Comparison of long-term antibody response to mRNA SARS-CoV-2 vaccine among peritoneal dialysis and hemodialysis patients

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Coronavirus disease 2019 (COVID-19) is associated with higher morbidity and mortality in patients on maintenance hemodialysis (HD) [1]. Vaccination against SARS-CoV-2 is the main priority to prevent COVID-19. Early humoral response among HD patients was lower compared to the general population [2-4]. Humoral response among peritoneal dialysis (PD) patients was evaluated in small groups, only. Evaluation of late antibody levels was not reported among this population.

This multicenter study assessed antibody levels 6 months after a two-dose regimen of the Pfizer BNT162b2 vaccine in PD compared to HD patients.

The study included two groups of participants, prevalence PD patients (>3 months of treatment) from 4 different PD units across Israel (n=64, PD group) and prevalence HD patients from two dialysis centers (n=118, HD group) were included. All patients had received two doses of Pfizer BNT162b2 mRNA vaccine 6 months ± 4 weeks before study inclusion. Patients with active malignancy, on immunosuppressive therapy (including steroids) or who had been infected with COVID-19 were excluded. Following approval of each local institutional review board and obtaining informed consents, blood samples for antibody level against the S1 subunit of the spike protein of SARS-CoV-2 were drawn.

Detailed Methods appear in **Item S1**.

PD patients were younger than HD (mean age 67.16±11.86 years, median 64 vs. 71.91±13.83 years, median 74, respectively (Mann Whitney U test p=0.005). The PD group included 45 (70.3%) men, 48.4% had diabetes mellitus (DM) compared with 76 men (64.4%) and 62.7% with DM in the HD group (p=0.42 and p=0.06, respectively). Ischemic heart disease was more common among HD participants whereas, hypertension was more common among PD. Demographics are summarized in Table 1. Six months (mean 23.59±1.65 weeks) after receiving second vaccine dose, 52 (81.3%) of the PD participants and 93 (78.8%) HD participants had antibody titers ≥50 AU/ml, which is considered a protective response (p=0.70). Mean antibody levels were not different between dialysis modalities, 400±622 AU/ml (median 133, 90% confidence interval 0-1831) among HD and 384±577 AU/ml (median 258, 90% confidence interval 16-982) among PD (Mann Whitney U test p=0.26). Antibody titer inversely correlated with age in the entire group and among HD group, but not PD patients (Spearman correlation = -

0.261; p<0.001, -0.260, p=0.005 and -0.169, p=0.18, respectively). Antibody titers were assessed across three age groups, <60-years-old (n=34), 60–75-years-old (n=80) and >75-years (n=68). Two HD patients and no PD patients younger than age 60 had antibody levels <50 AU/ml (5.9%), compared with 17 (21.3%) patients and 18 (26.5%) patients in the 60-75 years-old and >75 years-old, respectively (p=0.05). Antibody levels were not different between HD and PD across the three age groups (Figure 1).

This study describes antibody levels against S1 subunit of SARS-CoV-2 among HD and PD patients 6-months after a two-dose regimen of the BNT162b2 mRNA vaccine. Our findings demonstrate high percentage of patients in both dialysis modalities with significant antibody levels. No difference was documented between the two modalities. Antibody titers correlated with age. In the age group of younger than 60 years old, antibody levels <50 AU/ml were documented in only two HD patients, significantly different from the older population. Previous reports assessing antibody response among hemodialysis patients in earlier months after vaccination, reported lower intensity, delayed, heterogeneous response compared to the general population [2-4]. A small group of 23 PD patients included in a study by Agur et al. demonstrated similar response to the HD population [4]. A report comparing humoral response to whole-virus SARS-CoV-2 vaccination demonstrated a non-significant advantage among HD vs. PD patients [5]. Late antibody response among HD population reported by Nacasch et al., demonstrated antibody levels ≥50 AU/ml in 81% of patients, which correlated with immunosuppressive therapy and age [6]. While serology is commonly used as a surrogate marker of protection from viral infections, the clinical implications of antibody levels and protective threshold against COVID-19 are unknown. Post-vaccination titers were reported to be strongly predictive of immune protection. [7,8] A real-word study demonstrated correlation between breakthrough infection and low antibody titers one week before infection [9]. However, protective thresholds might vary between age groups and sub-populations.

The strength of this report is the relatively large number of PD participants and its multicenter design, which allowed us to avoid a “center effect”. The study assessed late serological response; earlier antibody levels were not available and therefore information regarding the dynamics of antibody titers after vaccination was not available. Other aspects of the immune system, most importantly the cellular response, were not assessed.

In summary, HD and PD patients maintained significant humoral response 6 months after a 2-dose regimen of vaccine. No difference between dialysis modalities was documented. Antibody levels correlated with age, so when considering giving a "booster" dose to these populations, the current report indicates prioritizing patients over the age of 60 years**.**

AUTHORS' CONTRIBUTIONS

Research area and study design: YE, SG, TT, AB; Data acquisition: YE, SG, TT, AB, NN, DE, KCH, SM, TZG; Data analysis and interpretation: YE, KCH, HLZ, YWW; Statistical analysis: HLZ, KCH; Supervision or mentorship: VP, SB, LS.

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. Background characteristics of the study participants

Characteristic	PD (n=64)	HD (n=118)	Chi square p-value	Mann-Whitney U test
Sex (male/female)	45/19	76/44	0.42	
Age, years, mean (SD)	67.16±11.86	71.31±13.89		0.005
Age distribution across age groups:			0.01	
<60 years, n (%)	13 (20.3)	21 (17.8)		
60-75 years, n (%)	36 (56.3)	44 (37.3)		
>75 years, n (%)	15 (23.4)	53 (44.9)		
Dialysis vintage (months)	34.88±25.73	35.10±27.61		0.9
Weight (mean, kg)	81.1±16.3	76.3±19.8		0.2
Diabetes mellitus, n (%)	31 (48.4)	74 (62.7)	0.06	
Ischemic heart disease, n (%)	15 (23.4)	47 (39.8)	0.03	
Hypertension, n (%)	58 (90.6)	93 (79.5)	0.05	
Lung disease, n (%)	5 (7.8)	11 (9.3)	0.7	
Laboratory results				
Albumin (gr/dl)	3.7±0.4	3.8±0.5		0.003
Urea	115.7±29.7	120.9±31.2		0.3
Hemoglobin (g/L)	11.0±1.3	10.8±1.1		0.4
C-reactive protein	1.95±4.1	1.83±3.2		0.8
Kt/V, mean (SD)	2.06±0.60*	1.298±0.27**	---	
Urine output (ml)	968±607	NA		

Note: Continuous variables that were not normally distributed were compared using Mann-Whitney U test
*Weekly Kt/V, **Duagirdas Kt/V

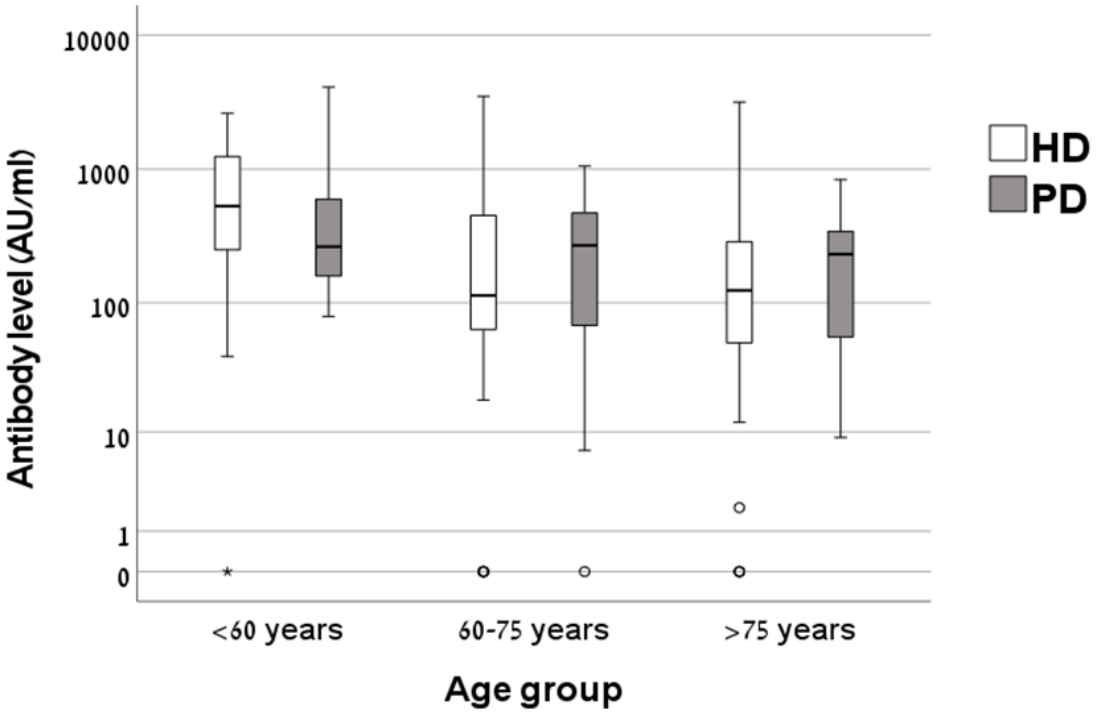

Figure 1. Box plot of humoral response of 3 age groups

Age groups were divided into: <60 years, 60-75 years and >75 years. There was no significant difference in antibody levels between HD and PD groups (p=0.362, p=0.358 and p= 0.424, respectively). The medians are marked by horizontal lines inside the boxes. Error bars represent the range between minimum and maximum antibody levels.

IgG anti-spike is presented as AU/ml units in logarithmic scale.