Factors predictive of anti-spike antibody titers after COVID-19 vaccination in hemodialysis patients

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Abstract

Background. Hemodialysis (HD) patients have a high prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and mortality, but they may have a weak response to coronavirus disease 2019 (COVID-19) vaccines.

Objectives. This study aimed to evaluate factors predictive of humoral response in HD patients vaccinated against SARS-CoV-2 infection.

Materials and methods. This is a 2-center observational study including HD patients who received the BNT162b2 mRNA vaccine followed by serological measurements 20 days and 4 weeks after the 1st and 2nd dose, respectively. Healthy controls were included. Anti-spike antibody was measured using the chemiluminescent immunoassay (CLIA) method. The quantile regression analysis was performed to assess factors associated with anti-spike antibody titers.

Results. Seventy-two HD patients and 22 healthy controls were included. Mean age of dialysis patients and controls was 72.5 \pm 11.5 years and 45.7 \pm 17.4 years, respectively. In the HD group, median levels of anti-spike antibody were 3 (interquartile range (IQR): 0.5–26) UI/mL and 391 (IQR: 55–1642) UI/mL after the 1st and 2nd dose, respectively, with response rates of 62.5% and 96.7%. The median level of the anti-spike antibody after the 1st dose in previously infected patients was 8571 (IQR: 2586—19147) UI/mL. There was a significant correlation between anti-spike antibody levels after the 2nd dose and age and anti-hepatitis B surface (HBs) antibody and serum albumin levels (Spearman's rho: r = -0.289, p < 0.001; r = 0.357, p = 0.027; r = 0.317; p = 0.026, respectively). The regression analysis showed a significant association of previous infection and anti-Hbs antibody level with anti-spike antibody level after the 1st dose of vaccine (p < 0.001). After a 5-month follow-up, 2 vaccinated patients contracted COVID-19.

Conclusions. This study showed a response rate of 96.7% to 2 doses of BNT162b2 mRNA vaccine in HD patients and 100% to a single dose in previously infected patients. The level of anti-spike antibody can be predicted by age, anti-Hbs antibodies, serum albumin, and previous infection. Despite the immunization of patients, preventive measures should be maintained in all dialysis units.

Key words: SARS-CoV-2, COVID-19 vaccine, hemodialysis, anti-spike antibody, hepatitis B vaccine

Background

Globally, vulnerable populations were severely afflicted by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic. Hemodialysis (HD) patients emerged as one of the high-risk groups for coronavirus disease 2019 (COVID-19). Once infected, their mortality rate reached 20–25% in several national and global reports. This led nephrology societies across the globe to call for effective preventive measures in these patients as well as to put them on priority lists for vaccination against COVID-19. 4–7

Despite the urgent need to vaccinate HD patients, this comorbid population is known to have low immunity and poor response to vaccines. Since decades, the best practice in HD patients has required administering vaccines against hepatitis B and pneumococcal infection. However, several studies revealed the weak immunization rates. the decline in the antibodies with time and consequently, a lack of chronic protection against the aforementioned diseases.^{8,9} In relation to COVID-19 vaccines, several recent studies showed a diminished humoral response intensity to 2 doses of the COVID-19 BNT162b2 (Pfizer-BioNTech) mRNA vaccine compared to healthy controls. 10-13 Despite the low levels of antibody titers, the rate of seropositivity seemed to vary between different reports. 14 Moreover, previously infected patients were found to mount their antibodies very early after the 1st dose. 10,15,16 Therefore, some patients might need 3 doses and others 1 dose only. On another note, the results have been contradictory regarding the correlation between the humoral response to COVID-19 vaccine and previous response to hepatitis B vaccine. 12,17

Objectives

This study aims to elucidate the factors affecting the humoral response of HD patients after the COVID-19 mRNA vaccine.

Materials and methods

Study setting

The vaccination campaign against COVID-19 started in Lebanon on February 14, 2021, with a prioritization of healthcare workers and elderly above 75 years of age. Hemodialysis patients received the BNT162b2 mRNA vaccine progressively, based on their age category (category 1A: ≥75 years, category 1B: 55–74 years; patients aged 16–54 years were vaccinated as the last category among HD patients). It took 5 months to cover the vaccination of all HD patients in the country.

The study included all chronic HD patients who received the vaccine and were tested for anti-spike antibody after

vaccination. Nephrologists who participated in the previous national study on COVID-19 prevalence in HD were contacted to include their patients.³ Only 5 nephrologists from 2 units performed serological testing in their patients following vaccination. The HD patients of these 2 units, Saint-George Ajaltoun and Bhannes hospitals, Lebanon, were finally included. These 2 units provided dialysis treatment for 123 patients before their first COVID-19 cases. Among these patients, 33 contracted COVID-19, 12 died from this disease and 9 from other causes. Not all infected patients received the vaccine. Until the end of July 2021, 82 patients received 2 doses of vaccine and 72 patients had the anti-spike antibody level measured.

Healthcare workers, some family members of patients and staff who were vaccinated and serologically tested were included as healthy controls.

Study design and participants

This is a retrospective study that collected data of HD patients who were administered the 1st dose of COVID-19 vaccine between February 15, 2021 and July 31, 2021. All HD patients in Lebanon who were tested for anti-spike protein antibody 20 days after their 1st dose and 4 weeks after their 2nd dose of vaccine were included.

The study got the approval of the ethics committee of Hotel-Dieu de France-affiliated to Saint-Joseph University, Beirut, Lebanon (approval No. CEHDF 1829) and was conducted in agreement with the Declaration of Helsinki of 1975.

Data collection

The outcome variable recorded for each patient was the level of anti-spike antibody after the 1st and 2nd dose of COVID-19 vaccine. Other variables collected were: age, sex, current smoking status, dialysis vintage, frequency of dialysis, number of weeks between the 2 doses of vaccine, comorbidities such as diabetes, hypertension, coronary artery disease (CAD), heart failure, cancer, and whether on immunosuppressive therapy or not. We also collected the hepatitis B vaccination status parameters for each patient: if fully vaccinated (yes/no), if immunized (yes/no) (defined as anti-hepatitis B surface (HBs) antibody levels above 10 UI/mL) and the last measured level of anti-Hbs antibody. Symptoms or side effects after vaccination were retrieved from medical charts: fever, myalgia, painful arm, headache, and other symptoms. Laboratory parameters included serum albumin level before vaccination and platelet count 1 month after the 2nd dose.

Anti-spike antibody measurement

The humoral response was evaluated using Elecsys Anti-SARS-CoV-2 S on the cobas e 411 analyzer (Roche Diagnostics, Basel, Switzerland). Elecsys Anti-SARS-CoV-2 S

is an electrochemiluminescence immunoassay (CLIA) intended for detection of antibodies against the receptor binding domain (RBD) of the spike (S) protein in human serum and plasma. The anti-SARS-CoV-2 S detected are mainly immunoglobulin G (IgG), in addition to immunoglobulin A (IgA) and immunoglobulin M (IgM). The Elecsys Anti-SARS-CoV-2 S assay uses a recombinant protein portraying the RBD of the spike antigen in a double-antigen sandwich assay format. Biotinylated SARS-CoV-2 S-RBD-specific recombinant antigen and SARS-CoV-2 S-RBD-specific recombinant antigen labeled with a ruthenium complex are first incubated to form a sandwich complex. During the 2nd incubation, the complex becomes bound to the solid phase via interaction of biotin and streptavidin, after addition of streptavidin-coated microparticles. The reaction mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. Then, application of a voltage to the electrode induces chemiluminescent emission which is measured with a photomultiplier. The results are determined via a calibration curve which is generated by a 2-point calibration and a master curve provided via the reagent barcode or e-barcode. The total duration of the assay is 18 min. When titers were above 250 UI/mL, dilution was performed up to 1/100. A cutoff of 0.8 UI/mL was used for interpretation. The sensitivity of the test is considered to be 89%, 98% and 100% after 14-20 days, 21-27 days and beyond 28 days, respectively. The specificity is almost 100%.

Statistical analyses

Continuous variables were presented as mean \pm standard deviation (SD) if normally distributed, and as median and interquartile range (IQR) if data were skewed; categorical variables were presented as numbers and percentages.

The t independent sample test was used to compare continuous variables that were normally distributed. The Mann–Whitney test was used to compare skewed data. A quantile regression analysis using the median (50^{th}) was performed to assess factors associated with anti-spike antibody levels after the 1^{st} vaccine dose, including all variables that had a p-value less than 0.2 in the univariate analysis. Spearman's rho correlation was used to estimate the association between anti-spike antibody levels after the 2^{nd} dose and serum albumin anti-Hbs antibody levels and other continuous variables. The statistical analysis was performed with IBM SPSS for Windows v. 26 (IBM Corp., Armonk, USA). A p-value ≤ 0.05 was considered statistically significant.

Results

Characteristics of HD patients

A total of 72 HD patients were included. Table 1 summarizes their characteristics. The mean age of patients

was 72.5 ± 11.5 years and 34.7% of them were females. Among the 60 infection-naïve patients, 2 patients did not get their 2^{nd} dose of vaccine, 1 died and 1 was admitted to the hospital for hip fracture. Among the 12 previously infected patients, only 4 received the 2^{nd} dose of vaccine.

The interval between the 1st dose and 2nd dose was 3 weeks in the eldest patients (those who were administered the vaccine in priority) and it was prolonged to 4–5 weeks in younger patients (based on the decision of the Ministry of Public Health). A total of 34 patients were 75 years old or older, and they completed their vaccination by the end of March 2021.

Two out of the 72 HD patients contracted COVID-19 during the follow-up period that ranged between 1 and 5 months. One of them, a 88-year-old male, who had negative anti-spike antibody titers after 2 doses of vaccine, was diagnosed with COVID-19 4 months after he completed his vaccination. He needed admission to the hospital for cough, dyspnea and oxygen therapy, and recovered after 5 days. Another patient, a 71-year-old female who had antispike antibody titers of 237 UI/mL after the 2nd dose, was diagnosed with COVID-19 two months after her 2nd dose. She had mild symptoms and did not require admission.

Characteristics of healthy controls

A total of 22 healthy controls were included with a mean age of 45.7 ±17.4 years (22-80 years) and 68.2% of them were females. Among these controls, 31.8% had a previous SARS-CoV-2 infection. All controls received the 2nd dose of vaccine 3 weeks after the 1st dose. The median level of anti-spike antibody following the 1st dose was 150 (IQR: 109.5-571) UI/mL. The median level of antispike antibody 1 month after the 2nd dose was 2000 (IQR: 1157-2000) UI/mL (maximum detection in controls was 3500 UI/mL). There was a significant difference in antispike antibody levels after the 1st dose of vaccine between previously infected and infection-naïve controls (N = 21, Z = -3.457, p < 0.001, Mann–Whitney test). There was no significant difference in the anti-spike antibody levels after the 2nd dose of vaccine between previously infected and infection-naïve controls (N = 17, Z = -1.213, p = 0.225, Mann-Whitney test).

Comparison between HD patients and healthy controls

The anti-spike antibody levels measured 20 days after the $1^{\rm st}$ vaccine dose and 4 weeks after the $2^{\rm nd}$ dose were both significantly higher in healthy controls compared to HD patients (Mann–Whitney test, p < 0.001 and p = 0.001, respectively). Figure 1 shows the high level of anti-spike antibody in previously infected patients compared to the levels after the $1^{\rm st}$ dose in healthy controls and infection-naïve HD patients.

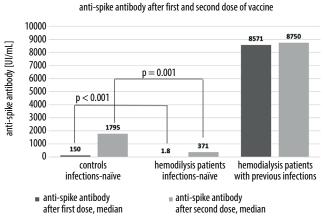


Fig. 1. Anti-spike antibody levels among different groups of patients

Factors associated with anti-spike antibody levels in HD patients

Sex, diabetes or CAD did not significantly affect the antispike antibody levels after the $1^{\rm st}$ and $2^{\rm nd}$ dose of vaccine. Heart failure patients presented a significantly weaker response with lower anti-spike antibody titers; previous infection caused a higher response of antibodies (Table 2). There was a positive correlation of anti-spike antibody levels after the $1^{\rm st}$ dose and after the $2^{\rm nd}$ dose of vaccine with age and anti-Hbs antibody and serum albumin levels (Table 3). The median of anti-spike antibodies after the $2^{\rm nd}$ dose of vaccine was 93.5 (IQR: 20.25-838.5) UI/mL in patients with an interval of 3 weeks between the $1^{\rm st}$ and

Table 1. Characteristics of hemodialysis (HD) patients and the statistical difference between the compared groups

Variable	HD patients (total = 72)	HD patients who were infection-naïve (n = 60)	HD patients previously infected (n = 12)	p-value
Age [years], mean ±SD	72.5 ±11.5	73.1 ±11.4	69.9 ±11.7	0.391*
Sex, n (% of females)	25 (34.7)	22 (36.7)	3 (25)	0.524
Dialysis vintage, median (IQR)	28 (14–60)	28 (14.5–60)	38.5 (9.7–74.2)	0.976**
Smoking status, n (%)	10 (13.9)	8 (13.3)	2 (16.7)	0.669***
Diabetes, n (%)	34 (47.2)	30 (50)	4 (33.3)	0.354***
Hypertension, n (%)	66 (91.7)	54 (90)	12 (100)	0.253 ^{\$}
CAD, n (%)	23 (31.9)	21 (35)	2 (16.7)	0.315***
Heart failure, n (%)	9 (12.5)	8 (13.3)	1 (8.3)	0.999***
History of cancer, n (%)	6 (8.3)	6 (10)	0 (0)	0.581***
Serum albumin level [mg/dL], mean ±SD	37.4 ±5	36.9 ±4.6	40.1 ±6.3	0.120*
Vaccinated against hepatitis B, n (%)	65 (90.3)	53 (88.3)	12 (100)	0.213 ^{\$}
Anti-Hbs antibody level >10 Ul/mL, n (%)	36 (50)	27 (45)	9 (75)	0.058 ^{\$}
Anti-Hbs antibody level mean ±SD median (IQR)	175.6 ±321.7 10.8 (0–109)	106.9 ±222.6 5.15 (0-50)	484.7 ±498.9 204 (17.25–818)	<0.001* 0.004**
Interval between the 2 doses of vaccine [weeks], mean ±SD	3.8 ±0.9	3.8 ±0.9	3.9 ±0.7	0.097*
Platelet count after the 2 nd vaccine dose, median (IQR)	181000 (156500–227500)	177000 (154500–207500)	208500 (166000–251000)	0.086**
Anti-spike antibody level after the 1st dose [UI/mL], median (IQR)	3 (0.5–26)	1.8 (0.5–7.9)	8571 (2585–19147)	<0.001**
Anti-spike antibody level after the 2 nd dose [UI/mL], median (IQR)	391 (55–1642)	371 (50–1157)	8750 (1936–26250)	0.003**
Anti-spike antibody level titer positive after the 1st dose, n (%)	45 (62.5)	33 (55)	12 (100)	0.003\$
Anti-spike antibody level titer positive after the 2 nd dose (%)	96.7 (total = 60)	96.5 (total = 58)	100 (total = 4)	0.474***
Adverse events after vaccination				
Myalgia, n (%)	16 (22.2)	11 (18.3)	5 (41.7)	0.091***
Fever, n (%)	9 (12.5)	5 (8.3)	4 (33.3)	0.030***
Sore arm, n (%)	27 (37.5)	24 (40)	3 (25)	0.248***
Headache, n (%)	7 (9.7)	5 (8.3)	2 (16.7)	0.309***
Other – fatigue, n (%)	12 (16.7)	11 (18.4)	1 (8.3)	0.006\$
Other – chills, n (%)	4 (5.6)	1 (1.7)	3 (25)	0.006 ^{\$}

^{*}independent t-test was used to compare means of continuous variables with normal distribution; **Mann–Whitney U test was used to compare medians of skewed continuous variables; $^{5}\chi^{2}$ test and ***Fisher's exact test were used to compare categorical data. SD – standard deviation; IQR – interquartile range; CAD – coronary artery disease; HBs – hepatitis B surface.

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Table 2. Assessment of anti-spike antibody levels after the 1st and 2nd dose of vaccine among different groups of categorical variables and the statistical difference between categories

Versiolala	Anti-spike antibody level 20 days after the 1st dose				Anti-spike antibody level 28 days after the 2nd dose			
Variable	N (71)	median (IQR)	p-value*	Z	N (61)	median (IQR)	p-value*	Z
Sex Male Female	46 25	2.85 (0.5–26) 3 (0.7–25.3)	0.652	-0.452	40 21	357.5 (32.05–1049) 948.5 (71.91–1932)	0.120	-1.556
Previous infection Yes No	12 59	8571 (3057–17765) 1.8 (0.5–7.9)	<0.001	-5.426	4 57	8750 (2124–22,500) 371 (52–1119)	0.001	-2.928
Smoking Yes No	10 61	4.8 (0.4–35) 3 (0.6–25.32)	0.856	-0.182	9 52	1590 (59–2352) 374 (56.4–1157.5)	0.296	-1.047
Dialysis frequency 2/week 3/week	6 65	1.6 (0.8–7) 3.2 (0.53–35)	0.579	-0.579	7 54	101 (26–338) 526 (60.8–1739)	0.141	-1.494
Diabetes Yes No	34 37	1.8 (0.4–14) 7.1 (0.8–39)	0.127	-1.526	29 32	279 (32–1119) 743 (86.5–1642)	0.233	-1.191
Hypertension Yes No	65 6	5.9 (0.6–35) 0.5 (0–1.1)	0.049	-1.954	55 6	391 (60.8–1739) 295 (19–1032)	0.348	-0.969
CAD Yes No	23 48	0.6 (0.4–23) 6.5 (0.9–38)	0.058	-1.899	22 39	102 (24–979) 704 (101–1739)	0.084	-1.727
Heart failure Yes No	9 62	0.6 (0.37–0.9) 6.6 (0.6–35)	0.029	-2.187	8 53	28 (14–519) 494 (101–1739)	0.018	-2.372
History of cancer Yes No	6 64	9 (0.6–12) 2.75 (0.5–30.2)	0.767	-0.315	5 56	86 (26–1348) 401 (59.9–1642)	0.674	-0.447

^{*}Comparison based on Mann-Whitney test. CAD - coronary artery disease; IQR - interquartile range.

Table 3. Correlation of anti-spike antibody levels after the 1st and 2nd dose of vaccine with different continuous variables

Variable	· ·	ntibody level 2 r the 1 st dose	0 days	Anti-spike antibody level 28 days after the 2 nd dose			
variable	correlation coefficient	p-value		correlation coefficient	p-value	n	
Age	-0.289	0.015	71	-0.464	<0.001	61	
Anti-Hbs antibody level	0.357	0.002	71	0.283	0.027	61	
Serum albumin level before vaccination	0.317	0.007	71	0.285	0.026	61	
Dialysis vintage	0.124	0.303	71	0.208	0.108	61	
Platelet count after 2 nd dose	0.243	0.046	68	0.207	0.110	61	
Number of weeks between 2 doses of vaccine	0.158	0.212	64	0.340	0.007	61	

Spearman's rho correlation was used to assess the association between anti-spike antibody levels and different continuous variables; HBs – hepatitis B surface.

 2^{nd} dose. It was of 979 (IQR: 308.5-1962.5) UI/mL in patients who received the 2^{nd} dose 4 to 6 weeks after the 1^{st} dose of vaccine.

The quantile regression analysis was used to analyze the association of different factors with the anti-spike antibody levels after the $1^{\rm st}$ dose of vaccine (Table 4). Previous infection and ani-Hbs levels were significantly associated with higher anti-spike antibody titers after the $1^{\rm st}$ dose, and remained significant after adjustment to age, sex, diabetes, CAD, heart failure, and serum albumin level.

Discussion

Our study revealed a positive humoral response rate of 96.7% after 2 doses of Pfizer-BioNTech vaccine in HD patients. This is in line with other reports from Europe confirming a good percentage of seropositivity of HD patients after full vaccination. The reported rates in the literature were 82% in a prospective study from Germany, ¹⁸ 88% in a trial from Switzerland, ¹⁹ 90% in the Romanov study from France, ¹⁰ and 97.7% in a prospective multicenter

(Ref = yes)

Variable	Coefficient	SE	df	95% CI	p-value		
Intercept	9692.68	17.1818	53	[9658.22; 9727.15]	<0.001		
Age [years]	0.006	0.1027	53	[-0.200; 0.212]	0.951		
Serum albumin level	0.257	0.2625	53	[-0.270; 0.783]	0.333		
Anti-Hbs antibody level	0.051	0.0039	53	[0.043; 0.059]	<0.001		
Sex Male Female (Ref)	-1.076	2.1362	53	[-5.361; 3.209]	0.616		
Previous infection (Ref = yes)	-9700.65	3.37	53	[-9707.42; -9693.89]	<0.001		
Diabetes (Ref = yes)	-3.479	2.1297	53	[-7.750; 0.793]	0.108		
Hypertension (Ref = yes)	-0.617	3.6469	53	[-7.931; 6.698]	0.866		
CAD (Ref = yes)	0.044	2.4562	53	[-4.882; 4.971]	0.986		
Heart failure	1.244	3.2067	53	[-5.188; 7.676]	0.700		

Table 4. Multivariate quantile regression analysis of factors associated with anti-spike antibody levels 4 weeks after the 1st dose of vaccine

The median (50th) was used for quantile regression analysis. SE – standard error; 95% CI – 95% confidence interval; df – degrees of freedom; CAD – coronary artery disease; HBs - hepatitis B surface.

study from Spain.¹¹ Our findings also highlighted the fact that the 1st dose is not enough to induce an acceptable seroconversion rate or titer in infection-naïve patients. Although 62.5% of patients in our sample developed positive anti-spike antibody levels after the 1st dose, the median of these antibodies was as low as 3 UI/mL (IQR: 0.5-26). This is aligned with the findings of Billany et al. from UK,16 where antibodies were detectable in 79.8% of patients with a median level of 2.4 (IQR: 8). Lower response rates to the 1st dose of 18%, 21% and 35% were reported by Speer et al.,18 Longlune et al.13 and Torreggiani et al.,20 respectively. They had to administer a 3rd dose of vaccine to patients who did not respond to the routine regimen.¹³ In most of the studies, HD patients had a better response than kidney transplant (TX) patients but worse than healthy controls. 12,15,17-19,21,22 This was also the case in our sample where healthy controls showed significant higher titers of antibodies.

One interesting finding in our study is the statistically significant association between hepatitis B vaccine response (anti-Hbs antibody levels) and anti-spike antibody levels. To the best of our knowledge, 3 previous studies tried to find out if there was any relation between these 2 variables. Only a French cohort of 78 patients showed a positive correlation between hepatitis B and humoral responses to COVID-19 vaccines, which concurs with our results. In a cohort from Switzerland that studied 1198 HD patients, no such correlation was found.¹⁹ Their patients had longer dialysis vintage than our patients, but were younger. In another study of 81 patients from Switzerland, no association was demonstrated.¹⁷ Their vaccination schedule consisted of 3 doses of Engerix B 40 µg, which is slightly different from our patients' 4 doses. The lack of consistency across studies regarding this association needs further evaluation by comparing statistical methods used and enrolling more patients from other units worldwide.

In our sample, high serum albumin level was associated with a better response to the COVID-19 vaccine. This parameter is known to predict mortality in HD patients.²³ It has also been demonstrated recently to be associated with COVID-19 vaccine response in HD.12 Other factors that were highlighted to predict the humoral response to COVID-19 vaccine in other cohorts are age, dialysis vintage and better dialysis quality. 10-12,19 We showed an inverse correlation between age and antispike antibody levels among our patients. However, this was not consistent in the literature. Speer et al. detected lower anti-spike antibody levels at older age in healthy controls but not in HD patients.18 Stumpf et al. demonstrated age-related differences in TX patients but not in dialysis ones.19 On the other hand, Jahn et al., Yanay et al. and Attias et al. found significant lower antibody levels in HD patients over 60, 70 and 75 years, respectively. 21,22,24

Our results shed light on the distinctive characteristics of patients previously infected with SARS-CoV-2 and their positive response to vaccination. In fact, these patients had higher serum albumin levels, were younger and had significantly higher anti-Hbs antibody titers than infection-naïve patients in our sample. This is most probably due to the natural selection following COVID-19. Those who survived the disease were the ones with more robust immunity parameters. In addition, the strong response of these previously infected patients after a single dose of vaccine and the high incidence of fever following 1 dose suggests that they do not need a 2nd injection. In fact, this 2nd dose can be spared for patients who are non-respondents and would need a 3rd dose.

The pronounced peak of response after 1 dose in patients with a history of COVID-19 has also been demonstrated in several reports from the general population.²⁵

Finally, the fact that one of the immunized patients was diagnosed with COVID-19 two months after the $2^{\rm nd}$ dose emphasizes the importance of maintaining preventive measures in all dialysis units. This was highlighted as well by Yanay et al. who reported 4% of their patients infected 7 days after the $2^{\rm nd}$ dose. $2^{\rm nd}$

Limitations

The major limitation of our study is the small sample size. The shortage of serological kits to assess anti-spike antibody levels prevented more units from assessing the humoral response of their patients. However, despite the limited number of patients, this study confirmed once more the good response rate of HD patients to 2 doses of vaccine, highlighted the robust seropositivity after 1 dose of Pfizer-BioNTech vaccine in previously infected patients, and showed the importance of anti-Hbs antibody level as a predictor of the response of patients to COVID-19 vaccine.

Conclusion

In conclusion, this study showed a response rate of 96.7% to 2 doses of BNT162b2 mRNA vaccine in HD patients and of 100% to the $1^{\rm st}$ dose in previously infected patients. The levels of anti-spike antibody can be predicted by age, anti-Hbs antibody, serum albumin levels, and previous infection. Despite the immunization of patients, preventive measures should be maintained in all dialysis units.

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