

## ORIGINAL ARTICLE

## INITIAL IMPACT OF THE COVID-19 PANDEMIC ON THE CARE PROFILE FOR CRITICALLY-ILL PATIENTS ON HEMODIALYSIS

### HIGHLIGHTS

1. Often, critically ill patients with COVID-19 progress to kidney dysfunction.
2. In 2020, there were more hemodialysis sessions when compared to 2019.
3. COVID-19 was the main cause of entry into hemodialysis.

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### ABSTRACT

**Objective:** to compare the care profile for critically-ill patients on hemodialysis before and during the COVID-19 pandemic. **Method:** an observational study carried out in a hospital from São Paulo, Brazil. The participants were critically-ill patients on hemodialysis hospitalized in 2019 and 2020. The data were collected from documents of hemodialysis sessions and from medical records. Chi-square, Mann-Whitney, Shapiro-Wilk and Fisher's Exact tests were used for comparisons ( $p < 0.05$ ). **Results:** a total of 212 sessions were performed with 50 patients in 2019 and 873 sessions with 171 patients in 2020. In 2019, the patients were referred to intensive care and hemodialysis after  $4.62 \pm 6.38$  and  $17.26 \pm 24.53$  days, respectively, and in 2020 these periods corresponded to  $2.21 \pm 3.63$  and  $10.24 \pm 11.99$  days. There were more deaths in 2020 ( $p = 0.01$ ) and among patients with COVID-19 ( $p = 0.014$ ). **Conclusion:** more hemodialysis sessions were observed in 2020 when compared to pre-pandemic times, an unknown situation in the first months of the pandemic.

**DESCRIPTORS:** Critical Care; Acute Kidney Injury; Renal Failure; Renal Dialysis; COVID-19.

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## INTRODUCTION

The Coronavirus Disease-19 (COVID-19) affects several organs<sup>1</sup> and the mechanisms of action of the virus in these systems are not yet fully known; however, more severe patients frequently evolve to renal dysfunctions<sup>1-4</sup>. A research study pointed out that 50% of the patients hospitalized due to COVID-19 evolved to Acute Kidney Injury (AKI) at some point during hospitalization<sup>5</sup> and another one reported that 32% of these patients already had AKI upon hospital admission<sup>6</sup>.

Initially, it was believed that deterioration of the renal function was due to cardiac alterations generated by the virus, associated with predisposing factors such as sepsis, hypovolemia and nephrotoxins<sup>3,7</sup>. Later on, this dysfunction was attributed to an intense inflammatory process generated by the virus due to the increased production of inflammatory interleukins such as IL-6 and TNF-alpha<sup>1,8</sup>. As research progressed, various authors identified that entry of SARS-CoV-2 into human cells occurs through binding of the virus spike protein to the angiotensin-2 converting enzyme (ACE-2), a protein mainly expressed in lung cells, heart, blood vessels, intestine and kidneys, which might explain the changes in these tissues during course of the disease<sup>9,10</sup>. More recently, AKI development in patients with COVID-19 is believed to be linked both to the direct effects of the virus on the kidneys and to the mechanisms triggered by the systemic viral infection and medication use for the treatment of these conditions<sup>10</sup>.

A number of studies have reported that patients of advanced age, obese, diabetic, hypertensive and/or with chronic kidney disease are more likely to develop AKI during hospitalization<sup>5-6,9-10</sup>. Management of patients with COVID-19 and AKI occurs in several ways, from clinical monitoring to Renal Replacement Therapy (RRT)<sup>3</sup>. Among the patients hospitalized with SARS-CoV-2, those belonging to the male gender, with diabetes and high creatinine levels, and on mechanical ventilation, are at a greater risk for entering RRT<sup>11</sup>.

International studies point to changes in the care profile for critically-ill patients in need of RRT in relation to the years prior to the pandemic, and these results mentioned the need to expand hemodialysis services not only to treat patients with the disease, but also those who remained on RRT after the COVID-19 treatment<sup>1,4</sup>.

National studies on this theme are still scarce and it is necessary to know this new service profile according to the local reality to scale teams, mainly Nursing professionals, the largest workforce in hemodialysis services. These aspects motivated this study, which aimed at comparing the care profile for critically-ill patients on hemodialysis before and during the COVID-19 pandemic.

## METHOD

A retrospective and observational study carried out at the hemodialysis service of a university hospital in the city of São Paulo, Brazil. The casuistry consisted of critically-ill patients on RRT from April to July 2019 and from April to July 2020. Patients over 18 years of age who underwent RRT during hospitalization in the Intensive Care Unit (ICU) were included. Patients without hemodialysis care documents and/or without hospitalization data were excluded.

The data were collected from external hemodialysis care documents and from the patients' electronic medical records. External hemodialysis care documents are standardized notes that contain data related to the patients and to each session. These documents are filled in by the Nursing team during RRT in units outside the hemodialysis sector. The patients' electronic medical records constitute an electronic system that stores the Medical, Nursing and Multiprofessional teams' notes regarding the patients' treatment and clinical

practice during care at the institution.

For data surveying, an instrument was developed with the following variables: gender, age, reason for hospitalization, presence of comorbidities, creatinine value at admission, admission date to the service, RRT initiation date, ICU admission date, number of ICU sessions, complications and outcomes (transfer, discharge or death). There was anonymization of the data regarding the patients' names and hospital registration by a person not connected to the research to guarantee their non-identification during the analyses.

The data were processed using IBM's *Statistical Package for Social Science – Statistics for Windows* (SPSS) software, version 20.0. For the comparisons between the groups, the Chi-square, Mann-Whitney, Shapiro-Wilk and Fisher's Exact tests were performed, with a 5% statistical significance level ( $p < 0.05$ ).

The research followed the precepts set forth in the 1975 Declaration of Helsinki and in National Health Council Resolution No. 466 of 12/12/12, which was approved by the Research Ethics Committee of the Federal University of São Paulo under opinion number 4,992,140.

## RESULTS

A total of 221 patients participated in the study: 50 in 2019 and 171 in 2020. The appointments in 2019 were mainly in men with a mean age of  $57.44 \pm 15.65$  years old [min=31; max=79], acute kidney disorders were the main reasons for admission to the service and the most frequent comorbidities were pre-existing nephropathies, hypertension and diabetes. In 2020, there was predominance of appointments in men with a mean age of  $60.60 \pm 14.38$  years old [min=23; max=91], COVID-19 was the main reason for admission to the institution and the most common comorbidities were hypertension, pre-existing nephropathies and diabetes. The other baseline data can be seen in Table 1.

**Table 1** – Demographic and clinical characteristics of the participants at baseline. São Paulo, SP, Brazil, 2021

	2019	2020	p
<b>Number of participants, n (%)</b>	50 (100)	171 (100)	
<b>Gender, n (%)</b>			
Male	32 (64)	110 (64.3)	0.966 <sup>a</sup>
Female	18 (36)	61 (35.7)	
<b>Diagnosis at admission, n (%)</b>			
Acute kidney disorders	15 (30)	45 (26.3)	0.606 <sup>a</sup>
Sepsis	14 (28)	26 (15.2)	0.039 <sup>a</sup>
COVID-19	0 (0)	114 (66.7)	<0.001 <sup>a</sup>
Surgery	6 (12)	8 (4.7)	0.093 <sup>a</sup>
Trauma	2 (4)	5 (2.9)	1.000 <sup>a</sup>
<b>Comorbidities, n (%)</b>			

Arterial hypertension	34 (68)	135 (78.9)	0.108 <sup>a</sup>
Diabetes	32 (64)	77 (45)	0.018 <sup>a</sup>
Nephropathies	40 (80)	92 (53.8)	0.001 <sup>a</sup>
Heart diseases	16 (32)	51 (29.8)	0.768 <sup>a</sup>
Gastroenteropathies	15 (30)	16 (9.4)	<0.001 <sup>a</sup>
Neuropathies	13 (26)	27 (15.8)	0.099 <sup>a</sup>
Pneumopathies	2 (4)	10 (5.9)	0.738 <sup>a</sup>

a. Chi-square test

b. Mann Whitney Test

Source: The authors (2021).

In 2019, 90% of the patients had increased creatinine levels when entering the service, were referred to the ICU after  $4.62 \pm 6.38$  days [min=0; max=18] and initiated RRT  $17.26 \pm 24.53$  days after being hospitalized [min=0; max=123]. 212 RRT sessions were performed, with a mean of  $4.44 \pm 3.39$  sessions per patient, and the therapy lasted from 1 to 135 days.

In 2020, 77.7% of the patients had increased creatinine levels at baseline, were referred to the ICU after  $2.21 \pm 3.63$  days [min=0; max=23] and initiated RRT  $10.24 \pm 11.99$  days after being hospitalized [min=0; max=93]. There were 873 RRT sessions during the period, with a mean of  $5.13 \pm 4.48$  sessions per patient and permanence in RRT from 1 to 53 days. The other data on RRT can be seen in Table 2.

**Table 2** – Renal Replacement Therapy data. São Paulo, SP, Brazil, 2021

	2019	2020	p
<b>Number of cases per month, n (%)</b>			
April	11 (22)	22 (12.9)	0.179 <sup>a</sup>
May	11 (22)	38 (22.2)	0.979 <sup>a</sup>
June	15 (30)	51 (29.8)	0.986 <sup>a</sup>
July	13 (26)	60 (35.1)	0.384 <sup>a</sup>
<b>Number of dialysis sessions, n (%)</b>	212 (100)	873 (100)	
<b>Days on dialysis, Mean <math>\pm</math> SD</b>	$17.10 \pm 20.60$	$10.06 \pm 10.04$	0.002 <sup>b</sup>
<b>Type of dialysis - First session, n (%)</b>			
Conventional hemodialysis	47 (94)	142 (83)	0.014 <sup>a</sup>
Slow hemodialysis	2 (4)	29 (17)	
Peritoneal dialysis	1 (2)	0 (0)	
<b>Dialysis frequency - First week, n (%)</b>			
Daily	3 (6)	84 (49.1)	<0.001 <sup>a</sup>
Every other day	45 (90)	47 (27.5)	

Random days according to exams	2 (4)	40 (23.4)	
<b>Dialysis frequency - Last week, n (%)</b>			
Daily	0 (0)	56 (32.7)	<0.001 <sup>a</sup>
Every other day	48 (96)	68 (39.8)	
Random days according to exams	2 (4)	47 (27.5)	
<b>Complications during the sessions, n (%)</b>			
System coagulation	10 (4.7)	17 (1.9)	0.056 <sup>a</sup>
Hemodynamic instability	3 (1.4)	39 (4.5)	0.014 <sup>a</sup>
Cardiopulmonary arrest	0 (0)	6 (0.7)	0.304 <sup>a</sup>
Hematoma in arteriovenous fistula	1 (0.5)	2 (0.2)	1.000 <sup>a</sup>
<b>Outcome, n (%)</b>			
Hospital discharge	28 (56)	61 (35.7)	0.010 <sup>a</sup>
Death - Total	22 (44)	110 (64.3)	
Death within 14 days of intensive care	4 (18.2)	39 (35.4)	0.238 <sup>a</sup>
Death within 28 days of intensive care	7 (31.8)	27 (24.5)	0.591 <sup>a</sup>
Death after 28 days of intensive care	11 (50)	44 (21.8)	0.586 <sup>a</sup>

a. Chi-square test

b. Mann Whitney Test

Source: The authors (2021).

When comparing the variables with the outcomes, it was observed that there were more deaths in 2020 when compared to 2019 ( $p=0.01$ ) and that patients with COVID-19 ( $p=0.014$ ) and with hemodynamic instability during RRT ( $p=0.016$ ) were the ones who died the most. No statistical differences were found that would evidence a higher number of deaths among the patients with an initial diagnosis of sepsis and/or acute kidney disease. There were also no associations between death and presence of previous diseases such as hypertension, diabetes, nephropathy, heart disease, gastroenteropathies, neuropathies and pneumopathies.

## DISCUSSION

In the first months of the COVID-19 pandemic, all the information indicated that SARS-CoV-2, the virus that causes the disease, had tropism for the organs of the respiratory and digestive systems; however, over time, an increase in vasculopathies and heart and kidney diseases was observed among the infected patients<sup>1-4</sup>. When comparing the first months of the COVID-19 pandemic to the pre-pandemic scenario, the current study identified that, in 2020, there was an increase in the number of critically-ill patients treated with RRT and an increase in the number of sessions when compared to the same period in 2019, and that COVID-19 was the main reason for admission to the hemodialysis service and the leading cause of death among these patients.

Originating in Wuhan, China, COVID-19 gained notoriety in March 2020, when the World Health Organization declared the beginning of the pandemic and, in October of the same year, the virus had already infected more than 39 million people and caused



more than one million deaths worldwide<sup>4</sup>. Due to its high transmissibility and lethality, the disease led to an increase in the demand for health services to manage the symptoms, changing the service profile of these organizations<sup>8-12</sup>. It was also possible to observe this new reality observed in the current study, when an important increase in the RRT demand was evidenced in sectors outside the hemodialysis service, both due to the increase in the number of patients and to the higher number of sessions per patient in the first months of the COVID-19 pandemic when compared to the previous year.

SARS-CoV-2 infects cells by binding to ACE-2, an enzyme expressed on the surface of various cells, including kidney tissue cells. The interaction between the virus spike protein and ACE-2 allows access to cellular organelles, where viral RNA translation and replication takes place<sup>9</sup>. In addition to direct cellular infection, there are other factors that may contribute to AKI in patients with COVID-19, such as generalized inflammation, hypovolemia, use of nephrotoxic drugs and organ failure<sup>9-10</sup>. This scenario might explain why COVID-19 has become the main reason for hospitalization among critically-ill patients who developed AKI and who were treated with RRT<sup>5,13-15</sup>.

A number of studies have indicated high mortality rates for patients with COVID-19 and AKI, a result that is similar to the one found in this research<sup>4-6,15</sup>. More recently, the presence of kidney injury is considered to be a severity and mortality factor among patients with COVID-19<sup>8,16</sup>. SARS-CoV-2 causes a state marked by high production of inflammatory cytokines that lead to systemic inflammation and increased clotting, significantly altering organ function. As it is a condition that is difficult to control, mortality among those infected is high<sup>8</sup>.

In 2019, a stable number of critically-ill patients on RRT and in less need of unconventional therapies were observed, such as the use of slow hemodialysis and daily sessions. However, in the first months of the pandemic, there was an increase in the number of critically-ill patients who evolved with the need for RRT and, due to severity, therapy was required for a longer period of time than the conventional one, in addition to daily sessions to maintain hydroelectrolyte balance and hemodynamic stability, similarly to other studies<sup>13-14</sup>. Another difference found between the groups was fewer days on hemodialysis among the patients with kidney injury and COVID-19, a fact that can be explained by the high severity and mortality among the participants in 2020.

Although it was not the target of this study, the increase in the number of patients on RRT and in the number of sessions exerts a direct impact on the increased workload and requires more qualified professionals for the service, training of new workers and definition of care protocols for patients with and without COVID-19, as well as cleaning and disinfection routines for the devices<sup>17</sup>.

These results point to the urgent need to expand dialysis services during the COVID-19 pandemic, not only with regard to the acquisition of equipment and supplies, but also in the training of health professionals for the area, especially the Nursing team, is the largest workforce in these sectors. In a long-term view, the consequences of AKI developed during SARS-CoV-2<sup>10</sup> infection are still unclear, but it is possible that there will be an increased demand from patients in these conditions for a period after the pandemic.

This research had the limitation of being a retrospective and observational study carried out in a single health service and, therefore, other studies need to be carried out to compare the different national and international realities.

## CONCLUSION

In 2020, there was an increase in the number of patients and hemodialysis sessions

compared to 2019. In addition to that, there were more deaths in 2020, with changes generated by COVID-19 as the main causes.

This study made an important contribution by identifying a higher number of appointments when compared to pre-pandemic times, a situation until then unknown in the first months of the pandemic. In addition to that, it was observed that COVID-19 was not only one of the main reasons for admission to the hospital hemodialysis service, but that it was also the main cause of the changes that led to death among critically-ill patients on RRT.

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#### Role of Authors:

Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work - **Gallota C, Augusto F da S, Carneiro IA**; Drafting the work or revising it critically for important intellectual content - **Gallota C, Viana TG, Augusto F da S, Genovese RE, Balda CA, Carneiro IA**; Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved - **Gallota C, Viana TG, Augusto F da S, Genovese RE, Balda CA**. All authors approved the final version of the text.

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