, and staff. On March 17, lockdown measures were implemented in France. On March 18, we cancelled meals during dialysis sessions, and starting April 1, we performed nasopharyngeal testing with RT-PCR for all nursing staff and all patients who had not previously been diagnosed with COVID-19. The total screening of our cohort took 4 days (2 dialysis sessions and 2 different nurse teams). We did not make any changes in home medication regimens, specifically not changing existing treatment with corticosteroids or immunosuppressive drugs.

For COVID-19–infected patients, we strictly monitored dry weight at each dialysis session with clinical methods and weekly monitoring of brain natriuretic peptide levels.

**RESULTS**

**Demographics and Baseline Characteristics of Patients**

There were 200 patients in our HD center included in this study. The dynamic course of COVID-19 diagnosis from emergence to development is presented in Figure 2.

A total of 200 HD patients and 40 care staff were screened for COVID-19. Thirty-eight patients (19%) had COVID-19 diagnosed; 36 patients tested positive with a nasopharyngeal RT-PCR test for SARS-CoV-2, of whom 4 were asymptomatic. The remaining 2 patients tested negative with RT-PCR for SARS-CoV-2 but had typical findings from CT of the chest (bilateral ground-glass opacities). Patient characteristics are described in Table 1. Five care staff tested positive for COVID-19 by RT-PCR. Three of these were asymptomatic and were diagnosed by systematic screening on April 1; the other 2 staff members presented with symptoms suggestive of COVID-19 and tested positive on March 25 and 27, respectively.

Most (79%) of the 38 COVID-19–infected patients were men, with a median age of 66.5 (range, 31-89) years, median weight of 76.9 (range, 41.0-126) kg, and average body mass index of 27.2 kg/m². Only 1 patient was an active smoker. Blood group antigens were A (13 patients; 34%), B (6 patients; 16%), AB (3 patients; 8%) and O (16 patients; 42%). Patients had been receiving HD for a median of 3.5 (range, 0.1-17.3) years. Two patients had a prior kidney transplant and 16 patients were on the kidney transplant waitlist. The cause of kidney failure was diabetes (12 patients), hypertension (9 patients), polycystic (4 patients), chronic interstitial disease (1 patient), chronic glomerulonephritis (1 patient), and undetermined (11 patients) nephropathies. Usual treatments included long-term corticosteroids (3 patients), angiotensin-converting enzyme inhibitors (8 patients), or angiotensin receptor blockers (11 patients). Comorbid conditions included hypertension (95%), dyslipidemia (66%), diabetes (45%), ischemic heart disease (45%), obesity (26%), and cardiac rhythm dysfunction (13%). Seven patients were infected with other viruses (hepatitis C virus, 4 patients; hepatitis B surface antigen positive, 2 patients; and HIV, 1 patient).

The most common symptom was fever (68%), followed by dry cough (63%), fatigue (35%), dyspnea
(29%), myalgia (8%), gastrointestinal symptoms (such as diarrhea, vomiting and abdominal pain; 8%), rhinorrhea and sore throat (8%), chest pain (3%), and ageusia (3%). No patients had anosmia.

All patients were receiving intermittent HD 3 times per week with a polysulfone membrane and acetic acid because we stopped hemodiafiltration and citric acid at the beginning of the COVID-19 epidemic. We experienced HD system or dialyzer clotting more frequently than usual for 3 patients, for whom we increased the dose of heparin. We did not systematically increase the dose of heparin for all COVID-19–positive patients. Two patients experienced arteriovenous fistula thrombosis. We did not observe any thromboembolic events.

Laboratory Findings

All patients had lymphopenia with lymphocytes <1.0 ×10⁹/L at disease onset. At the peak of the epidemic, the mean decrease in lymphocyte count was −415 ×10⁹/L (−1,360 to +200 ×10⁹/L). C-Reactive protein levels increased from diagnosis until the peak of disease symptoms (mean, 41-95 mg/L), then decreased as the symptoms disappeared (Table 2). Four patients displayed d-dimer counts >1,500 (range, 1,850-4,000) UI/L. Brain natriuretic peptide levels increased quickly at the beginning of the disease as patients lost weight, and troponin levels increased moderately (mean, 34-78 ng/L). Lactate dehydrogenase levels also increased from a mean of 260 to 336 UI/L. No change in hepatic function was observed in our population.

**Table 1. Clinical and Radiologic Characteristics**

| Characteristics          | All Patients (N = 38) | Patients Who Died (n = 8) | Survivors (n = 30) |
|--------------------------|-----------------------|--------------------------|--------------------|
| Age, y                   | 66.5 (31-89)          | 74 (63-85)               | 65 (31-89)         |
| Sex (male/female)        | 30/8                  | 8/0                      | 22/8               |
| Mean BMI, kg/m²           | 27.2                  | 26.9                     | 27.3               |
| Duration of dialysis, y  | 3.5 (0.1-17.3)        | 4.3 (0.5-17.3)           | 3.2 (0.1-14.2)     |
| Waiting for kidney transplant | 16 (42%)             | 2 (25%)                  | 14 (47%)           |
| Blood group A/B/AB/O      | 13/6/3/16             | 3/0/0/5                  | 10/6/3/11          |
| Initial nephropathy       |                       |                          |                    |
| Hypertension             | 9                     | 3                        | 6                  |
| Diabetes                 | 12                    | 2                        | 10                 |
| Chronic glomerulopathy   | 1                     | 0                        | 1                  |
| Chronic interstitial nephritis | 1                 | 1                        | 0                  |
| ADPKD                    | 4                     | 0                        | 4                  |
| Unspecified              | 11                    | 2                        | 9                  |
| Comorbid conditions      |                       |                          |                    |
| Hypertension             | 36 (94.7%)            | 7 (88%)                  | 29 (97%)           |
| Diabetes                 | 17 (44.7%)            | 2 (25%)                  | 15 (50%)           |
| Obesity                  | 10 (26.3%)            | 2 (25%)                  | 8 (27%)            |
| Ischemic cardiopathy     | 17 (44.7%)            | 5 (63%)                  | 12 (40%)           |
| Symptoms                 |                       |                          |                    |
| Fever                    | 26 (68%)              | 8 (100%)                 | 18 (60%)           |
| Cough                    | 24 (63%)              | 6 (75%)                  | 18 (60%)           |
| Ageusia                  | 1 (3%)                | 0 (0%)                   | 1 (3%)             |
| Dyspnea                  | 11 (29%)              | 6 (75%)                  | 5 (17%)            |
| Fatigue                  | 12 (32%)              | 2 (25%)                  | 10 (33%)           |
| GI symptoms              | 3 (8%)                | 0 (0%)                   | 3 (10%)            |
| Drugs                    |                       |                          |                    |
| ACEI/sartan              | 8 (21%)/11 (29%)      | 0 (0%)/1 (13%)           | 8 (27%)/10 (33%)   |
| IS/CS                    | 1 (2.6%)/3 (7.9%)     | 0 (0%)/1 (13%)           | 1 (3%)/2 (6.6%)    |
| Chest CT                 |                       |                          |                    |
| Stage 1                  | 5                     | NA                       | 5                  |
| Stage 2                  | 7                     | NA                       | 7                  |
| Stage 3                  | 5                     | NA                       | 5                  |
| Stage 4                  | 1                     | NA                       | 1                  |
| Stage 5                  | 1                     | NA                       | 1                  |

Note: Values expressed as median (range), number, or number (percent). Stage 1 = minimal, stage 2 = moderate, stage 3 = extensive, stage 4 = severe, and stage 5 = critical.

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; ADPKD, autosomal dominant polycystic kidney disease; CS, corticosteroids; CT, computed tomography; GI, gastrointestinal; IS, immunosuppression; NA, not applicable.
As hemoglobin levels decreased from 11.0 to 10.6 g/dL with infection, we adapted the erythropoietin dosage in accordance with the recommendations, to maintain hemoglobin levels at >10 g/dL. Unfortunately, we do not have any information about the erythropoietin strategy for hospitalized patients.

Radiologic Findings
As shown in Table 1, a total of 19 patients treated in outpatient settings had abnormalities on CT of the chest. We used the graduation of pulmonary parenchyma lesions described by the Société d’Imagerie Thoracique. Ground glass opacities were the most common radiologic findings on CT of the chest and classified as stage 1 (minimal, 5 patients), stage 2 (moderate, 7 patients), stage 3 (extensive, 5 patients), stage 4 (severe, 1 patient), and stage 5 (critical, 1 patient).

Case Occurrence Time Line and Protective Measures
Because we had many cases of COVID-19 and wanted to eliminate healthy carriers as potential sources of contamination, we applied individual protective measures. When RT-PCR tests became readily available, we performed SARS-CoV-2 RT-PCR testing on all patients and all staff without previously known infection. Systematic SARS-CoV-2 RT-PCR testing was performed for all patients and caregivers on April 1, 2020 (Fig 2), which led to the positive diagnosis of 4 asymptomatic patients, who were subsequently isolated in the COVID-19 sector. Five staff were found to be infected, including 4 nurses and 1 nursing assistant with RT-PCR-positive tests.

The management of dialysis patients with COVID-19 was carried out according to strict protocols to minimize the risk to other patients and personnel taking care of these patients, which highlights the usefulness of generalized barrier measures for all patients and the strengthening of generalized personnel protection measures for caregivers.

Outcomes
All affected patients lost weight during the first disease period. The mean weight decrease was 2.4 kg (from 0.5 to 9.5 kg). Thirty patients survived. Fifteen patients (42%) were admitted to the hospital, including 4 in intensive care units (ICUs). Two of the 4 patients in ICUs survived. Six of the 8 patients who died were denied ICU admission because of their high number of comorbid conditions and not because of the patient’s advance directives.

No patient received antiviral therapy, hydroxychloroquine, dexamethasone, or tocilizumab. Eight patients died (21% and 23% of all and symptomatic COVID-19–positive patients, respectively, corresponding to 4% of patients at the center) because of COVID-19, with multiorgan failure and sepsis the most common causes of death. The median time from the onset of respiratory symptoms to ICU admission was very short, ranging only from 1 to 2 days, and median survival from the onset of symptoms to death was 10 (range, 4–15) days. The duration of hospitalization was 10 (range, 5–23) days and time in the ICU was 13 days.

Besides usual treatments, 84.2% of patients with COVID-19 received antibiotics: roxithromycin and ceftriaxon combination (11 patients), amoxicillin/clavulanic acid combination (7 patients), and others (14 patients).

Other measures in the treatment of these patients were taken: decrease in the target weight to improve respiratory function, limiting the use of hemodiafiltration, reducing dialysis time in some cases, and increasing the dose of anticoagulant.

DISCUSSION
In a single HD center in Paris, France, we had a high prevalence of COVID-19 among patients. Through

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**Table 2. Laboratory Characteristics**

|                         | Baseline | At Diagnosis | Peak of the Disease | Delta (baseline/maximum) |
|-------------------------|----------|--------------|---------------------|-------------------------|
| Hemoglobin, g/dL (ref: 10-12) | 11.2 (7.9-13.5) | 11.0 (7.4-13.5) | 10.6 (6.3-14.6) | 0.5 (<1.7/+2.7) |
| White blood cell count, ×10^9/L (ref: 4,000-10,000) | 5,627 (2,200-8,900) | 5,106 (1,900-8,800) | 7,275 (2,900-13,300) | 2,094 (<200/+8,100) |
| Lymphocyte count, ×10^9/L (ref: 1,100-4,400) | 1,155 (480-2,720) | 830 (330-1,860) | 670 (140-1,740) | -415 (-1,380/+200) |
| Platelet count, /μL (ref: 150-400) | 185 (23-326) | 164 (61-320) | 257 (113-624) | 48 (-127/+422) |
| C-Reactive protein, mg/L (ref: <5) | 7.7 (1-38) | 40.9 (1.3-309) | 94.8 (1.8-432) | 97 (<0.9/+397) |
| d-Dimer (ref: <500) | NA | 1,498 (200-4,000) | NA | NA |
| BNP, pg/L (ref: <100) | 508 (18-3,770) | 605 (10-3,258) | 813 (91-3,279) | 362 (-103/+1,508) |
| Troponin, ng/L (ref: <34) | NA | 34 (1-101) | 78 (7-289) | 40 (<4/+174) |
| Lactate dehydrogenase, UI/L (ref: 125-220) | NA | 260 (175-394) | 336 (191-731) | 75 (<86/+531) |

**Note:** Values expressed as mean (range).

Abbreviations: BNP, brain natriuretic peptide; ref, reference value; NA, not applicable.
extensive efforts, including universal RT-PCR testing of all patients and staff, cohorting patients suspected of having or with COVID-19, and addressing other key logistical issues, including waiting room crowding, we were able to mitigate the effects of COVID-19, with a minority of cases occurring more than 2 weeks after the initial patient was diagnosed. HD patients with COVID-19 were universally lymphopenic and frequently had abnormal chest imaging results. Among HD patients with COVID-19, mortality was high at 21%.

The logistical issues in HD, such as collective transportation to HD, waiting room crowding, and the repeated requirement to attend HD along with the close physical proximity of patients to each other and to staff during HD, could significantly increase the risk for infection in this setting. Ten patients were positive the first week and 13 were positive the second week, representing 60% of the cases, with a dramatic decline after we instituted aggressive mitigation efforts.

We were among the first dialysis centers to be affected in Ile de France, with our first case occurring before France’s national quarantine measures were in place. The early timing may explain some of the challenges we faced.

1. We implemented enhanced personal protection equipment, with personnel and patients wearing surgical masks, on April 10. The 27-day delay between the start of the epidemic in France and the implementation of this policy can be explained by the shortage of masks in France.

2. An HD center is a relatively open space with personnel, such as medical staff, nurses, facility workers, and patients moving within the premises. Patients require frequent transportation to and from the center to receive their treatment 3 times per week and are able to practice limited social distancing while continuing their life-saving dialysis treatments. The necessity of in-person interactions between dialysis patients and health care workers may have been factors in the high incidence of COVID-19–positive patients in the center.

3. Universal RT-PCR tests were not easily available in France in the beginning of the epidemic. Our first cases had to be tested in local public hospitals with long wait times for tests and long turnaround times. We were able to manage our own tests in our center and increase systematic patient screening after March 18. Systematic RT-PCR screening led to the identification of positive patients, leading to effective isolation.

We believe that the addition of diagnosis with CT of the chest with on-demand RT-PCR testing would increase the diagnostic sensibility and decrease the number of false-negative patients. We also used weekly blood analysis because unexplained lymphopenia associated with a high C-reactive protein level should orient us quickly toward a COVID-19 diagnosis.

Finally, we have adapted our dialysis prescriptions by limiting the use of hemodiafiltration, reducing dialysis time in some cases, and increasing the dose of anticoagulant. No specific COVID-19 treatment has been implemented in our HD patient population. At this time in the epidemic, specific treatments were available in France for only severe hospitalized cases. Patients who died of COVID-19 had figured among the first affected patients in our center. Our therapeutic strategy quickly evolved, on one hand with implementation of a double probabilistic antibiotic therapy to limit cases of secondary infection, and on the other hand, a rapid decrease in target weight in response to patients who lost weight to improve respiratory function.

Epidemiologic data for patients receiving maintenance HD during the SARS-CoV-2 outbreak are limited and only several cases have been reported. However, it is important that follow-up was only 4 days (February 9 to 13) in the report of Wang et al.

The first series of cases came from Wuhan, China. From January 14, 2020 (first confirmed case), to February 17, 2020 (epidemic extinction day), the authors reported 37 COVID-19 confirmed cases in 230 HD patients (16.09%). In most patients, COVID-19 symptoms were mild, with no patients admitted to ICUs. COVID-19–positive dialyzed patients had less lymphopenia than our population and lower serum levels of inflammatory T cells, T helper cells, killer T cells, natural killer cells, and cytokines and milder clinical disease compared with non-HD patients with COVID-19. During that epidemic, 7 patients died, including 6 with COVID-19 and 1 without COVID-19. The causes of death were apparently not related to pneumonia but due to cardiovascular and cerebrovascular diseases and hyperkalemia, unlike our patients who died. The outcome of the 4 staff members was favorable.

Collectively, this study suggests that despite HD patients being at high risk for being infected with SARS-CoV-2, they are likely to experience mild disease that does not develop into full-blown pneumonia, probably due to the reduced function of the immune system and decreased cytokine storms.

In our case, despite having the same incidence observed in the study by Ma et al of SARS-CoV-2–positive hemodialyzed patients (19 of 200 patients) and early management, we have a higher fatality rate (1 death in 5 patients). Furthermore, there are many reasons for weight loss in dialysis patients, but it might be prudent to highlight the importance of careful attention to fluid and weight management for infected patients, especially during the earliest phase of infection.

In Brescia’s protocol, Alberici et al reported that of 21 patients (17 receiving antiviral therapy and hydroxychloroquine and 4 receiving dexamethasone and
tocilizumab), there was a 23% death rate in COVID-19–infected HD patients. The mortality was the same in our nontreated patients. Hence, we supposed that maintenance HD patients are at increased risk for mortality and complications in COVID-19 because of a very high number of comorbid conditions.

In summary, we report the first Parisian cluster of COVID-19 in an HD center. This is an observational study, which found a 19% incidence of COVID-19 in a population of 200 individuals. Mortality in this particularly fragile population is high (21% of affected patients, which represented 4% of all in-center patients). We had some challenges in implementing physical distancing measures in the dialysis center and needed to change the center’s organization. Almost all patients were symptomatic. Systematic screening by universal RT-PCR of all patients and staff allowed us to identify asymptomatic patients and nurses who could be isolated. These measures were highly valuable in our center to limit the spread of the virus and should be considered in HD centers.

Further observations will be needed to more fully understand the clinical spectrum and treatment approaches for COVID-19 in this patient population.

ARTICLE INFORMATION

Authors’ Full Names and Academic Degrees: Caroline Creput, MD, PhD, Christine Fumeron, MD, Daniel Toledano, MD, Mirela Diaconita, MD, and Hassan Izzedine, MD, PhD.

Authors’ Affiliations: Nephrology and Hemodialysis Unit, Diaverum, Paris, France. (CC, CF, DT, HI); and Department of Nephrology, Papepiers Private Hospital, Ramsay Générale de Santé, Paris, France (HI).

Address for Correspondence: Caroline Creput, MD, PhD, Nephrology and Hemodialysis Unit, Diaverum, Paris, France. E-mail: caroline.creput@diaverum.com

Authors’ Contributions: Research idea and study design: CC, CF, DT, HI; data acquisition: CC, CF, DT, MD; data analysis/interpretation: CC, CF, DT, HI; supervision or mentorship: CC, HI. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

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How did maintenance hemodialysis patients in France fare during the COVID-19 pandemic?

Methods and Cohort
- Single Center in Paris
- Universal RT-PCR screening of 200 maintenance hemodialysis patients and of staff
- From 13th March, 2020 to 15th April, 2020, a time of high community prevalence of COVID

Clinical Findings of Patients with COVID
- Fever: 68%
- Dry cough: 63%
- Lymphopenia: 100%
- Fatigue: 35%
- Dyspnea: 29%
- Asymptomatic: 11%

Conclusion: Mortality in this hemodialysis population exceeded 20%. Most but not all patients were symptomatic. Systematic screening allowed identification and isolation of asymptomatic patients, likely preventing additional cases.

Outcomes
- 38 patients positive
- 8 patients (21%) died
- 15 patients admitted (4 in ICU)

Reference: Creput C et al. COVID-19 in patients undergoing hemodialysis: prevalence and asymptomatic screening during a period of high community prevalence in a large Paris center. Kidney Medicine, 2020
Visual Abstract by Namrata Parikh, MD, DNB

@NamrataParikh