**Letter to the Editor**

**Trends in COVID-19 Outcomes in Kidney Transplant Recipients During the Period of Omicron Variant Predominance**

Florentino Villanego, MD, PhD,\(^1\) Luis Alberto Vigara, MD, PhD,\(^1\) Marta Alonso, MD, PhD,\(^1\) Cristhian Orellana, MD, PhD,\(^1\) Ana María Gómez, MD, PhD,\(^1\) Myriam Eady, MD, PhD,\(^2\) María Gabriela Sánchez, MD, PhD,\(^3\) Rosa Gómez, MD, PhD,\(^4\) Teresa García, MD, PhD,\(^1\) and Auxiliadora Mazuecos, MD, PhD\(^1\)

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron variant has spread rapidly worldwide.\(^1\) In Spain, it became predominant as of December 2021. Greater transmissibility and less severity have been described in the general population.\(^2\) However, no data have been reported on kidney transplant (KT) patients during the Omicron-predominant period. In addition, KT recipients have received a third dose of the mRNA vaccine after its approval in Spain in September 2021.

We performed a multicenter retrospective cohort study to analyze coronavirus disease-19 outcomes among our KT population throughout 2 successive epidemic waves in a period with changes in the viral variants and in the vaccination schedule: Spanish fifth wave (June–November 2021; Delta predominance, \(n = 27\)) and sixth wave (December 2021–February 2022; Omicron predominance, \(n = 117\)).

The incidence of SARS-CoV-2 infection in our cohort of KT patients was 4.3-fold higher during the last sixth wave (Table 1). The percentage of vaccination was very high and similar in both periods, but as expected, more patients had received a third dose in the last wave (11.5% versus 93.8%; \(P < 0.001\)). Fortunately, clinical picture has changed with less presence of fever and prevailing upper respiratory tract symptoms. There is a trend to a lower pneumonia and hospitalization incidence but without statistical differences. Additionally, critical patients, defined by intensive care unit admissions (22.2% versus 2.6%; \(P < 0.001\)), need for ventilatory support (18.5% versus 2.6%; \(P = 0.001\)), and mortality (29.6% versus 4.2%; \(P < 0.001\)) have significantly reduced.Recipient age, fever, and infection during the fifth wave were risk factors for death.

SARS-CoV-2 Omicron variant presents 15 mutations in the spike protein, conferring greater affinity toward the angiotensin-converting enzyme 2 receptor, which could explain the increased transmission rate observed.\(^1\) In addition, vaccines are less effective, although a milder clinical picture is described in fully vaccinated people.\(^1\) We also observed that infection rate is high and severity is lower in KT recipients compared with previous periods.\(^3,4\) However, mortality is much higher than in the general population (mortality rate in Spain: 0.9%).\(^2\)

As previously reported, a significant number of KT patients do not develop a humoral immune response after vaccination, even receiving a third dose, which could explain these results.\(^5\)

Our study has some limitations. Despite most cases have been reported, some outpatients might not have informed to their transplant centers, and the number of cases could have been underestimated in both periods. Furthermore, there is some overlap between the 2 variants, because in the last period some patients certainly would have caught delta. On the other hand, although peak incidence has already been reached, the epidemic wave is not over yet. These data should be taken as a trend at this time of higher rate of infections.

In conclusion, the incidence of SARS-CoV-2 infection in KT has increased, coinciding with the appearance of the Omicron variant. Although widespread vaccination with third dose has probably been able to reduce the consequences associated with this contagious new variant, the severity and mortality are still higher than in the general population, highlighting the need for new therapeutic and preventive strategies.

**REFERENCES**

1. Araf Y, Akter F, Tang YD, et al. Omicron variant of SARS-CoV-2: Genomics, transmissibility, and responses to current COVID-19 vaccines. J Med Virol. 2022;94:1825–1832.

---

*Received 9 February 2022. Revision received 11 February 2022.*

*Accepted 15 February 2022.*

\(^1\) Department of Nephrology, Hospital Universitario Puerta del Mar, Cádiz, Spain.

\(^2\) Department of Nephrology, Hospital Universitario de Jerez, Jerez de la Frontera, Spain.

\(^3\) Department of Nephrology, Hospital Universitario de Puerto Real, Puerto Real, Spain.

\(^4\) Department of Nephrology, Hospital Punta de Europa, Algeciras, Spain.

F.V. and A.M. designed the study, analyzed the data, and drafted the article. All authors revised the article, made substantial contributions, and approved the final version of the article.

The authors declare no funding or conflicts of interest.

Correspondence: Auxiliadora Mazuecos, MD, PhD, Department of Nephrology, Hospital Universitario Puerta del Mar, Av. Ana de Viya, 21, 1009, Cádiz, Spain. (auxiliadora.mazuecos.sspa@juntadeandalucia.es).

Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0041-1337/20/1066-e304

DOI: 10.1097/TP.0000000000004126
TABLE 1.
Characteristics of all kidney transplant patients included in the study

|                                | June–November 2021 | December 2021–February 2022 | P     |
|--------------------------------|---------------------|-----------------------------|-------|
| KT infected/KT population, n (%) | 27/952 (2.8)        | 117/961 (12.1)              | <0.001|
| Males, n (%)                   | 17 (63)             | 73 (62.4)                   | 0.95  |
| Recipient age, median [IQR], y  | 57 [47–65]          | 58 [47–67]                  | 0.56  |
| Time post-KT to COVID-19, median [IQR], mo | 88 [44–123]      | 83 [30–184]                 | 0.95  |
| Vaccination, n (%)             | 26 (96.3)           | 112 (96.6)                  | 0.94  |
| Two doses of vaccine, n (%)    | 23 (88.5)           | 7 (6.2)                     | <0.001|
| Three doses of vaccine, n (%)  | 3 (11.5)            | 105 (93.8)                  | <0.001|
| Type of third dose of vaccine  |                     |                             |       |
| mRNA-1273 Moderna, n (%)       | 3 (100)             | 74 (70.5)                   | 0.15  |
| BNT162b2 Pfizer-BioNTech, n (%)| 0                   | 30 (29.4)                   | 0.15  |

Immunosuppressive therapy at COVID-19 diagnosis

|                                | June–November 2021 | December 2021–February 2022 | P     |
|--------------------------------|---------------------|-----------------------------|-------|
| Prednisone, n (%)              | 25 (92.6)           | 110 (94)                    | 0.78  |
| Tacrolimus, n (%)              | 25 (92.6)           | 108 (92.3)                  | 0.96  |
| Mycophenolate, n (%)           | 22 (81.5)           | 95 (81.2)                   | 0.97  |
| mTOR inhibitors, n (%)         | 4 (14.8)            | 12 (10.3)                   | 0.49  |
| Cyclosporine, n (%)            | 1 (3.7)             | 7 (6)                       | 0.64  |

Immunosuppressive therapy within 2 y pre-COVID-19 diagnosis

|                                | June–November 2021 | December 2021–February 2022 | P     |
|--------------------------------|---------------------|-----------------------------|-------|
| Thymoglobulin, n (%)           | 4 (14.8)            | 11 (9.4)                    | 0.41  |
| Basiliximab, n (%)             | 1 (3.7)             | 6 (5.2)                     | 0.75  |
| Rituximab, n (%)               | 0                   | 1 (0.7)                     | 0.62  |

Clinical features

|                                | June–November 2021 | December 2021–February 2022 | P     |
|--------------------------------|---------------------|-----------------------------|-------|
| Asymptomatic, n (%)            | 3 (11.1)            | 26 (22.2)                   | 0.19  |
| Fever, n (%)                   | 15 (55.6)           | 43 (36.8)                   | 0.07  |
| Upper respiratory tract symptoms, n (%) | 16 (59.3)      | 85 (72.6)                   | 0.17  |
| Gastrointestinal symptoms, n (%) | 8 (29.6)           | 8 (6.8)                     | 0.001 |
| Pneumonia, n (%)               | 8 (29.6)            | 19 (16.2)                   | 0.11  |

COVID-19 management

|                                | June–November 2021 | December 2021–February 2022 | P     |
|--------------------------------|---------------------|-----------------------------|-------|
| Hospitalized, n (%)            | 10 (37)             | 25 (21.4)                   | 0.08  |
| Ventilator support, n (%)      | 5 (18.5)            | 3 (2.6)                     | 0.001 |
| ICU admission, n (%)           | 6 (22.2)            | 3 (2.6)                     | <0.001|
| ICU admissions in hospitalized patients, n (%) | 6 (60)          | 3 (12)                      | 0.02  |

COVID-19 outcomes

|                                | June–November 2021 | December 2021–February 2022 | P     |
|--------------------------------|---------------------|-----------------------------|-------|
| Dead, n (%)                    | 8 (29.6)            | 4 (3.3)                     | <0.001|
| Dead in hospitalized patients, n (%) | 6 (60)           | 4 (16)                      | 0.01  |

Multiple logistic regression analysis for COVID-19-related death

|                                | OR (95% CI) | P     |
|--------------------------------|-------------|-------|
| Males                          | 0.77 (0.16-3.69) | 0.747 |
| Recipient age                  | 1.13 (1.03-1.24) | 0.008 |
| Time from KT to COVID-19       | 0.99 (0.99-1.01) | 0.783 |
| Fever                          | 14.39 (2.22-93.20) | 0.005 |
| Fifth wave                     | 12.97 (2.33-72.12) | 0.003 |

Comparison between those infected in June to November 2021 and December 2021 to February 2022.

CI, confidence interval; COVID-19, coronavirus disease 2019; ICU, intensive care unit; IQR, interquartile range; KT, kidney transplantation; mRNA, messenger RNA; mTOR, mammalian target of rapamycin; OR, odds ratio.

2. Government of Spain Ministry of Health. Actualización nº 557. Enfermedad por el coronavirus (COVID-19). February 04, 2022. Available at https://www.sanidad.gob.es/profesionales/saludPublica/ccayes/alertasActual/nCov/documentos/Actualizacion_557_COVID-19.pdf. Accessed February 6, 2022.

3. Crespo M, Mazuecos A, Rodrigo E, et al; Spanish Society of Nephrology COVID-19 Group. Respiratory and gastrointestinal COVID-19 phenotypes in kidney transplant recipients. Transplantation. 2020;104:2225–2233.

4. Callaghan CJ, Mumford L, Curtis RMK, et al; NHSBT Organ and Tissue Donation and Transplantation Clinical Team. Real-world effectiveness of the Pfizer-BioNTech BNT162b2 and Oxford-AstraZeneca ChAdOx1-S vaccines against SARS-CoV-2 in solid organ and islet transplant recipients. Transplantation. 2022;106:436–446.

5. Stumpf J, Tonnus W, Paliege A, et al. Cellular and humoral immune responses after 3 doses of BNT162b2 mRNA SARS-CoV-2 vaccine in kidney transplant. Transplantation. 2021;105:e267–e269.