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ORIGINAL ARTICLE

Impact of first-wave COronaVIrus disease 2019 infection in patients on haemoDIALysis in Alsace: the observational COVIDIAL study

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ABSTRACT

Background. There are only scarce data regarding the presentation, incidence, severity and outcomes of coronavirus disease 2019 (COVID-19) in patients undergoing long-term haemodialysis (HD). A prospective observational study was conducted in eight HD facilities in Alsace, France, to identify clinical characteristics of HD patients with COVID-19 and to assess the determinants of the risk of death.

Methods. All HD patients tested positive for COVID-19 from 5 March to 28 April 2020 were included. Collected data included patient characteristics, clinical features at diagnosis, laboratory data, treatments and outcomes.

Results. Among 1346 HD patients, 123 tested positive for COVID-19. Patients had a median age of 77 years (interquartile range 66–83), with a high number of comorbidities (3.2 ± 1.6 per patient). Symptoms were compatible in 63% of patients. Asthenia (77%), diarrhoea (34%) and anorexia (32%) were frequent at diagnosis. The delay between the onset of symptoms and diagnosis, death or complete recovery was 2 (0–5), 7 (4–11) and 32 (26.5–35) days, respectively. Treatment, including lopinavir/ritonavir, hydroxychloroquine and corticosteroids, was administered in 23% of patients. The median C-reactive protein (CRP) and lymphocyte count at diagnosis was 55 mg/L (IQR 25–106) and 690 Ly/μL (IQR 450–960), respectively. The case fatality rate was 24% and determinants associated with the risk of death were body temperature {hazard ratio [HR] 1.96 [95% confidence interval (CI) 1.11–3.44]; $P = 0.02$} and CRP at diagnosis [HR 1.01 (95% CI 1.005–1.017); $P < 0.0001$].

Conclusions. HD patients were found to be at high risk of developing COVID-19 and exhibited a high rate of mortality. While patients presented severe forms of the disease, they often displayed atypical symptoms, with the CRP level being highly associated with the risk of death.

Keywords: COVID-19, epidemiology, haemodialysis, mortality

INTRODUCTION

Since late December 2019, an outbreak of a novel coronavirus, called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), occurred in Wuhan, China. The first case of coronavirus disease 2019 (COVID-19) in France was diagnosed on 24 January in Paris. A cluster was identified on 3 March, following an evangelist gathering between 17 and 21 February in Alsace, France. Since then, the northeastern regions of France have been severely struck by the pandemic (1178 in-hospital deaths in Alsace as of 28 April among 14 810 total in-hospital deaths in France and 1.89 million inhabitants in Alsace).

Early reports have suggested that patients with chronic kidney disease could be more susceptible to a severe form of COVID-19 {odds ratio [OR] 3.03 [95% confidence interval (CI) 1.09–8.47]} [1, 2]. However, there are only scarce data regarding the presentation, incidence, severity and outcomes of COVID-19 in HD patients. Currently, available information is based on case reports or small case series [3–5]. Given the rapid pace of the pandemic, we were compelled to gather an epidemiologic overview of COVID-19 HD patients and their specificities to optimize medical care.

Herein we report the results of an observational study in a cohort of HD patients from eight HD facilities in Alsace, France. This study provides an overview of the clinical presentation and outcomes of COVID-19 in HD patients in centres

KEY LEARNING POINTS

What is already known on this topic?

- as of 28 April 2020, there were 129 859 cases of confirmed COVID-19 and 23 660 deaths in France.
- there are only scarce data regarding the presentation, incidence, severity and outcomes of COVID-19 in patients undergoing long-term haemodialysis (HD).

What this study adds?

- HD patients often displayed an atypical presentation, such as gastrointestinal involvement, less hyperthermia, a much more severe form of COVID-19 and delayed viral clearance.
- the incidence and mortality rate of COVID-19 were much higher in HD patients than in the general population.
- C-reactive protein and body temperature at admission were predictive of the risk of death.

What impact may this have on practice or policy?

- screening indications should be comprehensive in this population to ensure adequate isolation and repeated reverse transcription–polymerase chain reaction testing would be advisable before ending isolation in COVID-19 HD patients.
- we suggest strict implementation of 'barrier gestures' in these patients in whom strict containment cannot be secured due to the regular need for dialysis.
- because of the substantial vulnerability of our patients, the prioritized distribution of personal protective equipment in a period of relative shortage or more extensive indications for hospitalization should be considered.

on the front line of COVID-19 during the first French wave of the epidemic.

MATERIALS AND METHODS

Data were collected from 5 March, the first confirmed dialysis case of COVID-19, to 28 April 2020 from adult (≥18 years old) patients undergoing long-term HD and testing positive for COVID-19. A positive test for COVID-19 was defined by either a positive reverse transcription–polymerase chain reaction (RT-PCR) test on a nasopharyngeal swab or compatible radiologic findings on a low-dose computed tomography (LD-CT) scan. Eight HD facilities in three cities participated in the study: Strasbourg [Clinique St Anne, Association pour l'utilisation du rein artificiel en Alsace (AURAL) Bergson, Hôpitaux Universitaires de Strasbourg], Colmar (AURAL Colmar, Hôpitaux Civils de Colmar) and Mulhouse (Hôpital Emile Muller, Diaverum private centre, AURAL Mulhouse). These eight facilities provided HD treatment for 1346 patients in Alsace.

The collected data were as follows:

(i) General characteristics and demographics.

(ii) Comorbidities, including age >75 years, functional disabilities, obesity (body mass index >30 kg/m^2), history of cancer (<5 years), current immunosuppression (history of transplantation, autoimmune disease, chemotherapy <5 years), chronic respiratory disease (e.g. chronic obstructive pulmonary disease, sleep apnoea treated with continuous positive airway pressure, need for long-term oxygen therapy), stroke, peripheral arterial disease, ischaemic heart disease and diabetes. A histroy of high blood pressure was not taken into account, due to its nearly ubiquitous prevalence in this population.

(iii) Diagnostic methods: RT-PCR on a nasopharyngeal swab, LD-CT scan indicating the extent of the impairment (minimal if <10% of the pulmonary parenchyma, mild if 10–25%, mild–severe if 25–50%, severe if 50–75%, critical if >75%).

(iv) Clinical presentation at diagnosis: date of onset of symptoms, date of diagnosis and dat of hospitalization, if needed. Clinical features and the severity of the infection at the time of diagnosis were documented [asymptomatic, moderate if not requiring oxygen supply or mild symptoms either with ambulatory care or hospitalization, severe if admission required for oxygen supply or severe symptoms, critical if hospitalization in an intensive care unit (ICU) or oxygen supply >10 L/min].

(v) Laboratory characteristics at diagnosis: C-reactive protein (CRP), procalcitonin (PCT), lymphocyte count, serum albumin, electrolyte disorders (either plasma potassium <3.5 mmol/L or serum calcium <2.20 mmol/L or serum magnesium <0.70 mmol/L).

(vi) Treatment: oxygen therapy (none or need for a nasal cannula or simple face mask with flow rate in liters per minute), non-invasive ventilation or assisted ventilation, antibiotic and specific treatments (none, lopinavir/ritonavir combination, hydroxychloroquine, corticosteroids). The delay between initiation of therapy and the date of diagnosis and the onset of symptoms was also documented.

(vii) Laboratory evolution: at Day 7 and Day 14 (CRP, PCT, lymphocyte count, serum albumin, lactate dehydrogenase and ferritin).

(viii) Clinical outcomes: hospitalization, length of hospital stay, hospitalization in the ICU, evolution at Days 3, 7, 10, 14 and 21 after diagnosis (stability, improvement, deterioration or deceased) and weight loss. The patient's condition on 28 April was also noted: discharged from hospital care, still hospitalized, transferred to a rehabilitation centre, ambulatory care or deceased. Recovery status and recovery time were reported. Complete recovery was defined as two

Table 1. Patient characteristics

Characteristics	Results	Available/total, *n*/*N*
Demographics at the time of diagnosis		
Age (years), median (IQR)	77 (68–83)	123/123
Age >75 years, *n* (%)	71 (58)	123/123
Gender (male), *n* (%)	70 (57)	122/123
Functional disability, *n* (%)		109/123
Total autonomy	37 (34)	
Partial autonomy	56 (51)	
None	16 (15)	
Kidney disease, *n* (%)		117/123
Diabetic	42 (36)	
Glomerulonephritis	17 (14.5)	
CIN/uropathy	18 (15.5)	
Vascular	14 (12)	
APKD	10 (8.5)	
Unknown	16 (13.5)	
Comorbidity at the time of diagnosis, *n* (%)		
Presence of comorbidity	118 (97.5)	121/123
Number of comorbidities, mean ± SD	3.2 ± 1.6	118/123
Cancer	24 (20)	
Immunosuppression	18 (15)	
Stroke	26 (22)	
Peripheral arterial disease	41 (35)	
Ischaemic heart disease	54 (46)	
Diabetes	63 (53)	119/123
Chronic respiratory disease	40 (34)	119/123
Obesity	40 (36)	112/123
Clinical features at the time of diagnosis, *n* (%)		
Fever	61 (57)	107/123
Body temperature (°C), mean ± SD	37.8 ± 1	100/123
Cough	77 (69)	112/123
Dyspnoea	55 (51)	107/123
SpO_2 (%), median (IQR)	95 (90–98)	95/123
SpO_2 <93%	42 (44)	
Asthenia	82 (77)	106/123
Diarrhoea	35 (34)	102/123
Anorexia	33 (32)	103/123
Myalgia	20 (20)	102/123
Anosmia	6 (6)	103/123
Other ENT symptoms	14 (14)	103/123
Headache	11 (11)	103/123
Severity of the disease, *n* (%)		120/123
Asymptomatic	4 (3)	
Moderate	62 (52)	
Severe	43 (36)	
Critical	11 (9)	

CIN, chronic interstitial nephropathy; BMI, body mass index; SpO2: pulsatile saturation in oxygen; ENT, ear, nose and throat.

consecutive negative RT-PCRs on nasopharyngeal swabs after a minimum time of 24 days after the onset of symptoms and with at least 48 h without symptoms.

Statistical analysis

Quantitative data are described as median and interquartile range (IQR) or mean and standard deviation (SD) according to the normality of the distribution. Distribution normality was tested graphically and with the Shapiro–Wilk test. Comparisons were performed using the Student's *t*-test or the Mann–Whitney test, as appropriate. Qualitative data are described according to the frequency for each modality and compared with Fisher's exact test.

Risk factors for death were analysed with a multivariate Cox model including variables with a P-value <0.2 in the univariate comparison between deceased and surviving patients. Statistical significance was defined as $P < 0.05$. All statistical analyses were performed with STATA/MP 13.1 (StataCorp, College Station, TX, USA).

RESULTS

Between 5 March and 28 April, 123 patients undergoing long-term haemodialysis (HD) were infected with COVID-19 (Mulhouse, $n = 64$; Strasbourg, $n = 45$; Colmar, $n = 14$), representing 9.1% of all patients undergoing long-term HD in our centres ($n = 1346$). The cumulative and incident cases in included HD facilities are presented in Supplementary data, Appendix 1.

Patient characteristics, demographics and comorbidities at the time of diagnosis are summarized in Table 1. Of note, a history of high blood pressure was found in 97.5% of patients.

Diagnosis

The median time between first symptoms and diagnosis was 2 days (IQR 0–5). The origin of the contamination was unknown in the majority of cases (62.5%). Otherwise, the contamination mostly occurred in patients living in institutions (40%) or intrafamilial settings (29%). Of note, 21% of infections were due to nosocomial contamination (already in a hospital unit or rehabilitation unit for at least 7 days for another reason before the onset of symptoms) and 10% were related to an evangelist gathering cluster in Mulhouse. There was no evidence of either vertical or horizontal transmission within the HD units.

The clinical features and severity of the disease at the time of diagnosis are presented in Table 1. Symptoms were found to be compatible with COVID-19 infection (a combination of at least two symptoms among fever, cough and dyspnoea) in 63% of patients.

The primary method of diagnosis was RT-PCR of a nasopharyngeal swab for 112 patients, which was contributive in 88%. LD-CT scan was performed on 64 patients and was contributive in 88% and confirmed the diagnosis in 13 patients that had an initially negative RT-PCR. The extent of the impairment (available for 49/64 patients) on LD-CT scan was minimal in 13 (26.5%), mild in 21 (43%), mild–severe in 6 (12%), severe in 7 (14.5%) and critical in 2 (4%) patients.

Laboratory findings at the time of diagnosis are provided in Table 2. Of note, the median maximal CRP level was 112 mg/L (IQR 56–203) and was reached after a median delay of 7 days (IQR 4–12) after the onset of symptoms.

Treatment

Sixty per cent of the patients required oxygen support therapy at the time of diagnosis. When oxygen therapy was needed, the median time between the onset of symptoms or time of diagnosis and maximal oxygen therapy was 8 days (IQR 3–11) and 2 days (IQR 0–8), respectively (data available in 29 patients).

Table 2. Laboratory characteristics of HD patients with COVID-19

Characteristics	At diagnosis ($N = 123$)	Day 7 post-diagnosis ($N = 102$)	Day 14 post-diagnosis ($N = 83$)	Normal range
CRP (mg/L), median (IQR)	55 (25–106), $n = 113$	55 (15–113), $n = 81$	19 (7–58), $n = 58$	0–4
Procalcitonin (µg/L), median (IQR)	0.805 (0.475–2.115), $n = 32$	1 (0.5–3.54), $n = 31$	0.42 (0.2–2.03), $n = 14$	0–0.5
Lymphocyte count (Ly/µL), median (IQR)	690 (450–960), $n = 109$	635 (425–1010), $n = 76$	870 (600–1250), $n = 57$	1.000–4.000
Serum albumin (g/L), mean ± SD	35 ± 6, $n = 70$	NC	32 ± 7, $n = 39$	35–50
Ferritin (µg/L), median (IQR)	NA	1188 (840–2060), $n = 41$	NA	23–322
LDH (U/L), median (IQR)	NA	280 (215–346), $n = 31$	NA	120–246

n, Number of available data/number of patients; LDH, lactate dehydrogenase; NA, not available.

Table 3. Treatment in HD patients with COVID-19

Treatment	Results	Available/total, *n*/*N*
Antibiotic treatment, *n* (%)	76 (77)	99/123
Cephalosporin	56 (78)	
Macrolide	24 (33)	
Specific treatment, *n* (%)	23 (23)	100/123
Lopinavir/ritonavir	10 (38.5)	
Hydroxychloroquine	12 (46)	
Corticosteroid	5 (19)	
Oxygen therapy, *n* (%)	68 (60)	114/123
Artificial ventilation	5 (4)	
Initial oxygen therapy (L/min), median (IQR)	0 (0–2)	109/123
Maximal oxygen therapy (L/min), median (IQR)	2 (0–6)	111/123

Antibiotic therapy was initiated in 77% of patients after a median delay of 0 days (IQR −1–1) and 3 days (IQR 1–5) after diagnosis and symptoms onset, respectively. A putative antiviral therapy was initiated at the discretion of the physician in 23% of patients after a median delay of 2 days (IQR 1.5–3.5) and 4.5 days (IQR 3–9.5) after diagnosis and symptoms onset, respectively. This treatment was discontinued in 4/23 patients due to intolerance or medical contraindication. The main reasons for non-prescription of a specific therapy were the clinician's choice and the absence of guidelines in HD patients (65%).

An overview of treatments is provided in Table 3.

Outcomes at the time of writing

Hospitalization was required in 71% of patients after a median time of 2 days (IQR 0–5) after symptoms onset, seven of whom were transferred to the ICU. The median hospital stay was 9 days (IQR 4–14).

At the time of writing, follow-up data on 117/123 patients were available: 39 (33%) were discharged from the hospital, 11 (9%) remained hospitalized, 27 (23%) had only ambulatory care, 11 (9%) were transferred to a rehabilitation centre and 29 (24%) had died. Complete recovery was observed in 30 (24%) patients after a median interval of 32 days (IQR 26.5–35) after the onset of symptoms. In survivors at Day 21 ($n = 63$), 52% had a sustained positive RT-PCR on a nasopharyngeal swab or had no control exam until this time. Supplementary data, Appendix 2 depicts the time interval until complete recovery, death or the end of the observation time. Of note, a mean weight loss of −2.4 ± 2.7 kg (SD −13–1.5) was observed.

Deceased patients

Twenty-nine (24%) patients died from COVID-19, three of whom died in the ICU. The median time between symptoms onset and death was 7 days (IQR 4–11). The Kaplan–Meier survival curve is presented in Figure 1 . A comparison of deceased and surviving patients is shown in Table 4.

At diagnosis, deceased patients presented a significantly older age, a more severe presentation, a higher CRP level, a higher body temperature and more often required oxygen therapy and at a higher flow. Patients who died more frequently had a typical presentation of the disease at diagnosis compared with survivors (85% versus 57%; P = 0.011), including dyspnoea (70% versus 45%; P = 0.027). Clinical features at diagnosis were critical in 31% (compared with 2% in survivors) and moderate in 31% (compared with 58% in survivors). Of note, compared with survivors, deceased patients more frequently had diabetic kidney disease (48% versus 32%) or an autosomal polycystic kidney disease (APKD) (15% versus 7%). None of the specific comorbidities was associated with the risk of death, while only a history of ischaemic heart disease tended to be

Table 4. Comparison of deceased and surviving patients

Characteristics	Deceased patients ($n = 29$)	Surviving patients ($n = 94$)	P-value	Available in each group/total, *n/N*
Demographics at the time of diagnosis				
Age (years), median (IQR)	80 (72–88)	75.5 (64–83)	0.04	(29/94)/123
Age >75 years, *n* (%)	19 (66)	52 (55)	0.39	123/123
Gender (male), *n* (%)	18 (62)	52 (56)	0.67	122/123
Functional disability, *n* (%)			0.13	109/123
Total autonomy	5 (20)	32 (38)		
Partial autonomy	14 (56)	42 (50)		
None	6 (24)	10 (12)		
Comorbidity, *n* (%)	28 (100)	90 (97)	1	121/123
Number of comorbidities, mean ± SD	3.4 ± 1.3	3.1 ± 1.6	0.28	(28/90)/123
Obesity, *n* (%)	8 (33)	32 (36)	1.0	112/123
Severity of the disease at diagnosis, *n* (%)			<0.001	120/123
Asymptomatic	0 (0)	4 (4)		
Moderate	9 (31)	53 (58)		
Severe	11 (38)	32 (35)		
Critical	9 (31)	2 (2)		
Clinical features at the time of diagnosis				
Body temperature, mean ± SD	38.2 ± 1	37.7 ± 1	0.056	(24/76)/123
SpO_2, median (IQR)	92 (85–97)	96 (90–98)	0.07	(22/73)/123
Laboratory and LD-CT scan characteristics, median (IQR)				
CRP at diagnosis (mg/L)	95 (49–192)	44.5 (19–92)	0.0003	(25/88)/123
CRP peak (mg/L)	220 (117–272)	98.5 (44–147)	0.0002	(23/70)/123
Procalcitonin at diagnosis (ng/mL)	1.7 (0.83–5.7)	0.8 (0.34–1.7)	0.12	(5/27)/123
Lymphocyte count at diagnosis (Lym/µL)	530 (420–910)	720 (461–995)	0.36	(23/86)/123
CRP at D7 (mg/L)	157 (72–222)	43 (14–94)	0.0004	(11/70)/102
Lymphocyte count at Day 7 (WBC/µL)	410 (300–550)	670 (450–1040)	0.017	(10/66)/102
Extent of impairment on the initial LD-CT scan, *n* (%)			0.54	48/62
Minimal	2 (22)	11 (28)		
Mild	5 (56)	16 (41)		
Mild to severe	0 (0)	6 (15)		
Severe	1 (11)	5 (13)		
Critical	1 (11)	1 (3)		
Therapy during period of care, *n* (%)				
Antibiotic treatment	19 (78)	57 (71)	0.56	99/123
Specific treatment	8 (28)	15 (21)	0.55	94/123
Oxygen therapy	24 (92)	44 (50)	<0.005	114/123
Artificial ventilation	4 (15)	1 (1)	0.009	114/123
Initial oxygen therapy (mL/min), median (IQR)	2 (0–4)	0 (0–2)	0.0028	(26/83)/123
Maximal oxygen therapy (mL/min), median (IQR)	15 (4–15)	0 (0–3)	<0.0005	(25/86)/123

SpO_2, pulsatile saturation in oxygen.

Table 5. Multivariate analyses of factors associated with the risk of death

Factors	HR	P-value	IQR
Age	1.03	0.18	0.987–1.072
Partial or no autonomy	0.66	0.59	0.14–3.05
Oxygen therapy	1.13×10^{16}	1.0	
SpO_2 at diagnosis	0.97	0.31	0.90–1.03
Body temperature at diagnosis (per 1°C)	1.96	0.02	1.11–3.44
CRP at diagnosis (per 1 mg/dL)	1.01	<0.0001	1.005–1.017

Multivariate analysis performed on only 83 patients due to missing data.
SpO_2, pulsatile saturation in oxygen.

more frequent in deceased patients (61% versus 41%; $P = 0.084$).

A Cox model was subsequently constructed for multivariate analysis. Included in this model were age, autonomy (total autonomy or not), pulsatile saturation in oxygen (SpO_2) and oxygen therapy at diagnosis, body temperature and CRP at diagnosis. PCT was not included due to the amount of missing data. When taking into account all of the clinical symptoms, only body temperature at diagnosis was associated with the risk of death {hazard ratio [HR] 1.96 [95% confidence interval (CI) 1.11–3.44]; $P = 0.02$}. CRP at diagnosis was also associated with the risk of death [HR 1.01 (95% CI 1.005–1.017); $P < 0.0001$].

The results of the multivariate analysis are presented in Table 5, while the Kaplan–Meier survival curves according to CRP quartile are shown in Figure 1.

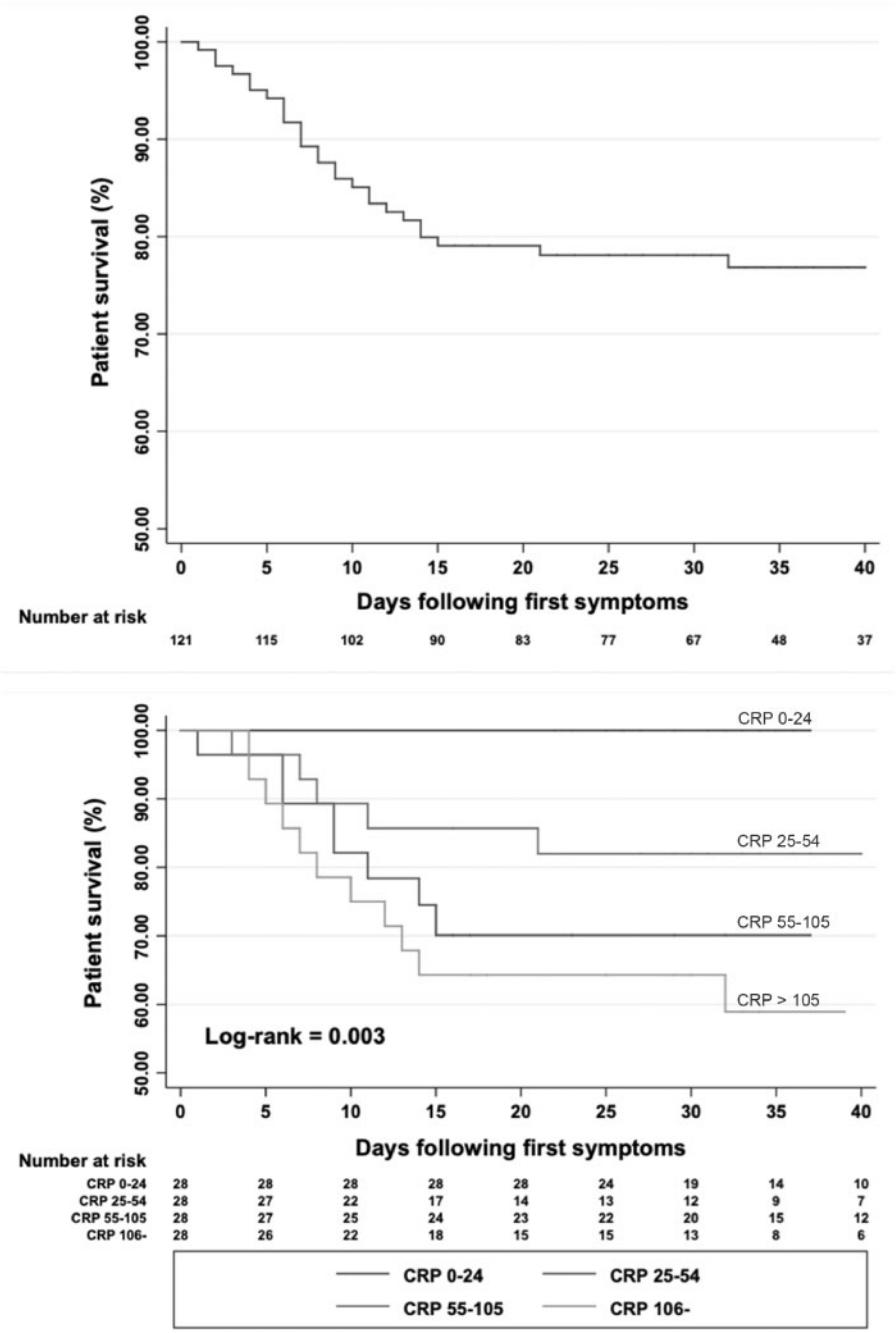

FIGURE 1: Kaplan–Meier survival curves in HD patients after onset of symptoms and according to CRP quartile.

DISCUSSION

The rapid outbreak of the COVID-19 pandemic represented an unexpected challenge for the medical community. Although the epidemic curve is descending in many countries, the imminent end of containment measures raises the risk of a second wave [6, 7], and any new disease-related information would be useful to improve care. Given the lack of knowledge relative to specific and vulnerable patients, we report herein on a series of patients undergoing long-term HD in eight facilities in Alsace, France, where the first cluster of COVID-19 occurred.

The incidence of COVID-19 was much higher in our HD patients than in the background population (9.1% versus 0.16%). There are various putative explanations. First, our HD population carried comorbidities at risk of COVID-19 infection. Second, physical distancing is challenging during HD sessions, in the waiting room, during transport to HD facilities and in living facilites (many patients live in nursing homes). Finally, these patients are in contact with healthcare providers three times a week, such that screening was likely more thorough than in the general population. There was no evidence for transmission within our HD units, as the first cases occurred in patienta treated in separate rooms and containment measures were immediately applied for all suspected patients. Indeed, each patient presenting to the HD unit with any symptom suggestive of COVID-19 was admitted to a dedicated isolated room until the RT-PCR result was available. All patients with

proven COVID-19 remained thereafter in an isolated room to avoid nosocomial transmission.

In the first reports in the Chinese population [2, 8], only 25–50% of patients had at least one comorbidity, which is far below our findings. Compared with hospitalized US patients who had more similar clinical characteristics and a significant number of comorbidities (88% with at least one comorbidity) [9], our patients were older and slightly less obese. Notwithstanding, our patients more frequently had diabetes, chronic respiratory disease and a history of cancer. The question of whether end-stage kidney disease (ESKD) *per se* or the comorbidities associated with ESKD worsens the outcome remains to be determined.

Compared with HD patients of the nationwide French Renal Epidemiology and Information Network (REIN) registry [10], patients in our cohort were older (74 ± 15 versus 69 ± 15 years) and were more likely to have APKD (8.5% versus 5.8%), obesity (36% versus 29%), chronic respiratory disease (34% versus 19%), cancer (20% versus 12%), ischaemic heart disease (45.6% versus 29%), stroke (22% versus 13%) and peripheral arterial disease (34.7% versus 21%). These observations highlight the substantial vulnerability of our cohort, i.e. the 'frails upon the frails'. Moreover, the higher proportion of patients with partial (51.4% versus 8.5%) or an absence of autonomy (15% versus 8.5%) would explain both the higher vulnerability of these patients and the frequent need for external or institutional help, which could be a vector of contamination. This suggests that 'barrier gestures' should be strictly implemented in these patients in whom strict containment cannot be secured due to the need for dialysis. Screening indications should be comprehensive in this population to ensure adequate isolation when needed. Also, the favoured distribution of personal protective equipment in a period of relative shortage or wider indications for hospitalization should be considered.

Typical symptoms of COVID-19 infection have been initially described as fever, cough and dyspnoea [11]. Fever was inconsistent in our cohort compared with previous reports (57% versus 98%) [8, 11]. A lack of fever is frequent in infected HD patients, who tend to be slightly hypothermic in baseline conditions [12]. A considerable proportion of our patients presented with less typical symptoms, mostly asthenia, diarrhoea and anorexia. The latter has been previously described in the general COVID-19 population [8, 13–15] as well as in a case report of HD patients [16] and kidney transplants [17]. For example, diarrhoea, initially described as an uncommon symptom [8], was found in 34% of our patients. The extensive screening in our patients likely enabled the detection of atypical forms, although more frequent gastrointestinal involvement in patients with ESKD cannot be excluded.

Lymphopaenia was frequent in our cohort, as also previously described in the general COVID-19 population [8, 9, 11, 15], and associated with the severity of the disease [18]. This was attributed not only to a chronic endothelial dysfunction in ageing patients with chronic disease, but also to a direct cytotoxic action of the virus [15, 19]. Lymphopaenia should be considered both as part of the diagnosis and as a marker of the risk level of the disease [20]. In this study, CRP was higher than in previous studies conducted in the general COVID-19 population, even those patients with severe disease [8, 9, 11]. Of particular note, CRP was predictive of the risk of death in our cohort of COVID-19 HD patients. Such an association between CRP and disease severity was previously reported and associated with the extent of impairment on LD-CT scan (correlation coefficient 0.873, 0.734; $P < 0.001$) [21, 22]. Some authors have suggested the use of a predictive score based on CRP and lung volume involvement on LD-CT scan at the time of diagnosis [21, 22]. High PCT (>0.5 ng/mL), an uncommon finding in the general COVID-19 population [8, 9, 11], was more frequent in our cohort.

The mortality rate in our cohort was much higher than in the general COVID-19 population: 24% compared with the 1–5% mortality in the general COVID-19 population [23] and 8–15% mortality among patients >70 years old [9, 23]. An abysmal prognosis was previously described in a small cohort of kidney transplant recipients in the USA [17], with an early mortality rate of 28% at 3 weeks. A similar mortality rate of 26% was found in Italian [24] patients admitted to the ICU who had fewer comorbidities and were younger [median age 63 years (IQR 56–70)]. These findings thus emphasize the detrimental effect of ESKD and comorbidity burden over that of age. We did not find any association between age and risk of death in our cohort, in contrast to the general population. This discrepancy could be explained by the more advanced age of our cohort, as we compared old versus very old patients, which might have attenuated the differential risk. However, one should bear in mind that our HD population had a much higher mortality rate (16%) than that found in the general COVID-19 population (0.91%), with a steeper effect of age [10, 25]. Our results suggest an estimated mortality rate of 26.7%, but the exact case fatality rate (CFR) should take into account the asymptomatic patients, whose exact percentage was unknown in our population.

A noteworthy observation was the poor and prolonged viral clearance in our patients. Only 24% of our patients had viral clearance after a median of 32 days after onset of symptoms. while viral clearance was initially reported after a median time of 17–20 days in the general COVID-19 population [26, 27]. However, a recent study [28] found a viral clearance after a median of 24 days, with a maximum duration of 42 days, which is more in line with our population. Age and ESKD are well-identified causes of immune dysfunction, which could delay viral clearance [29]. In addition, the higher prevalence of a severe form of the disease could be associated with prolonged viral shedding [27]. Currently French guidelines [30] recommend the end of isolation 24 days after the onset of symptoms in immunocompromised patients, without control RT-PCR testing. Given the present data, it would seem cautious to perform another RT-PCR test before ending isolation. In our opinion, and considering the false negative rate of ∼30% [31, 32], a minimum of two consecutive negative swabs would appear to be a sound precaution.

Our study has certain limitations. The cohort was modestly sized and we could not perform a proper comparison due to the lack of other reported cohorts in HD patients. The number of missing data also represents a drawback. Finally, the absence of systematic screening in both the general and specific COVID-19 populations such as ours may limit our conclusions, especially regarding the CFR. Further larger studies are necessary to estimate the risk factors in the HD population. The high mortality rate in our patients also points to the need for randomized controlled studies on antiviral therapy.

CONCLUSION

In the present report, we describe a cohort of 123 HD patients presenting with symptomatic COVID-19 together with their clinical profiles and outcomes. HD patients were found to be at high risk of developing COVID-19. Several clinical characteristics, including atypical presentation, the predictive value of elevated CRP and delayed viral clearance, were worth noting and could be specific for this population. The outcomes were abysmal in this particularly vulnerable population, with a mortality rate of 24%.

SUPPLEMENTARY DATA

Supplementary data are available at ndt online.

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AUTHORS' CONTRIBUTIONS

N.K., F.C., T.K., D.B.-K., T.H. and M.I. designed the study. N.K., F.C., C.M., A.L.F., T.N., M.I., P.P. and S.B. collected the study data. N.K., T.K., D.B.-K., T.H. and F.C. performed the statistical analyses and drafted the manuscript. All authors participated in the critical revision and approval of the article.

CONFLICT OF INTEREST STATEMENT

None declared.

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