Research Article

Acute kidney injury in Colombian patients with COVID-19 who received kidney support therapy with genius® 90 technology

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Abstract

**Introduction:** Acute kidney injury (AKI) is one of the complications associated with severe COVID-19 infection, and it can present in up to 20% to 40% of the cases; of these, approximately 20% will require renal replacement therapy (RRT).

**Objective:** To establish clinical and laboratory characteristics in a group of patients from Colombia with COVID-19 infection and AKI that received intermittent and prolonged RRT with the GENIUS® 90 technology in between March and July 2020.

**Design:** Cross-sectional study.

**Results:** 78.9% of participants were men and 21.1% were women. The main comorbidities were the following: Hypertension (65.3%), diabetes mellitus (38.9%), obesity (26.3%), cancer (5.3%), Chronic obstructive pulmonary disease (11.6%), cardiovascular disease (23.2%), active smoking (11.6%). 33.7% had chronic kidney disease (CKD) in the average serum creatinine on admission was 4.4 mg/dl.

The following inflammatory markers were elevated: C-reactive protein (CRP), d-dimer and ferritin (20.3 mg/dl, 931mcg/l and 1174 ng/ml, respectively). 63.5% of patients underwent sustained low-efficiency dialysis (SLED) (6 to 12 hours) and the rest of the patients (36.35%) underwent conventional hemodialysis (less than 4 hours).

The mortality of the total patient sample was 36.9%, lower in patients with CKD than in patients with no previous renal disease history (18.7% and 40.1%, respectively).

**Conclusion:** Renal complications are frequent in patients with severe COVID-19. The development of AKI could be an isolated prognostic marker associated with an increase in mortality in patients with COVID-19, and one of the options is intermittent and prolonged RRT with the GENIUS® 90 system.
Introduction

COVID-19 is an infectious disease caused by the new coronavirus SARS-CoV-2, a virus that is highly related to SARS-CoV, which caused an epidemic in the year 2002. Since the first reported cases in December 2019, there has been an exponential increase in its numbers, and currently there exists a high number of cases of people infected with COVID-19, which is associated with a high percentage of morbidity and mortality.

Acute kidney injury is a condition in which a rapid deterioration of the kidney function occurs, with electrolyte disturbances, acid-base disturbances, a decrease in urine output and an accumulation of nitrogen waste products [1], it is one of the complications associated with COVID-19 infection and in a high number of cases it requires renal replacement therapy. There are several options of treatment including: Continuous renal replacement therapy, conventional hemodialysis, and prolonged intermittent therapies.

Prolonged hemodialysis consists in ultrafiltration which is almost exclusive in its diffusion mechanism [2]. It is a technique with high efficacy that utilizes low blood flow and a low dialysate, which has been established as a substitute for continuous renal replacement therapy in critically ill patients with hemodynamic instability. It has also been established as a transition therapy from continuous renal replacement therapy to intermittent hemodialysis [3,4]. It is safe and cost-effective, being a good option for patients with COVID-19. However, there are no published studies about the use of these therapies in patients with COVID-19 and AKI.

Materials and methods

This is a cross-sectional study held in a group of patients from Colombia with the diagnosis of COVID-19 and AKI that received PIRRT in between March and July 2020 in the cities of Bogotá, Cartagena, Barranquilla, Valledupar, Bucaramanga, Pereira, Ibague, Cali and Medellin.

Inclusion criteria: Patient is above 18 years of age, positive COVID-19 results by reverse transcriptase polymerase chain reaction (RT-PCR) or antibodies against SARS-CoV-2, acute kidney injury requiring conventional hemodialysis and prolonged therapies with the GENIUS® 90 technology. A non-probabilistic sampling was used by convenience for patients that met the inclusion criteria.

Exclusion criteria: Patient with end-stage kidney disease on previous renal replacement therapy.

The data was obtained from secondary sources, by medical chart reviewing of patients with COVID-19 and acute kidney injury requiring renal replacement therapy at Fresenius medical care- FM express program in nine cities of Colombia, between March and July of the year 2020.
without the disease, 11.0 (12.0-9.3), with a $p$ value of less than 0.05 (Table 2).

In our study, of all the patients, only 13 had procalcitonin measurements with a median of 4.2 (5.6-1.6) ng/ml, and 57 participants with ferritin reports, with a median of 1174 (1650-884) ng/ml. Additionally, on evaluation of the RRT given to patients, the median number of SLED sessions was 5.0 (9.0-1.0), while the median number of sessions for regular hemodialysis was 3 (4.0-1.0).

In general, the patients in the study were critically ill. Of all participants, 86.3% required intensive care unit level of care. Of these, 31.7% had CKD and 68.3% did not have the disease. The majority of patients required mechanical ventilation and around two thirds of the patient’s required at least one vasopressor. Additionally, when comparing the SOFA and APACHE scores on admission to the ICU amongst participants, the median of APACHE was 16.5 (22-9) points and the median of SOFA was 8 (11.7-4.0) for patients with CKD, while in patients without it. The median of APACHE and SOFA scores were 16 (21-0) and 8 (12-3) points, respectively, without a statistically significant difference ($p > 0.05$) (Table 3).

Finally, a mortality of 36.9% was identified in the total number of participants, with less mortality in patients with CKD, 6/32 (18.7%) in comparison to the patients without CKD, 29/63 (40.1%), with a statistically significant difference (Table 3).

**Discussion**

COVID-19 is infectious disease caused by RNA monocatenary virus SARS-CoV-2, which is not only a local pulmonary infection, but compromises multiple systems that can lead to multiple organ system dysfunction, given a dysregulated inflammatory response. The latter due to the action of the virus itself in the epithelial cells [1-4]. The virus attaches to the carbopeptidase receptor related to the angiotensin-converting enzyme 2 (ACE-2), found in

### Table 1: Clinical and socio-demographic characteristics.

| Variable                                      | Total (n = 95) | CKD 32 (33.7%) | No CKD 63 (66.3%) | $p$ value |
|-----------------------------------------------|---------------|----------------|-------------------|----------|
| Age, Me [IQR]                                | 64.0 [71.0-56.0] | 67.5 [71.0-61.0] | 62.0 [72.0-54.0] | 0.238    |
| Gender, n (%)                                |               |                |                   |          |
| Female                                        | 20 (21.1)     | 9 (28.1)       | 11 (17.5)         | 0.228    |
| Male                                          | 75 (81.9)     | 23 (71.9)      | 52 (82.5)         |          |
| Hypertension, n (%)                           |               |                |                   |          |
| Yes                                           | 62 (65.3)     | 27 (84.4)      | 35 (55.6)         | 0.005*   |
| No                                            | 33 (34.7)     | 5 (15.6)       | 28 (44.4)         |          |
| Type 2 Diabetes Mellitus, n (%)               |               |                |                   |          |
| Yes                                           | 37 (38.9)     | 17 (53.1)      | 20 (31.7)         | 0.043*   |
| No                                            | 58 (61.1)     | 15 (46.9)      | 43 (68.3)         |          |
| Obesity, n (%)                                |               |                |                   |          |
| Yes                                           | 25 (26.3)     | 5 (15.6)       | 20 (31.7)         | 0.092    |
| No                                            | 70 (73.7)     | 37 (84.4)      | 43 (68.3)         |          |
| Cancer, n (%)                                 |               |                |                   |          |
| Yes                                           | 5 (5.3)       | 1 (3.1)        | 4 (6.3)           | 0.506    |
| No                                            | 90 (94.7)     | 31 (96.9)      | 59 (93.7)         |          |
| COPD, n (%)                                   |               |                |                   |          |
| Yes                                           | 11 (11.6)     | 4 (12.5)       | 7 (11.1)          | 0.842    |
| No                                            | 84 (88.4)     | 28 (87.5)      | 56 (88.9)         |          |
| Cardiovascular disease, n (%)                 |               |                |                   | <0.001*  |
| Yes                                           | 22 (23.2)     | 16 (50.0)      | 6 (9.5)           |          |
| No                                            | 73 (76.8)     | 16 (50.0)      | 57 (90.5)         |          |
| Active Smoking, n (%)                         |               |                |                   | 0.918    |
| Yes                                           | 11 (11.6)     | 4 (12.5)       | 7 (11.1)          |          |
| No                                            | 84 (88.4)     | 28 (87.5)      | 56 (89.9)         |          |

### Table 2: Laboratory characteristics of patients initiating RRT.

| Variable                                      | Total (n = 95) | CKD 32 (33.7%) | No CKD 63 (66.3%) | $p$ value |
|-----------------------------------------------|---------------|----------------|-------------------|----------|
| Creatinine mg/dl, Me [IQR]                    | 4.40 [5.92-3.30] | 5.39 [7.48-3.46] | 4.31 [5.70-3.15] | 0.084    |
| Inflammatory Markers                         |               |                |                   |          |
| CRP mg/dl, Me [IQR]                           | 20.30 [41.60-7.60] | 23.2 [118.2-8.90] | 16.0 [37.8-4.70] | 0.547    |
| D-Dimer μg/l, Me [IQR]                        | 931.0 [2200.0-1400.0] | 1139.0 [2076.5-3987.0] | 783.3 [3380.0-9] | 0.492    |
| Complete Blood Count                         |               |                |                   |          |
| Hemoglobin g/dl, Me [IQR]                     | 10.70 [12.00-9.10] | 9.90 [11.35-8.50] | 11.0 [12.0-9.30] | 0.035*   |
| Acid Base Status and Electrolytes            |               |                |                   |          |
| pH, Me [IQR]                                  | 7.29 [7.37-7.17] | 7.31 [7.38-7.24] | 7.28 [7.34-7.16] | 0.235    |
| HCO3, mmol/l, Me [IQR]                        | 18.00 [21.2-14.2] | 18.1 [20.9-15.4] | 18.0 [21.3-13.7] | 0.923    |
| Lactate mmol/l, Me [IQR]                      | 1.93 [2.73-1.40] | 1.80 [2.72-1.28] | 2.00 [2.73-1.40] | 0.381    |
| PaO2/FiO2, Me [IQR]                           | 148.0 [205.0-78.0] | 173.5 [224.5-101.0] | 123.0 [190.0-71.0] | 0.053    |
| Sodium, mEq/l, Me [IQR]                       | 138.0 [141.0-133.0] | 137.5 [141.0-133.2] | 138.0 [142.0-133.0] | 0.374    |
| Potassium, mEq/l, Me [IQR]                    | 4.90 [5.80-4.00] | 4.85 [5.77-4.00] | 5.00 [5.80-4.00] | 0.812    |

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Cardiac, pulmonary, and renal injury: the SARS-CoV-2 virus can cause infection of the glomeruli and cardiopulmonary tissue, kidneys, and the immune system cells. In this way, it can cause infection of the glomeruli and the renal tubular epithelium [5]. AKI is common in patients with COVID-19, being present in approximately 20 to 40% of the patients admitted to the ICU. Of these, 20% require RRT during the course [3,8].

The mechanisms behind kidney damage are unclear and likely multifactorial in origin. There are several potential mechanisms of kidney injury in COVID-19 infection; cytokine damage is one of the proposed mechanisms, with a direct toxic effect of the cytokines on the renal tubules. Other mechanisms include organ crosstalk, for example, if patients develop cardiomyopathy and consequently cardiorenal syndrome, or alveolar damage leading to medullary hypoxia [6]. Systemic effects such as hypotension, positive fluid balance and rhabdomyolysis may also lead to acute kidney injury [6]. In a study of 26 autopsies with patients with COVID-19, diffuse erythrocyte aggregation with endothelial damage and obstruction were found in the peritubular and glomerular capillaries [7]. There was also diffuse damage of the proximal tubules with loss of the brush border, vacuolar degeneration and necrosis. It is also thought that kidney disease may be caused by SARS-CoV-2 entering the kidney cells via the ACE-2 receptor, and can cause damage by inducing tubular damage via deposition of MAC complexes on tubules and infiltration CD68+ macrophages in the tubule-interstitium [7].

In our study we found that the median of age of patients with AKI secondary to COVID-19 was similar to other published studies such as Hirsch, et al. and Chan, et al. [9,10]. However, a meta-analysis published recently composed primarily of Chinese patients showed a great variability in the age, including patients from 47 to 70 years old [11].

In the Spanish register acute kidney failure COVID-19 [12], it was found that more than 60% of the patients were hypertensive, around 30% of the patients were diabetic, 32% were obese, 14% had COPD and less than 10% were cancer patients.

While it is true that CKD is a major risk factor for AKI, as shown by Hirsch, et al. [10], the majority of our patients did not have CKD at baseline, suggesting that even though kidney function is preserved, patients are still at risk of developing AKI.

The median of creatinine on admission in our study differs from the one reported in other studies [9,10]. This is due to the fact that the serum creatinine obtained in our study was previous to the start of RRT; additionally, our data came from medical charts, not having the baseline serum creatinine previous to hospitalization.

The average level of d-dimer and CRP were both high in all the patients as expected in COVID-19 infection, even higher than in other published studies like Richardson, et al. in the United states of America [11], were the mean CRP value was 13 mg/dl and d-dimer was 438 mcg/L. Of the total of our patients, the procalcitonin and ferritin levels were higher in comparison with the values in the study published by Richardson, et al. [11].

The average blood gas analysis in our study showed metabolic acidosis and moderate hypoxemia, which reflects in the severity of COVID 19 infection in the participants. Of the total sample, a high number of patients required ICU level of care, and of these, more than ninety-percent required mechanical ventilation and the majority required vaspressors. These findings are higher than the ones reported in Rubin, et al. were 77% of the patients’ required mechanical ventilation and the mean SOFA score was 6.

Global mortality in our patients was 36.9%, similar to other studies such as Hirsch et al, were the mortality was 34.8% [8]. It is worth to highlight that the mortality was lower in patients with CKD than in patients without CKD. Within the analysis of this study a hypothesis is generated, that the natural immunosuppressive state in CKD patients may protect against the cytokine storm by COVID-19 [13-15], that is present in patients that are previously healthy without any immunosuppression. However, randomized clinical trials have to be made to corroborate the latter, given that for now, only studies with descriptive methodology have been published.

### Table 3: Characteristics of patients in the intensive care unit (ICU).

| Variable                                      | Total (n = 95) | CKD 32 (33.7%) | No CKD 63 (66.3%) | p value |
|-----------------------------------------------|---------------|----------------|-------------------|---------|
| ICU level of care requirement, n (%)          |               |                |                   |         |
| Yes                                           | 82 (86.3)     | 26 (81.3)      | 56 (88.6)         | 0.068   |
| No                                            | 13 (13.7)     | 6 (18.7)       | 7 (11.1)          |         |
| Mechanical Ventilation, n (%)                 |               |                |                   |         |
| Yes                                           | 80 (97.5)     | 25 (96.1)      | 55 (98.2)         | 0.068   |
| No                                            | 2 (2.5)       | 1 (3.9)        | 1 (1.8)           |         |
| Use of at least one vasopressor, n (%)        |               |                |                   |         |
| Yes                                           | 70 (85.3)     | 22 (88.7)      | 48 (76.1)         | 0.324   |
| No                                            | 12 (14.7)     | 10 (31.3)      | 15 (26.8)         |         |
| SOFA score on ICU admission, Me [IQR]         | 8.00 [12.00-3.00] | 8.00 [11.7-4.00] | 8.00 [12.0-3.00] | 0.366   |
| APACHE score on ICU admission, Me [IQR]       | 16.00 [21.0-0 | 16.5 [22.0-9.00] | 16.0 [21.0-0]    | 0.374   |
| Patient’s final status, n (%)                 |               |                |                   |         |
| Alive                                         | 60 (63.1)     | 26 (81.3)      | 34 (53.9)         | 0.009*  |
| Deceased                                      | 35 (36.9)     | 6 (18.7)       | 29 (40.1)         |         |

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One of the strengths in our study is that even though there is data published regarding AKI in COVID-19 patients. This is the first study to not only include patients with AKI and confirmed or highly probably COVID-19, but also with intermittent or prolonged RRT with the GENIUS® 90 technology. Additionally, patients from several cities of Colombia were included, which labels it as a multicenter study for extrapolation of the results.

Its main limitation is that it’s a cross sectional study, which makes it impossible to appreciate the impact of our RRT through time. Furthermore, a small percentage of the patients included have a negative COVID-19 RT-PCR, but with high clinical suspicion and positive serology (probable cases). Finally, there was no information obtained in regards to urine output and the baseline creatinine, which did not allow the classification of AKI by severity.

Conclusion

Renal complications are frequent in patients with severe COVID-19 and its clinical presentation is variable, including hematuria, proteinuria and acute kidney injury requiring RRT. The development of AKI could be an isolated prognostic marker associated with an increase in mortality in patients with COVID-19, and one of the options is intermittent and prolonged RRT with the GENIUS® 90 system. The GENIUS® 90 technology is available in Colombia over 10 years ago and is operated by FM express program of Fresenius Medical Care Colombia, and through this study, we aimed to characterize Colombian patients with AKI by COVID-19 that received intermittent and prolonged RRT.

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