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Immunogenicity of BNT162b2 SARS-CoV-2 Vaccine in a Multicenter Cohort of Nursing Home Residents Receiving Maintenance Hemodialysis

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To the Editor:

We recently reported that almost all maintenance hemodialysis (HD) patients mount specific antibodies within a month after COVID-19 onset (1). However, evidence concerning the immunogenicity of SARS-CoV-2 vaccines in this immuno-deficient population is scarce (2).

We prospectively assessed the response to the BNT162b2 spike mRNA vaccine in a multicenter cohort of maintenance HD patients living in nursing homes and compared their antibody response with that observed in a group of non-dialyzed nursing home residents.

Following the approval by the European Medicines Agency of mRNA vaccines developed by BioNTech-Pfizer and Moderna, nursing home residents were prioritized for vaccination by Belgian health authorities. We included all nursing home residents on in-center HD at five hospitals from the UCLouvain network. A cohort of non-dialyzed nursing home residents, matched for COVID-19 history, served as controls. All participants received two doses of BNT162b2 spike mRNA vaccine, 21 days apart. Serum samples were taken on Day 28 after the first dose, i.e. at the time of the peak of neutralizing antibodies in Phase 1 trials (3), and also on Days 49 and 77, the latter only in HD patients. Comorbidities listed by the CDC (Atlanta, Georgia) as risk factors for severe COVID-19, were recorded (4).

Serum samples were tested with two electro-chemiluminescent immunoassays: an anti-SARS-CoV-2 qualitative immunoassay using a recombinant nucleocapsid antigen (anti-SARS-CoV-2 N) (Roche Elecsys), and an anti-SARS-CoV-2 S quantitative immunoassay testing for antibodies against the spike protein receptor-binding domain (anti-SARS-CoV-2 RBD) (Roche Elecsys). Both tests have a very high sensitivity and specificity, and the anti-RBD immunoassay correlates well with neutralization tests (Supplementary Material).

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Groups were compared using Mann-Whitney, Kruskal-Wallis or chi-square tests, as appropriate. Statistical analyses were performed using Stata (v16) and GraphPad Prism (v8). All tests were two-tailed and a P-value <0.05 was considered significant.

Thirty-four HD patients and 45 controls were included. SARS-CoV-2 infection was previously diagnosed in 10 HD patients (by qPCR on a nasopharyngeal swab) and 12 controls (by periodic serologic testing), (p=0.8). Controls were significantly older and had fewer comorbidities than HD patients (Table 1). Anti-SARS-CoV-2 N antibodies were detected in all but three HD patients with prior COVID-19, two of whom first tested positive by qPCR on the day of the first vaccine dose. All HD patients and controls without known prior COVID-19 were seronegative for anti-SARS-CoV-2 N antibodies.

On Day 28, the proportion of subjects without history of COVID-19 who developed anti-spike RBD antibodies was similar in HD patients (19/24, 79%) and controls (28/33, 85%), (p=0.6). All controls and HD patients with prior COVID-19 mounted an anti-RBD response, except one HD patient who first tested positive by qPCR on the day of first vaccination. Anti-RBD levels were similar in HD patients and controls, both in groups with and without prior COVID-19 (Table 2). The humoral response in HD patients was sustained until Day 77. Responders to the vaccine did not differ from non-responders concerning demographics and comorbidities (Table 1, Supplementary Material), except for the presence of anti-N antibodies (more prevalent in responders, p=0.04) and liver disease (more prevalent in non-responders, p=0.007). By June 1st, 2021, no case of severe COVID-19 was observed neither in HD patients nor in controls.

Around 80% of the included nursing home residents on maintenance HD mount anti-spike antibodies one week after the second BNT162b2 mRNA vaccine dose, despite advanced age and multiple comorbidities. Moreover the humoral response was sustained until Day 77 after the first

dose. Nevertheless, although this did not reach statistical significance (likely due to the small sample size), anti-RBD level on Day 28 was much lower in HD patients than in controls without COVID-19 history (25 and 199, respectively). Yet, no severe COVID-19 was observed among HD patients by June 1st, 2021, however their lower peak antibody titers may be associated with a shorter duration of clinical efficacy, as observed with other vaccines (5). Grupper et al. recently documented a humoral response in 54/56 (96%) vaccinated HD patients (6). However, their patients were younger (mean age 74), were not tested for serologic evidence of prior COVID-19 and the level of anti-RBD antibodies was measured one month after the second vaccine dose, all three factors potentially complicating the comparison with our results (3,7). In a recent nationwide mass-vaccination study, the clinical effectiveness of the BioNTech-Pfizer vaccine was similar across age groups (with >70,000 subjects aged >70 years) (8).

Our results demonstrate the immunogenicity of the vaccine in elderly patients under maintenance HD, with extensive comorbidities. Since the immunogenicity of other vaccines and duration of specific immunity is lower in HD patients than in the general population (5), serological follow-up may help determine optimal immunization schedules.

As recently documented in the general population (7), anti-RBD levels are 10-fold higher in vaccinated HD patients with preexisting than in those without COVID-19. Moreover 8 out of 10 seropositive HD patients elicited rapid and maximal immune responses, with anti-spike levels higher than the upper level of measurement (>250U/mL), even 7-13 days after the first dose in two of them.

A definite strength of this study is its multicentric design. Clear limitations are the small sample size, and the focus on a specific population of frail and very ill patients.

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In conclusion, around 80% of nursing home residents on maintenance HD develop anti-spike antibodies one week after the second dose of the BNT162b2 mRNA COVID-19 vaccine, and this response is sustained over two months after the second dose. Follow-up studies are needed to assess the durability of the vaccine response in this high-risk population.

Supplementary Material
Supplementary File (PDF)
Item S1; Table S1.

Supplementary Material Descriptive Text for Online Delivery
Supplementary File (PDF). Item S1; Table S1.

Article Information

Authors' Contributions: Research area and study design: LL, AS, BK,MJ; data acquisition: LL, AS, EVR, AR, GC, GG, JMP, PB, MDS; data analysis and interpretation: LL, AS, JM, MJ; statistical analysis: JM; supervision or mentorship: MJ, JCY, BK, HRV. LL and AS contributed equally to this work. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

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Table 1. Baseline characteristics.

	Controls n=45	Hemodialysis n=34	P-value
Age, median (IQR), years	88 (85-90)	81 (74-87)	<0.001
Female gender – no. (%)	29 (64)	19 (56)	0.44
Hypertension – no. (%)	23 (51)	25 (74)	0.04
Diabetes – no. (%)	2 (4)	14 (41)	<0.001
Obesity – no. (%)	4 (9)	6 (18)	0.25
Cardiovascular disease – no. (%)	10 (22)	14 (41)	0.07
Stroke – no. (%)	2 (4)	10 (29)	0.002
COPD or asthma – no. (%)	4 (9)	5 (15)	0.42
Liver disease – no. (%)	0 (0)	3 (9)	0.04
Dementia – no. (%)	0 (0)	6 (18)	0.003
History of cancer – no. (%)	7 (16)	4 (12)	0.63
Active cancer – no. (%)	2 (4)	4 (12)	0.22
Immunosuppressive therapy – no. (%)	4 (9)	0 (0)	0.07
HIV infection – no. (%)	2 (4)	0 (0)	0.21
History of COVID-19 – no. (%)	12 (27)	10 (29)	0.79

COPD, chronic obstructive pulmonary disease; HIV, human immunodeficiency virus.

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Table 2. Immune response to SARS-CoV-2 vaccination among hemodialysis and control individuals.

	Comparison between groups on day 28 after first dose			Longitudinal follow-up in hemodialysis patients		
No history of COVID-19	**Controls n=33**	**Hemodialysis n=24**	**P-value**	**Day 28 n=24**	**Day 49 n=24**	**Day 77 n=22**
Presence of anti-N Ab, no. (%)	0 (0)	0 (0)	-	0 (0)	0 (0)	0 (0)
Presence of anti-RBD Ab, no. (%)	28 (85)	19 (79)	0.6	19 (79)	21 (88)	20 (91)
Anti-RBD Ab, median (IQR), U/ml	199 (9-250)	25 (5-250)	0.4	25 (5-250)	190 (33-250)	118 (26-250)
History of COVID-19	**Controls n=12**	**Hemodialysis n=10***	**P-value**	**Day 28 n=10**	**Day 49 n=10**	**Day 77 n=10**
Presence of anti-N Ab, no. (%)	12 (100)	7 (70)*	0.04	7 (70)	9 (90)	9 (90)
Anti-N Ab, median (IQR)	94 (34-158)	25 (1-56)	0.8	25 (1-56)	50 (13-64)	44 (31-59)
Presence of anti-RBD Ab, no. (%)	12 (100)	9 (90)	0.3	9 (90)	10 (100)	10 (100)
Anti-RBD Ab, median (IQR), U/ml	250 (250-250)	250 (250-250)	0.6	250 (250-250)	250 (250-250)	250 (250-250)

*****Including the two HD patients who tested positive by qPCR on a nasopharyngeal swab on the day of the first vaccine dose.

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