LETTER TO THE EDITOR

Clinical impact, reactogenicity and immunogenicity after the first CoronaVac dose in dialysis patients: a Phase IV prospective study

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CoronaVac (Sinovac Life Sciences, Beijing, China), an inactivated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine, has been approved for emergency use by 35 countries. A real-world Chilean study including 10.2 million persons showed prevention of symptomatic disease in 65.9% and severe coronavirus disease 2019 (COVID-19) in 87.5% [1]. In Brazil, CoronaVac has been included in the national vaccination program since 1 January 2021.

Among patients on chronic dialysis, the COVID-19 mortality risk was 21 times higher than that for matched historical controls [2]. Chronic kidney disease patients have been excluded from vaccine trials and had no early priority for vaccination. Therefore this single-center, Phase IV prospective 12-month follow-up study was devised to assess the clinical impact, reactogenicity and immunogenicity of CoronaVac.

Between 29 April 2021 and 8 May 2021, 198 patients ages 20–75 years were enrolled to receive a two-dose schedule of CoronaVac (3 μg each dose, 28 days apart). The study was approved by the local ethics committee and was registered at ClinicalTrials.gov (NCT04801667). All patients signed an informed consent form. On Day 28, a questionnaire was used to capture adverse reactions to the vaccine. Antibody response on Day 28 was assessed using the AdviseDx SARS-CoV-2 immunoglobulin G (IgG) II assay (Abbot Laboratories, Abbott Park, IL, USA). Values >50 AU/mL were considered positive.

The characteristics and outcomes of the study population (n = 198) are shown in Table 1. They were predominantly male, with a median age of 50 years [interquartile range (IQR) 40–56], diabetes mellitus in 21% and a median time on dialysis of 32 months (IQR 15–63).

The prevalence of anti-SARS-CoV-2 nucleocapsid protein on Day 0 was 27% (n = 54). For immunogenicity analysis, 137 patients who were seronegative for IgG anti-SARS-CoV-2 were included (56 had either positive IgG at Day 0 or a previous confirmed COVID-19 diagnosis and 5 had no serologic test available). Seroconversion 28 days after the first dose was 44% [95% confidence interval (CI) 36–53] with a median IgG value of 40 AU/mL (IQR 12–95) (Figure 1). Among those who were IgG positive, the median IgG value was 99 AU/mL (IQR 90–143). Patients >45 years of age and those on chronic-use prednisone 5 mg/day for failed renal allografts showed a lower seroconversion rate.

After the first vaccine dose, 4 (2%) patients had a COVID-19 diagnosis confirmed by reverse transcription polymerase chain reaction or antigen test at a median time of 14 days (IQR 11–15). Of these, two required hospitalization and one died 42 days after the first dose of the vaccine.

The most common adverse reaction after the first dose was local pain/tenderness (16%). Systemic symptoms (fever, myalgia, headache and diarrhea) occurred in ≤8% of the patients and no severe adverse reactions were observed.
Table 1. Baseline demographic characteristics, outcomes, adverse reactions and immunogenicity of the first dose of CoronaVac on dialysis patients

| Parameters                                                                 | Overall (N = 198) | Immunogenicity cohort (n = 137) | P-value | IgG-positive D28 (n = 60) | IgG-negative D28 (n = 77) | P-value |
|---------------------------------------------------------------------------|-------------------|---------------------------------|---------|---------------------------|---------------------------|---------|
| Demographic characteristics                                              |                   |                                 |         |                           |                           |         |
| Age (years), median (IQR), n (%)                                          | 50 (40–56)        | 48 (48–56)                      | 0.99    | 46 (56–56)                | 51 (43–57)                | 0.03    |
| 20–60                                                                     | 176 (89)          | 122 (89)                        | –       | 52 (87)                   | 70 (89)                   | –       |
| >60                                                                       | 22 (11)           | 15 (11)                         | –       | 8 (13)                    | 7 (8)                     | –       |
| Male gender, n (%)                                                        | 106 (54)          | 74 (54)                         | 0.93    | 32 (54)                   | 42 (55)                   | 0.88    |
| Dialysis method, n (%)                                                    | 0.23              |                                 | 0.40    |                           |                           |         |
| Haemodialysis                                                             | 127 (64)          | 79 (58)                         | –       | 37 (62)                   | 42 (65)                   | –       |
| Peritoneal dialysis                                                       | 71 (36)           | 58 (42)                         | –       | 23 (38)                   | 35 (45)                   | –       |
| Time on dialysis (months), median (IQR)                                   | 32 (15–63)        | 29 (13–58)                      | 0.36    | 29 (13–69)                | 28 (12–49)                | 0.58    |
| Chronic kidney disease aetiology, n (%)                                   |                   |                                 |         |                           |                           |         |
| Diabetes mellitus                                                         | 41 (21)           | 26 (19)                         | 0.96    | 10 (17)                   | 16 (21)                   | 0.58    |
| Hypertension                                                              | 24 (12)           | 17 (12)                         | –       | 9 (15)                    | 8 (10)                    | –       |
| Glomerulonephritis                                                        | 41 (21)           | 30 (22)                         | –       | 16 (27)                   | 14 (18)                   | –       |
| Polycystic kidney disease                                                 | 19 (10)           | 15 (11)                         | –       | 6 (10)                    | 9 (12)                    | –       |
| Unknown                                                                   | 54 (26)           | 33 (24)                         | –       | 11 (18)                   | 22 (29)                   | –       |
| Others                                                                    | 19 (10)           | 16 (12)                         | –       | 8 (13)                    | 8 (10)                    | –       |
| Diabetes mellitus                                                         | 51 (26)           | 34 (25)                         | 0.85    | 14 (23)                   | 20 (26)                   | 0.72    |
| Cardiovascular disease                                                     | 60 (30)           | 37 (27)                         | 0.51    | 19 (32)                   | 18 (23)                   | 0.28    |
| Previous transplant                                                       | 65 (33)           | 40 (29)                         | 0.48    | 13 (22)                   | 27 (85)                   | 0.08    |
| Use of prednisone                                                         | 36 (18)           | 24 (17)                         | 0.88    | 5 (8)                     | 19 (25)                   | 0.01    |
| Albumin (mg/dL), mean ± SD                                                | 3.99 ± 0.4        | 3.98 ± 0.42                     | 0.87    | 3.97 ± 0.46               | 3.98 ± 0.39               | 0.75    |
| Outcomes (N = 198)                                                        |                   |                                 |         |                           |                           |         |
| COVID-19 diagnosis after the first dose, n (%)                            | 4 (2)             | –                               | –       | –                         | –                         | –       |
| Age (years), median (IQR)                                                 | 51 (36–63)        | –                               | –       | –                         | –                         | –       |
| Time from first dose to COVID-19 (days), n (%)                            |                   |                                 |         |                           |                           |         |
| <7                                                                       | 0                 | –                               | –       | –                         | –                         | –       |
| 8–14                                                                     | 2 (50)            | –                               | –       | –                         | –                         | –       |
| >14                                                                      | 2 (50)            | –                               | –       | –                         | –                         | –       |
| Need for hospitalization                                                   | 2 (50)            | –                               | –       | –                         | –                         | –       |
| Need for intensive care                                                   | 2 (50)            | –                               | –       | –                         | –                         | –       |
| Death                                                                    | 1 (25)            | –                               | –       | –                         | –                         | –       |
| Adverse reactions to the vaccine, n (%)                                   |                   |                                 |         |                           |                           |         |
| Local pain or tenderness                                                  | 31 (16)           | –                               | –       | –                         | –                         | –       |
| Myalgia                                                                  | 15 (8)            | –                               | –       | –                         | –                         | –       |
| Headache                                                                 | 11 (6)            | –                               | –       | –                         | –                         | –       |
| Runny nose                                                                | 10 (5)            | –                               | –       | –                         | –                         | –       |
| Sore throat                                                               | 6 (3)             | –                               | –       | –                         | –                         | –       |
| Diarrhea                                                                  | 3 (2)             | –                               | –       | –                         | –                         | –       |
| Fever                                                                    | 2 (1)             | –                               | –       | –                         | –                         | –       |
| Serologic status before vaccination, n (%)                                 |                   |                                 |         |                           |                           |         |
| Negative                                                                 | 144 (73)          | 137                             | –       | –                         | –                         | –       |
In this ongoing prospective study, the first dose of CoronaVac vaccine was safe for dialysis patients, with a few mild adverse events. The seroconversion rate after the first dose was lower than that reported among healthcare workers receiving CoronaVac but was similar to that of other studies with dialysis patients and messenger RNA (mRNA) vaccines. Older age and the use of low-dose maintenance prednisone after a failed transplant were associated with a lower antibody response. These factors also impair the immunologic response to other vaccines, such as hepatitis B, in this population.

The small number of events and the short follow-up time prevent drawing any conclusions about the clinical effectiveness of the first dose of the vaccine.

In conclusion, our preliminary results are in agreement with previously published studies of mRNA vaccines, indicating a lower seroconversion rate among patients on renal replacement therapy. This reinforces the urgent need to maintain sanitary measures for individual protection and promote vaccination of household contacts and caregivers. Furthermore, it suggests that other immunization strategies, perhaps with higher or additional doses, or even the combination of vaccines developed using different platforms, deserve to be studied in this group of individuals.

**AUTHORS’ CONTRIBUTIONS**

J.M.P., M.P.C., C.M.T., H.T.S. and D.T.C. participated in the research design. J.M.P., M.P.C., C.M.T., A.L.A., S.R.M. and H.T.S. wrote the article. M.P.C., C.M.T. and H.T.S. participated in the data analysis.

**CONFLICT OF INTEREST STATEMENT**

The authors declare no conflicts of interest.
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DATA AVAILABILITY STATEMENT

Due to ethical concerns, supporting data can only be made available to bona fide researchers subject to a non-disclosure agreement.

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