Peritoneal dialysis in the era of COVID-19: experience of a Tunisian center

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Received: 18 May 2022 / Accepted: 25 June 2022 / Published online: 1 August 2022 © The Author(s) under exclusive licence to Italian Society of Nephrology 2022

Abstract
The COVID-19 pandemic has transformed the health landscape by hampering the management of patients with chronic diseases. Providing optimal healthcare has become a critical issue, especially for patients with end-stage renal disease (ESRD) receiving in-center dialysis. Peritoneal Dialysis (PD) has the advantage of being a home-based therapy. Several papers about COVID-19 in the chronic kidney disease (CKD) population have been published, but few studies focused on the PD population, with limited case series. In this paper, we share our strategy for managing PD patients during the pandemic and describe the characteristics of 24 episodes of COVID-19 that occurred in our PD patients. Also, we report the impact of the pandemic on different outcomes and discuss the challenges of renal replacement therapy (RRT) in the time of COVID-19 and the advantages of PD. During the period from December 2019 to September 2021, 127 patients received PD in our center. Among them, we recorded 24 episodes of COVID-19 that occurred in 20 patients, corresponding to an incidence of 8.4 per 1000 patient-months. None of the 20 patients with COVID-19 were vaccinated and there was a significant male gender predominance in the COVID-19 group compared to the non-COVID-19 group. The prevalence of diabetic nephropathy and primary glomerulonephritis were also significantly higher in the COVID-19 group. The revealing symptoms were asthenia, dry cough, and the deterioration of general conditions in 100%, 75%, and 63% of the patients, respectively. A biological inflammatory syndrome was found in 30% of the patients. Chest computed tomography (CT) scan, performed in 5 patients, showed features of COVID pneumonia with an average extent of damage of 55%. The rate of patients starting PD during the study period was comparable to that before the pandemic. Furthermore, we did not find a significant difference between the infected and the non-infected groups regarding the incidence of peritonitis, PD technique failure, and mortality (6.1 [0–1.46] vs 3.9 [0.15–0.64] deaths per 1000 patient-months. COVID-19 does not seem to have influenced the outcomes of our patients treated with PD even before the launch of mass immunization in our country. Thus, PD can be a great option for RRT in the era of the COVID-19 pandemic since many issues could be managed remotely to avoid regular hospital visits and contribute to maintaining social distancing, which is the cornerstone of breaking the chain of transmission of the novel virus.

Keywords COVID-19 · Pandemic · Peritoneal dialysis · Management

Introduction
The COVID-19 pandemic, which is in its second year now, had a crucial role in transforming the health landscape by impeding the management of chronic diseases. In this paper, we report our experience in managing peritoneal dialysis (PD) patients during the pandemic.

Our PD unit, operating through the Department of Internal Medicine “A” at Charles Nicolle university hospital in Tunis, included:
- A mini operating room for peritoneal catheter placement and removal.
- A consultation office for patient education, periodic follow-up and preparation for kidney transplant (KTx).
- A day hospital for iron and antibiotic delivery and other nursing care.

The medical staff includes a senior doctor with two resident doctors. The paramedical staff includes a chief nurse and two other nurses and a caregiver specialized in PD care. Among the 127 PD patients treated in our unit, we retrospectively collected data of all the cases (20) of COVID-19 that occurred between December 2019 and September 2021. We used Real-Time Reverse Transcriptase Polymerase Chain reaction (RT-PCR) to confirm the infection after nasopharyngeal swabbing.

We compared data and outcomes between patients with COVID-19 and non-COVID-19 PD patients. We used the chi 2 test (or Fisher test if appropriate) to compare proportions. We calculated the incidence rates by relating the number of events to the duration of follow-up during the study period. We calculated the 95% confidence intervals (95%, CI) using the usual formulas in order to compare incidences in the two groups. The difference is considered significant when there is no overlap between intervals.

**Our strategy for managing PD patients during the epidemic waves:**

The first case of COVID-19 in the world was reported in December 2019 [3] and it was declared a pandemic by the WHO in March 2020 [4]. Tunisia reported the first confirmed case of COVID-19 in March 2020 [5], and the first case in our PD patients was confirmed in April 2020. During our study period, Tunisia experienced 4 epidemic waves. The peaks were observed in October 2020, February 2021, April 2021, and July 2021 [6].

During this pandemic and more particularly during the epidemic waves, as nephrologists, we had two primary goals:

- Keeping our patients safe, and
- Meeting the needs of patients who require COVID-19-related and unrelated hospitalization.

PD patients are trained to perform their dialysis at home and can therefore avoid in-center hospital visits, unlike patients on hemodialysis (HD). Thus, PD patients can avoid undue exposure to the novel coronavirus.

Our strategy consisted of supporting patients to remain at home safely with remote contact (phone) and monitoring. Consultation became telephonic rather than face-to-face.

There were calls about routine check-ups, calls from anxious patients asking for advice, and others from patients reporting particular complaints that were managed remotely. However, there were some circumstances where face-to-face consultation was deemed necessary by clinicians, especially when serious complications like infectious peritonitis were suspected. Patients who reported symptoms that might be related to SARS-Cov2 infection were asked to stay at home and avoid contact with other people during the period recommended by the National Authority for Assessment and Accreditation in Healthcare (INEAS): 14 days during the first peak, 10 days during the second, and the third ones, then 7 days. Some of them were asked to contact the national Mobile Emergency and Resuscitation Service (SAMU) to be tested and evaluated. Other patients, in whom we suspected another health problem requiring further explorations, were asked to come for in-hospital consultation. The decision was based on a number of criteria summarized in Table 1.

For patients who were asked to come for face-to-face consultation and those who requested unplanned consultations, the barrier measures were respected and there was systematic temperature measurement and questions about COVID-19 symptoms and contact with people positive for the novel virus. If COVID-19 was suspected, nasopharyngeal swabbing for PCR was done. During the epidemic waves, hospitalizations were limited.

- For non-COVID-19 health problems: patients were admitted if they could not be managed with ambula-

| Patients asked to come for consultation | Patients asked to contact the SAMU |
|---------------------------------------|-----------------------------------|
| Patients with confirmed or suspected PD-related complications | Patients who are worried about their symptoms |
| Peritonitis/tunnel infection based on the ISPD guidelines | Patients whose symptoms get worse |
| Patients with non-infectious complications of PD | Patients who present severe symptoms |
| Patients who describe serious symptoms not attributable to COVID-19 | Patients who do not present severe symptoms but who are deemed at higher risk of complications from COVID-19 based on their clinical history and comorbidities |

**SAMU** mobile emergency and resuscitation service, **PD** peritoneal dialysis, **ISPD** International Society for Peritoneal Dialysis
ory care, i.e., in-hospital treatment was required or their symptoms worsened.

– Patients who came for COVID-19-related symptoms instead of contacting the SAMU and presented severe symptoms were admitted to the local COVID-19 unit and switched temporarily to HD.

Once the COVID-19 vaccine was available in Tunisia, our patients were among the priority populations. We encouraged them to get vaccinated.

**Characteristics of COVID-19 in our patients**

During a cumulative study period of 2858.3 months, 24 episodes of COVID-19 infection were recorded in 20 patients corresponding to an incidence of 8.4 per 1000 patient-months (95% CI [5–11.8]). Four patients experienced 2 episodes of COVID-19, an average of 5.25 months apart. No patient was vaccinated before the first episode of COVID-19 infection and 2 patients experienced a second episode after getting fully vaccinated. The vaccine became available in Tunisia in April 2021, 17 months after the beginning of our inclusion period; most of our patients were initially reticent to get vaccinated.

There were 14 men and 6 women with a sex-ratio of 2.3 in the COVID-19 group contrasting with that of 0.94 in non-infected patients ($p = 0.04$). The median age was 39 years in patients who experienced COVID-19 (range: 22–60 years) without significant differences with that of the non-infected patients.

Diabetes (25%) and primary glomerulonephritis (30%) were the main causes of end stage renal disease (ESRD) in the infected patients (supplementary figure A). In the non-infected group, the rate of diabetic nephropathy was 13% and the rate of primary glomerulonephritis was 10%, the difference between the two groups was statistically significant, $p < 0.01$ and $p < 0.03$, respectively.

Diabetes and hypertension were the most common comorbidities observed in the COVID-19 group (supplementary table A) with rates of 25% and 70%, respectively; these rates are statistically similar to those of 15.9% and 89.4% observed in the non-infected group.

All patients were on automated PD for an average duration of 3 years, and 3 of them had a history of peritonitis.

The revealing symptoms were dominated by asthenia, dry cough and altered general conditions (supplementary figure B). Fever was present in 9 patients (45%). Two patients had low blood pressure due to dehydration. Four patients presented with peripheral oxygen desaturation in ambient air, including one during her second episode of COVID-19.

Laboratory tests revealed that C-reactive protein level (CRP) was high in all the patients, and most of them had lymphopenia (91%). The main biological parameters recorded in the infected patients are summarized in supplementary table B.

Chest computed tomography (CT) scan was carried out in 5 patients; it was positive in 4 of them with an average extent of damage of 55%.

A concomitant infection was diagnosed in three cases and consisted of a superinfected skin ulcer in the first, bacterial peritonitis in the second, and bacterial pneumonia in the third patient. For treatment we followed our national guidelines [1]. Seven patients were admitted to the hospital and one of them was hospitalized in the intensive care unit (ICU) for high oxygen needs. All of them received azithromycin, vitamin C and zinc supplementation. A preventive dose of heparin was prescribed in eight patients.

During hospital stays, patients were switched to HD. Two patients died, one from respiratory failure despite high flow oxygen therapy; the patient was not intubated due to lack of ICU beds, while the other patient died in unspecified circumstances.

Table 2 summarizes the rates of patients who started PD, dropped out of PD (PD failure), the incidence of peritonitis and death during the study period in the overall population and in each group (COVID/ non-COVID). Among the 30 patients who dropped out of PD, 17 (57%) were switched to HD, 10 (33%) died, two patients were lost to follow-up, and one patient underwent kidney transplantation.

We did not notice a significant change in the rate of patients who started PD each year between 2018 and 2021, ranging from 21 to 24%.

| Outcome        | N  | %    | Monthly incidence % | 95% CI      | $p$  |
|----------------|----|------|---------------------|-------------|-----|
| **Mortality**  |    |      |                      |             |     |
| Total          | 12 | 9.4  | 0.42                | [0.18–0.66] |     |
| COVID-19 (+)   | 2  | 10   | 0.61                | [0–1.46]    | NS  |
| COVID-19 (–)   | 10 | 9.3  | 0.39                | [0.15–0.64] |     |
| **Peritonitis**|    |      |                      |             |     |
| Total          | 26 | 20.5 | 0.91                | [0.59–1.26] |     |
| COVID-19 (+)   | 6  | 30   | 1.84                | [0.36–3.31] | NS  |
| COVID-19 (–)   | 20 | 18.7 | 0.78                | [0.44–1.14] |     |
| **PD failure** |    |      |                      |             |     |
| Total          | 32 | 25.2 | 1.12                | [0.7–1.5]   |     |
| COVID-19 (+)   | 4  | 20   | 1.23                | [0.02–2.43] | NS  |
| COVID-19 (–)   | 28 | 26.2 | 1.1                 | [0.7–1.51]  |     |
| **Entry in PD**|    |      |                      |             |     |
| Total          | 33 | 26   | 1.15                | [0.76–1.55] |     |
| COVID-19 (+)   | 6  | 30   | 1.84                | [0.37–3.31] | NS  |
| COVID-19 (–)   | 27 | 25   | 1.07                | [0.66–1.47] |     |
Mortality was higher in the COVID-19 group compared to the non-COVID-19 group 6.1 vs 3.9 deaths per 1000 patient-months, however this difference was not statistically significant.

Regarding the medical and nursing staff, two of the nurses and the caregiver and one of the resident doctors experienced COVID-19 during the study period. The suspected source of contamination was out-of-hospital in three of them and contact with a positive patient in one case. None of the infected healthcare professionals had yet been vaccinated when they tested positive for COVID-19.

Discussion and conclusions

During the COVID-19 pandemic, PD patients were described as “the forgotten group” [2]. Despite several papers being published during these 2 years about COVID-19 in patients with CKD [3–7], few cases of COVID-19 in the PD population have been reported. Sachdeva et al. shared data of 11 cases of COVID-19 in PD patients, 8 cases in Jiang’s series [3], and only two cases were reported in Valeri’s series [8]. The incidences of COVID-19 in the PD population reported in the literature are close to those of the general population [3]. Jiang HJ et al. reported an incidence of 2.44 per 1000 person-months and their data covered the period when the vaccine was not available, similarly to our population, however, the incidence of COVID-19 was higher in our study (8.4 per 1000 person-months). This can be explained by the high rate of patients newly admitted to PD during the study period in our series (26%), and the required visits for education.

The low incidence can be explained by the fact that PD is a home-based treatment, which is the main advantage over HD during the pandemic. Consultations and prescriptions can be provided remotely to limit hospital visits and to avoid contact with other people. Moreover, the infected or contact patients can be isolated at home rather than in a specific dialysis unit, while HD patients with suspected or confirmed COVID-19 need isolation during dialysis, resulting in a shortage of healthcare providers and HD machines. Healthcare providers may be infected while treating HD patients resulting in a shortage of dialysis team members due to illness or quarantine. In response to these problems, some strategies are recommended for reducing the frequency and duration of dialysis which, however, may be detrimental to its quality [5]. Moreover, HD strategies for infected patients consume considerable amounts of medical resources and may threaten the quality of health care provided to patients with non-COVID-related diseases.

COVID-19 has received the most attention during the pandemic among other health problems. Providing adequate dialysis in the era of the COVID-19 pandemic became a real challenge.

Some authors discussed the potential disadvantages of PD in patients with COVID-19 infection, such as the problem of increased intraperitoneal pressures, which can worsen breathing difficulties. Hypervolemia related to the decrease in the ultrafiltration rate in case of associated peritonitis can also worsen dyspnea [5].

Moreover, gastrointestinal symptoms are very common in COVID-19 [9] but it is still unclear whether the virus increases the risk of bacterial translocation and peritonitis.

In our center, mortality in the COVID-19 group was higher compared to the other group (6.1 [0–1.46] vs 3.9 [0.15–0.64] deaths per 1000 patient-months), but this difference was not statistically significant, which is similar to that reported in the literature [3].

The low mortality in this population suggests that the PD population is not a high-risk population. In a recent cohort study including 436 CKD patients, 30-day mortality was significantly higher in HD patients with COVID-19 compared to PD patients with COVID-19 [4].

PD may be the safer dialysis modality given the fact that it is a home-based therapy, but large cohorts are lacking to better investigate the outcomes of COVID-19 in this population.

In our study, mortality, peritonitis and PD failure were more frequent but not significantly so in the COVID-19 group. Given the limited number of cases, no conclusions can be drawn about the virulence in this population.

In the past decades, the use of PD among patients with ESRD has declined in our center. This decline was mainly due to the urgent start of RRT with HD through a central venous catheter. At the time of COVID-19, the lack of PD use seems to have been addressed thanks to the efforts implemented to fight the pandemic. COVID-19 has pushed us to reconsider this therapy by challenging the conventional approaches and exhausting our resources. We had a slight increase in the rate of patients who started PD. Further studies are needed to confirm the superiority of PD at the time of the COVID-19 pandemic.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s40620-022-01396-9.

Acknowledgements We would like to acknowledge the nursing team of the PD unit of the Department of Internal Medicine “A” at Charles Nicolle hospital in Tunis (Mrs Halima Jouini, Mrs Imen Chihouay, Mrs Ibtisssem Brahmi, and Mr Akrem Nahdi), and the nursing team of the HD unit, for their hard work and dedication during the COVID-19 pandemic. They have performed above and beyond under such challenging conditions.

Declarations

Conflict of interest The authors of this manuscript have no relevant financial or non-financial interests to disclose.
Ethical statement The analyses involved existing parameters in an anonymized database where the user cannot identify individuals. The local ethical principles for data collection were respected.

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