



SARS-CoV-2 Infection Evolution Among Nephrologists During the Pandemic: Clinical Features and Impact of Vaccination

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E xposure of health care workers (HCWs) to SARS-CoV-2 has resulted in high rates of COVID-19.¹ Nephrologists have been at the front line as patients on kidney replacement therapy present more severe COVID-19 and need continuous medical assistance.¹ Vaccination decreases rates and severity of COVID-19.² However, real-world evidence of booster vaccine dose acceptance, safety, and impact on further infections among nephrologists is not available.

This national survey (Supplementary Methods) evaluated the impact of the SARS-CoV-2 pandemic in Spanish nephrologists across the different waves and the effectivity of initial and booster vaccine doses on breakthrough COVID-19. In Spain, vaccination was not mandatory for HCWs.

Among 348 nephrologists (66% female, 45 \pm 12 years) completed the online who survey (Supplementary Table S1), comorbidities were uncommon (8% hypertension, 2% diabetes mellitus, 15% dyslipidemia, <1% chronic kidney disease or albuminuria). Exposure to patients with COVID-19 was very frequent (median of 24 [22-24] months with at least 1 case during the period), and 74% of the nephrologists worked in COVID-19 units. There were 12 nephrologists (3%) who had not completed the initial vaccination schedule and 33 (9%) who had not received a booster dose (Supplementary Table S1).

SARS-CoV-2 infections and reinfections were registered mainly in the sixth wave (Supplementary Figure S1). Across the different waves, some features such as symptoms and prescribed treatments significantly varied (Supplementary Table S2). Importantly, only a low percentage of nephrologists reported access to appropriate personal protective equipment during the first wave (P < 0.001). The source of contagion differed across waves, changing from predominantly professional to social (P < 0.001) (Supplementary Table S2).

Overall, 146 nephrologists (42%) developed at least 1 SARS-CoV-2 infection (Supplementary Table S1). Regarding clinical presentation, 18 (12%) were asymptomatic, 80 (55%) had cough, 71 (49%) fever, 69 (47%) myalgia, 69 (47%) asthenia, and 63 (43%) rhinorrhea. There were 9 nephrologists (6%) who developed infiltrates in chest X-ray, and 5 (3%) required admission. Infected nephrologists were younger (P <0.001), more frequently fellows or consultants (P =0.029), in night shifts (P = 0.004), assigned to COVID-19 units (P < 0.001), incompletely vaccinated (P =0.005), or missing a booster dose (P < 0.001)(Supplementary Table S1). Furthermore, 20 nephrologists (14%) suffered a reinfection. The only factor associated to reinfection was an incomplete initial vaccination schedule (5% not reinfected nephrologists had an incomplete initial vaccination schedule vs. 20% of reinfected nephrologists, P = 0.032).

The impact of vaccination was assessed after November 1, 2021, when booster vaccination was available for HCWs. To assess the impact of the booster dose, we excluded nephrologists who had an incomplete initial vaccination and those with prior COVID-19. New-onset COVID-19 was more common among the 13 nephrologists missing a booster dose (11, 84%) than among the 225 nephrologists who received a booster dose (40, 17%). No demographic or clinical differences were detected between nephrologists receiving and not receiving a booster dose (Supplementary Table S3). Factors associated to infection after a booster dose in univariate analysis were younger age (P < 0.001), night shifts (P = 0.007), working in COVID-19 units (P = 0.008), and missing a booster dose (P < 0.001) (Supplementary Table S4). A multivariate model using Cox regression adjusted for age, night shift, and working in COVID-19 units revealed that missing a booster dose (hazard ratio, 5.027, 95% CI [2.56–9.87], P < 0.001) was an independent predictor for new-onset COVID-19 (Table 1). Kaplan–Meier plot reveals a significant association between missing a booster dose and COVID-19 during follow-up (median 351 [341-362] days) (log-rank 28.0, P < 0.001) (Figure 1).

The key finding of the present real-world study is the effectivity of a booster dose of SARS-CoV-2 vaccine to prevent further infections among nephrologists who had received a full initial vaccination schedule and did not have a prior SARS-CoV-2 infection.

COVID-19 is common among HCWs, and mitigating COVID-19 is key to preserve the health of HCWs and a well-functioning health care system during pandemic waves.³ Telemedicine has been used to avoid social contact and protect both HCWs and patients.³ We did not observe an impact of telemedicine on breakthrough infections among nephrologists. However, the uptake of telemedicine was low (31% at any time). This suboptimal use of telemedicine may be related to the usual work environment of nephrologists, a mainly hospitalbased specialty with necessary contact with in-center dialysis patients and with frequent night shifts.⁴ A high direct exposure to SARS-CoV-2-infected patients likely contributed to infection of nephrologists. The total exposure time was very high; close to 100% of the months (median 24 of 24 months). Moreover, working on COVID-19 units and not being a head of service were associated to COVID-19. In this regard, protective equipment arrived late to HCWs in Spain. In-hospital

 Table 1. Multivariate Cox regression for predictors of SARS-CoV-2

 infection after booster dose approval in nephrologists in Spain

Variables	HR (95% CI)	Р
Age (yr)	0.97 (0.95-1.00)	0.051
Night shifts (yes)	2.15 (0.80-5.79)	0.128
Work in COVID-19 units (yes)	1.77 (0.72–4.43)	0.210
Booster dose (no)	5.24 (2.64–10.3)	<0.001

HR, hazard ratio.

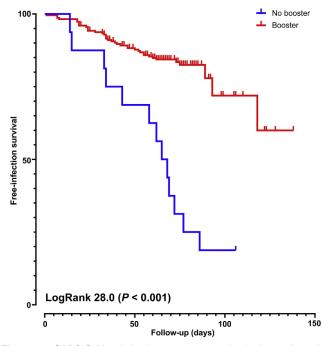


Figure 1. SARS-CoV-2 infection among nephrologists after the availability of the booster dose. The analysis included 238 nephrologists who were initially vaccinated and had not presented any previous SARS-CoV-2 infection at the time of booster approval.

protective measures were considered suboptimal in the first wave by 87% of nephrologists. This first wave collapsed the health care system in Madrid and required a full lockdown with the population forced to remain at home. Therefore, nephrologists were infected mainly in the professional environment. The availability of appropriate protective equipment in hospitals, the high incidence of COVID-19 in the population, especially during the sixth epidemic wave, and the relaxation of social distancing measures in the following waves changed the origin of SARS-CoV-2 contagion to mostly a social context.

Uptake of SARS-CoV-2 vaccines and booster doses was high among nephrologists, similar to the Spanish population. Despite these measures, the number of infected nephrologists peaked during the sixth wave (December 2021 to January 2022), after booster vaccination was offered, but driven by the Omicron variant that had higher rates of escape from vaccines or natural immunity after infection.⁵ However, booster doses and natural immunity seem to enhance neutralization capacity against all known SARS-CoV-2 variants.⁶ Our study reveals that among Spanish nephrologists not previously infected with SARS-CoV-2, booster vaccine doses decreased the risk of SARS-CoV-2 infection 5-fold versus nonboostered subjects. There is controversy regarding booster dosing in persons with prior COVID-19. Indeed, immunity derived from infection and a 2dose vaccine schedule may be stronger than from 3 doses.⁷ However, we could not address this issue.

Although previous data had revealed a protective effect of booster doses against COVID-19 in HCWs, our study is the first to include new variants, such as Omicron.⁸ Our data support that booster dosing also reduced infections among working age, for the most part healthy and young HCWs in the sixth Spanish wave that corresponds to the Omicron era, thus contributing to the health care system resilience during the pandemic waves.

Among limitations, this is a survey-based study and participation was voluntary, which could have led to bias, and some data may be missing. Second, we lack data on humoral and cellular immunities. However, most participants were working and healthy, so an immune response would be expected after vaccination. Third, we do not have information about the reasons for not being vaccinated. Spanish nephrologists selfreported reasons for not being vaccinated include lack of appointment, pregnancy, contraindication, or previous COVID-19.⁹ Finally, some questions were subjective, such as the appropriate personal protective equipment or the contagion source.

In conclusion, after completing an initial SARS-CoV-2 vaccination, receiving a booster dose could help to prevent further infections in the Omicron era among nephrologists not previously infected by SARS-CoV-2. These results should encourage HCWs to be vaccinated and receive a booster dose even if they are healthy, as the long-term effects of COVID-19 are still poorly characterized and preventing infections among HCW minimizes the disruption to the health care system during pandemic waves.

APPENDIX

List of Members of the Spanish Society of Nephrology Council

The Spanish Society of Nephrology Council includes Patricia de Sequera, Gabriel de Arriba, Borja Quiroga, Miquel Blasco, Gema Fernández Fresnedo, Marian Goicoechea, Sagrario Soriano, Emilio Sánchez-Álvarez, Francisco Javier Pérez Contreras, Auxiliadora Mazuecos, Marian Goicoechea, Manuel Gorostidi, María José Soler, and Mariano Rodríguez Portillo.

DISCLOSURE

BQ has received honoraria for conferences, consulting fees, and advisory boards from Vifor-Pharma, Astellas, Amgen, Bial, Ferrer, Novartis, AstraZeneca, Sandoz, Laboratorios Bial, Esteve, Sanofi-Genzyme, and Otsuka. AO has received consultancy or speaker fees or travel support from Astellas, AstraZeneca, Amicus, Amgen, Fresenius Medical Care, Bayer, Sanofi-Genzyme, Menarini, Kyowa Kirin, Alexion, Otsuka, and Vifor Fresenius Medical Care Renal Pharma and is Director of the Catedra Mundipharma–UAM of diabetic kidney disease and the Catedra AstraZeneca–UAM of chronic kidney disease and electrolytes. MG has received honoraria for conferences, consulting fees, and advisory boards from Vifor-Pharma, Novo Nordisk, Medtronic, Sanofi, Otsuka, AstraZeneca, and GlaxoSmithKline. ESÁ has received honoraria for conferences, consulting fees, and advisory boards from AstraZeneca, Vifor, Astellas, Novo Nordisk, and Baxter. PdS reports receiving honorarium for conferences, consulting fees, and advisory boards from Amgen, Astellas, AstraZeneca, Baxter, Braun, Fresenius, Nipro, and Vifor-Pharma and is the present president of the Spanish Society of Nephrology.

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AUTHOR CONTRIBUTIONS

BQ: conception and design, acquisition of data, analysis and interpretation of data, and drafting the manuscript. AO: conception and design, interpretation of data, and revision of the manuscript. ESA: conception and design, acquisition of data, and revision of the manuscript. MG: conception and design, acquisition of data, and revision of the manuscript. PS: conception and design, interpretation of data, and revision of the manuscript.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Supplementary Methods.

Figure S1. Evolution of SARS-CoV-2 infection and vaccination across the different pandemic waves. This analysis includes 302 subjects with registered SARS-CoV-2 infection date and vaccination date. In 34 subjects, initial vaccination date was missing. In 21 subjects, booster dose date was missing.

 Table S1. Baseline characteristics of SARS-CoV-2 infected and noninfected nephrologists.

Table S2. Clinical features of infected nephrologists with SARS-CoV-2 across the different pandemic waves. This table includes 140 participants with recorded infection date.

Table S3. Differences between nephrologists with or without a booster vaccine dose. This analysis includes only those nephrologists free of prior infection that completed the initial vaccination schedule.

Table S4. Univariate analysis for factors associated to SARS-CoV-2 infection in vaccinated nephrologists. This analysis includes nephrologists without prior SARS-CoV-2 infection that were initially vaccinated.

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