

Management and Outcomes of patients on maintenance dialysis during the COVID-19 pandemic: a report from Geneva, Switzerland

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Abstract

Background Patients on maintenance hemodialysis are at high risk for serious complications from COVID-19 infection including death. We present an overview of the local experience with dialysis units management and reorganization, local epidemiology and outcomes during the COVID-19 outbreak in Geneva, Switzerland.

Methods All SARS-CoV-2 positive outpatients on maintenance dialysis were transferred from their usual dialysis facility to the Geneva University Hospitals dialysis unit to avoid creation of new clusters of transmission. Within this unit, appropriate mitigation measures were enforced as suggested by the institutional team for prevention and control of infectious diseases.

Results From February 25 to May 18, 2020, 19 of 246 patients on maintenance dialysis were tested positive for SARS-CoV-2, representing an incidence rate of 97.6 cases per 100,000 person-days. Eighteen patients were on maintenance hemodialysis and one on peritoneal dialysis. Twelve of these infections were detected during the first two weeks after mitigation strategies were enforced. Most common symptoms were fever (89%), cough (84%) and fatigue (68%). Two patients required orotracheal intubation. Six patients on maintenance hemodialysis who had previously tested positive for SARS-CoV-2, all of them male, died (32%). Five deaths were COVID-19 related and one death was due to dialysis withdrawal at the patient's request.

Conclusion Strict mitigation measures seemed to be effective to control infection spread among patients on maintenance dialysis. COVID-19 infection is associated with a high fatality rate. Large scale epidemiological studies are needed to assess the efficacy of preventive measures in decreasing infection and mortality rate within the dialysis population.

Background

Coronavirus related disease (COVID-19) outbreak, caused by the novel coronavirus named SARS-CoV-2 was declared a pandemic by the World Health Organization (WHO) on March 12, 2020 ¹. Since the diagnosis of four cases of pneumonia in Wuhan, China in late December 2019, SARS-CoV-2 infection has spread with unparalleled transmission rate resulting in more than six million confirmed cases, responsible for over 400,000 deaths worldwide ².

In the effort to reduce viral transmission rate, community spread, as well as overwhelmed health systems, jurisdictions worldwide adopted containment and/or mitigation strategies, such as travel restrictions to and from high risk areas, social distancing, quarantine for confirmed or suspected cases, and cancellation of large-scale public events and gatherings ²⁻⁴. At the individual level, the WHO is recommending hygiene measures, such as avoiding contact with confirmed cases and frequent hand washing ⁵.

Patients with end stage kidney disease on maintenance dialysis have a high prevalence of cardiovascular disease, diabetes, hypertension, and old age⁶, which all put them at high risk for a severe COVID-19 infection and death^{4,7,8}. Whereas most outpatient activity for patients with chronic conditions could be temporarily held, in-center hemodialysis sessions require the physical presence of patients. Moreover, not all dialysis facilities can guarantee adequate distance between patients due to space restrictions. In addition, patients are required to travel several times per week to the dialysis units, often using public transportation, thus exposing themselves to the risk of community transmitted infection. Infected patients would expose other patients and medical staff to SARS-CoV-2 with the risk of creating clusters within dialysis units which may result in catastrophic outcomes for this extremely vulnerable population⁹.

In our study, we present an overview of local experience with dialysis unit management and reorganization, local epidemiology and short-term outcomes during COVID-19 outbreak in Geneva, Switzerland.

Methods

Screening and Prevention Strategies

All confirmed SARS-CoV-2 infections were reported to cantonal health authorities who provided daily updated data on local epidemiology.

First Epidemiological Phase 25.02.2020–13.03.2020 (Mostly Imported Cases)

At the beginning of the local epidemic, there was little evidence of community transmission of SARS-CoV-2. During this phase, patients were asked to call ahead their dialysis unit in case of fever and upper respiratory symptoms before coming for their session. Their body temperature was systematically measured upon arrival. If any symptoms were present or if the patient was febrile ($> 37.5\text{ C}^\circ$), a screening nasopharyngeal swab was performed in a dedicated room. Awaiting the results, the patient was dialyzed respecting a distance of at least 2 meters from other patients or in a separate room if the latter was available. All patients had to wear a surgical mask upon arrival and during the whole dialysis session. In addition, the dialysis units provided two masks to patients who used public transportation; patients were asked to wear them on their way home as well as on their way to the unit for the next session. Hospitalized patients were screened in their respective wards if suspected symptoms were present. If the test was positive for SARS-CoV-2 infection, patients were transferred to a dedicated medicine ward.

The same preventive measures were applied in the three affiliated outpatient dialysis facilities except that facemasks were not systematically provided to patients. In addition, visits were not allowed during dialysis session and the waiting rooms were reorganized to guarantee a two-meter space between chairs. Only one patient at a time was allowed in the locker room.

For patients treated by peritoneal dialysis, regular monthly visits in outpatient clinics were replaced by phone calls. Should an emergency condition require an in-hospital evaluation, the same preventive measures described above applied.

Second Epidemiological Phase 14.03.2020–18.05.2020 (Community Transmission)

At this stage, there was growing evidence of community viral spread. Nationwide and local response plans were activated to enforce mitigation. In the canton of Geneva, schools and non-essential businesses were closed as of March 15, 2020 and the Hospital went through reorganization and restructuring. During this phase, all three residents of the Nephrology Division at Geneva University Hospitals and five of the nine attending staff physicians were reoriented to care for patients admitted with COVID-19 in the Medicine Wards. All elective activity, including outpatient consults, was postponed. Patients who needed close follow-up were offered phone consultations with lab work in outpatient facilities outside the University Hospital.

It was decided, in joint collaboration with all outpatient dialysis facilities, that all SARS-CoV-2 positive outpatients on maintenance dialysis from affiliated units would be transferred at the Geneva University Hospitals dialysis unit in order to avoid creation of new clusters of transmission. Within this unit, confirmed or suspected COVID-19 outpatients were separated from non-infected patients in two distinct parts of the unit. In addition, a third shift was added to accommodate patients with COVID-19 and enforce the recommended two meters distance between patients during sessions. Within this shift, standard disinfection procedures for dialysis machines were applied. For patients who were dependent on public transportation, a private transport was organized in order to decrease risk of community transmission. Hospitalized patients were transferred to COVID-19 dedicated wards in case of suspicion of or confirmed infection.

Healthcare Workers Screening and Protection

At work, all staff had to wear surgical facemasks and keep a two meters distance from patients when possible. Nurses who worked in proximity with confirmed cases wore an N95 respirator, goggles, gloves and long sleeve impervious gown. Any staff member with fever (> 37.5 C°) or upper respiratory symptoms was systematically screened. Staff with a positive test had to self-isolate at home for at least 10 days and were allowed to resume their activity after day 10 if they had no symptoms for at least 48 hours or after day 14.

Patients' Education

Staff of each unit approached patients during their dialysis sessions since the beginning of the local epidemic in order to share information about the outbreak, explain the importance and rationale of containment measures, organizational and staff changes, give advice on individual prevention methods and answer patients' questions. Patient received an information letter and frequent updates were provided to patients through a dedicated website.

Hospital Care Units and Admission Criteria

Acute patient care at Geneva University Hospitals is provided in the Medical (or Surgical) Ward, the Intermediate care Units (IMCU) (offering monitoring and non-invasive positive pressure ventilation) or the Intensive Care Unit (ICU), as needed. Admission to the IMCU or the ICU was regulated using the consensus criteria drafted by the Swiss Academy for Medical Sciences¹⁰. The following exclusion criteria were applied: patients with unwitnessed or recurrent cardiac arrest, cardiac arrest without return of spontaneous circulation, vasopressor resistant circulatory failure, any disease with life expectancy < 12 months, end-stage neurodegenerative disease or severe dementia, patients with severe and irreversible neurological event-condition, NYHA class 4 heart failure, chronic obstructive pulmonary disease (stage GOLD 4D), or liver cirrhosis (Child-Pugh score > 8).

Our institution developed management protocols for patients admitted with SARS CoV-2 infection. Treatment with hydroxychloroquine (single dose of 800 mg) and/or lopinavir/ritonavir (200/50 mg twice daily for 5 days) could be prescribed at the discretion of the attending physician in the absence of contraindications.

Data collection

In Switzerland, all patients on maintenance dialysis are listed in a national registry and have provided informed written consent for their anonymized data to be used for quality control or clinical research purposes. The study was approved by the research ethics committee of the canton of Geneva (ID 2020 – 01281). Data on demographic characteristics, baseline comorbidities, COVID-19 status, related symptoms or laboratory findings, and outcomes were retrospectively collected. For this study, the modified Charlson comorbidity index was used¹¹.

Statistical Analysis

Results are presented as mean \pm standard deviation, median with interquartile range, or number (percentage). Between groups comparisons were performed with the Student t test, the chi-square or the Mann-Whitney test, as appropriate. IBM SPSS Statistics (version 24.0, Armonk, NY) was used.

Results

Local Epidemiology

The first SARS-CoV-2 infection in Switzerland was confirmed on February 24, 2020 and the first case in the canton of Geneva on February 27, 2020. On May 18th, 2020, the canton of Geneva counted a total of 5,122 confirmed SARS-CoV-2 infection cases (Fig. 1), an incidence rate of 12.3 cases per 100,000 person-days. Fifty five percent of infected patients were women. During the same time period, 270 COVID-19 related deaths were reported, representing a mortality rate of 5%¹². Among patients who died, 55% were men and 90% were over 70 years old.

Dialysis Patients' Outcomes

In the canton of Geneva, four dialysis units treat a total of 246 hemodialysis and peritoneal dialysis patients. Two of them provide in-center dialysis for outpatients, whereas those at University Geneva Hospitals and at Hôpital de la Tour provide in-center dialysis for both outpatients and inpatients. In this unit, there are two dialysis shifts from Monday to Saturday. Demographics of patients on maintenance dialysis are summarized in Table 1.

Table 1
Baseline characteristics of patients on maintenance dialysis by infection status

Characteristics	Not infected by SARS CoV-2 (N = 227)	Infected by SARS CoV-2 (N = 19)	p
Mean age (years)	67 ± 16	65 ± 17	0.68
Male gender (%)	146 (64%)	12 (74%)	0.70
BMI	25 ± 5	28 ± 5	0.02
Diabetes (%)	84 (37%)	12 (62%)	0.03
Modified CCI	8 ± 3	8 ± 3	0.69
Dialysis vintage (mo)	32 (15–59)	32 (14–49)	0.60
Patients on HD	200 (88%)	18 (95%)	0.71
Data are presented as mean ± SD, median (IQR) or n (%)			
Abbreviations: BMI, body mass index; CCI; Charlson comorbidity index; HD, hemodialysis			

From February 25 to May 18, 2020, a total of nineteen patients (8%) from all dialysis units were tested positive for SARS-CoV-2, representing an incidence rate of 97.6 cases per 100,000 person-days (95% confidence interval 62.3–153.0). Thirteen patients (68%) were men and six women (32%). All infections were detected during the second epidemiological phase after March 13, 2020 but most of them (12/19) were identified in the first two weeks after mitigation strategies were enforced (Fig. 1). Eight of these infections were hospital-acquired (while initially admitted in non-COVID wards). To note, the only SARS-CoV-2 positive patient on peritoneal dialysis was hospitalized prior to testing positive. Baseline characteristics of patients by infection status are shown in Table 1. Infected patients had higher prevalence of diabetes and higher body mass index than non-infected patients.

On presentation, most common symptoms were fever (89%), cough (84%) and fatigue (68%). Fourteen patients (74%) presented with multifocal opacities on chest x-rays. Two patients required orotracheal intubation and both of them survived. One patient developed bilateral multi-segmental acute pulmonary embolisms and was treated with anticoagulation. Three patients were treated with hydroxychloroquine, two with lopinavir/ritonavir, and three with the combination of both agents.

Within this 13-week time period, nine patients died, six of whom were positive for SARS-CoV-2. Five deaths were COVID-19 related and one death was due to dialysis withdrawal at the patient's request. Four patients had a preexisting advance healthcare directive and one patient did not fulfill admission criteria to the ICU. One patient was initially admitted to the IMCU but clinically improved and was transferred to the Medicine ward. However, he later developed respiratory distress and comfort care was then provided. Characteristics of infected patients by outcome are shown in Table 2. Patients who died were older than patients who survived (78 ± 7 versus 59 ± 19 years), had a higher body mass index (29 ± 6 versus 26 ± 4) and higher modified Charlson comorbidity index (10 ± 1 versus 7 ± 3).

Table 2
 Characteristics of patients on maintenance dialysis with SARS CoV-2 infection by outcome

Characteristics	Survived (n = 13)	Died (N = 6)
Mean age (years)	59 ± 19	78 ± 7
Male gender	8 (62%)	6 (100%)
Diabetes (n)	8 (62%)	4 (67%)
BMI	26 ± 4	29 ± 6
Modified CCI	7 ± 3	10 ± 1
Dialysis vintage	38 (7–73)	30 (15–51)
Patients on HD	12 (92%)	6 (100%)
Clinical presentation on diagnosis		
fever	11 (85%)	6 (100%)
cough	11 (85%)	5 (83%)
dyspnea	5 (38%)	4 (67%)
fatigue	7 (54%)	6 (100%)
diarrhea	2 (15%)	1 (17%)
Laboratory tests on diagnosis		
WBC (x1000/μl)	5.9 (4.9–8.3)	11.2 (5.6–13.2)
Neutrophils (%)	81 (73–89)	83 (41–89)
Lymphocytes (%)	10 (6–18)	8 (7–9)
Peak C-reactive protein (mg/L)	71 (23–280)	188 (159–302)
Chest x-ray (n/n)		
Multifocal opacities (%)	9 (69%)	5 (83%)
Outcomes		
Treated as outpatients	3 (23%)	0
Intubation required	2 (15%)	0
Hospital days to discharge or death	18 (3–28)	11 (5–26)

Data are presented as mean (SD), median (interquartile range) or n (%)

Abbreviations: BMI, body mass index; CCI; Charlson comorbidity index; HD, hemodialysis; WBC, white blood cell count; ICU, intensive care unit; IMCU, intermediate care unit.

Characteristics	Survived (n = 13)	Died (N = 6)
ICU- IMCU days to discharge or death	11 (4–24)	4
Data are presented as mean (SD), median (interquartile range) or n (%)		
Abbreviations: BMI, body mass index; CCI; Charlson comorbidity index; HD, hemodialysis; WBC, white blood cell count; ICU, intensive care unit; IMCU, intermediate care unit.		

House Staff Outcomes (all dialysis units)

During the same period, a total of seven staff members, six nurses and one physician, were tested positive for SARS-CoV-2.

Mitigation Measures Easing

Mitigation measures were highly effective at the cantonal level with infection rate, death rate, hospitalizations and ICU admissions considerably dropping after the second week and for three consecutive weeks. This allowed gradual easing of the measures by April 27, 2020 with some businesses resuming their activities and outpatient consultations or elective procedures being rescheduled. Further easing of measures was initiated on May 11, 2020 with to date a persistently low infection and death rate. No new infections among dialysis patients were diagnosed since the gradual easing of measures.

Discussion

To our knowledge, this is the first report describing the COVID-19 epidemic in an administrative region including all patients on maintenance hemodialysis from the beginning of the epidemic until the end of mitigation strategies. We show three important findings: first, incidence of SARS CoV-2 infection may be higher in patients on maintenance hemodialysis and confers a high mortality risk; second, most cases were identified during the first two weeks of mitigation demonstrating that social distancing and other preventive measures were successful in slowing down infection spread in this vulnerable population; third, a significant proportion of infections were hospital-acquired underlying the importance of identifying in-hospital clusters of transmission. Of importance, no direct contamination within hemodialysis units was documented.

The prevalence of SARS-CoV-2 infection appears to be higher among patients on maintenance dialysis compared with the general population. However, the real incidence of the infection in the general population remains to be determined as testing was not systematically performed, especially at the beginning of the epidemic, and it is likely that many mild cases were undetected. On the other hand, the threshold for testing was very low in patients on maintenance dialysis.

Twelve patients were infected in the first two weeks after mitigation enforcement while eight patients were infected in the hospital. When considering incubation time of SARS-CoV-2¹³, the majority of infections were acquired before the beginning of mitigation strategies. Therefore, infection control

measures for patients on maintenance dialysis should be part of a wider strategy and established as early as possible in the outbreak's timeline in order to be efficient.

Few reports have recently been published on dialysis units ongoing experience during the COVID-19 outbreak. They provide epidemiological data on infection and mortality rates within their dialysis population ¹⁴⁻¹⁷.

During the current outbreak, national authorities and infection control experts drafted specific guidance for dialysis centers. For example, the American Center for Disease Control (CDC) and the British National Institute for Healthcare and Excellence (NICE) provided such guidance ^{18,19}. Moreover, several calls for action were made signaling the urgent need for vigilance and proposing measures to deal with current outbreak within dialysis units ²⁰⁻²³. Containment measures are more effective when they are taken as early as possible and should be part of a clear nationwide strategy and response plan ^{24,25}.

In addition, current health crisis required an important reorganization and restructuring of health institutions worldwide. In our institution, medical outpatient activity was significantly decreased, non-urgent and elective surgeries were cancelled or postponed. Medical and surgical wards along with their staff were converted to admit COVID-19 patients and new dedicated wards were created to deal with the large influx of patients. Physicians and nurses from the University Hospital hemodialysis unit were also recruited in the wards or the ICU. The reduced medical staff resources created yet another challenge for the treatment of hemodialysis patients during the outbreak.

Patients on maintenance dialysis, due to comorbidities and older age, might not be offered admission to the ICU in case of severe disease ¹⁰. In our institution, none of the five patients who died due to CoViD-19 would have been a candidate for ICU admission according to local rationing criteria (although four of these patients had an advance medical directive refusing ICU admission). This stresses out even more the vulnerability of the dialysis population during the current outbreak and the importance of infection prevention. It also highlights the importance to timely discuss with patients and their families their goals of care and their values.

Our study has significant limitations. The number of patients is relatively small and the whole effect of the pandemic may have not been captured as more infections may occur in the weeks to come while lockdown will progressively be lifted. Nevertheless, 3 weeks after measures easing, no new infections have been diagnosed. In addition, we may have missed asymptomatic or pauci-symptomatic infections as we were unable to preventively test all patients on maintenance dialysis. However, inclusion of all patients in maintenance dialysis at the cantonal level with no losses to follow-up represent important strengths of this report.

Conclusion

In conclusion, COVID-19 outbreak represents an unprecedented challenge for dialysis facilities worldwide with high infection and case fatality rate. Early and strict mitigation measures enforced at Geneva University Hospitals in Switzerland seemed to be effective to control infection spread among patients on maintenance dialysis. Large scale multi-center epidemiological studies are eagerly awaited to assess the efficacy of preventive measures in decreasing infection and mortality rate within the dialysis population and to increase readiness for future outbreaks.

Abbreviations

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

CoViD-19 – Coronavirus disease 2019

WHO – World Health Organization

Declarations

Ethics approval and consent to participate

All patients have provided written informed consent for their anonymized data to be used for quality control or clinical research purposes. The study was approved by the research ethics committee of the canton of Geneva “Commission cantonale d'éthique de la recherche” (CCER Genève, ID 2020-01281).

Consent for Publication

We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal. All authors have read and approved the manuscript and agree with its submission to “BMC Nephrology”.

Availability of data and material

Data was retrieved from the Swiss Dialysis Registry and is summarized in tables 1 and 2. Anonymous raw data could be provided for specific reasons upon request.

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Author contributions

All authors have read and approved the manuscript and agree with its submission to “BMC Nephrology”.

IZ – Drafted the manuscript, participated in literature review and data collection

TAM – Critically revised the manuscript, participated in literature review and data analysis

TE, VB, MZ, NM, FR, RW, AI – Critically revised the manuscript, participated in data collection

PYM – Critically revised the manuscript, participated in data interpretation

PS – Supervised the study, critically revised the manuscript, participated in literature review, responsible for data collection and analysis

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Competing interests

None declared.

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Figures

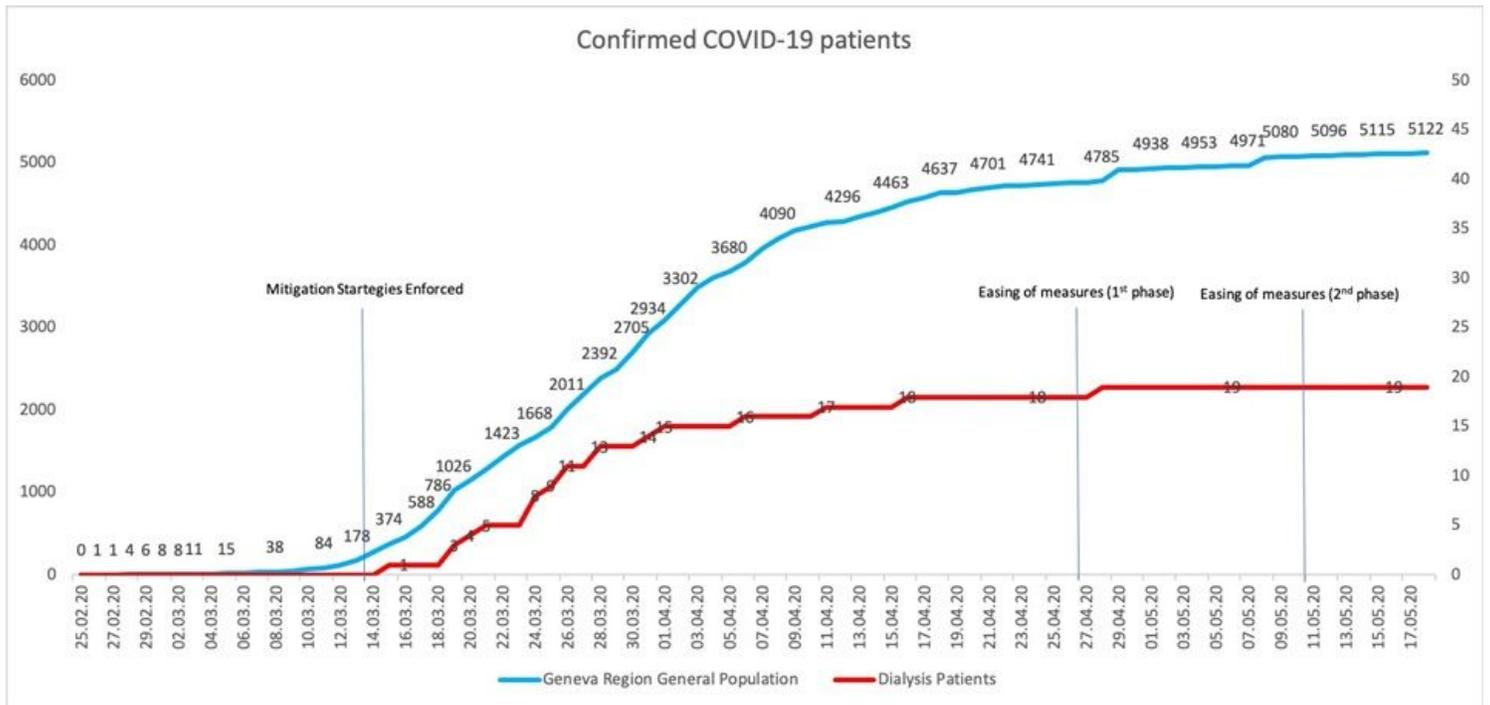


Figure 1

Cumulative frequency of SARS CoV-2 in the general population and in patients on maintenance dialysis.