

## LETTER TO THE EDITOR

# Humoral responses to BNT162b2 SARS-CoV-2 and hepatitis B vaccines are associated in patients on maintenance hemodialysis: a single-centre experience in Belgium

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Maintenance hemodialysis (HD) patients are at high risk for life-threatening coronavirus disease 2019 (COVID-19) [1]. Recent studies have documented a strong humoral response after severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccination in this population [2], even in older patients [3], in contrast to kidney transplant recipients [4]. Previous reports have also shown a poor humoral response after hepatitis B virus (HBV) vaccination in chronic kidney disease patients with comorbidities (e.g. older age, diabetes, immunosuppression) [5, 6]. We therefore hypothesized that this weak response to the HBV vaccine could serve as a potential indicator of response to SARS-CoV-2 vaccination. However, data linking humoral responses to both vaccines remains scarce and contradictory [7, 8].

We retrospectively studied the association between the humoral response to HBV and BNT162b2 spike mRNA vaccines in a cohort of adult patients on in-centre maintenance ( $\geq 3$  months) HD at Cliniques universitaires Saint-Luc and its satellite site. We excluded 58 patients who had a history or serologic evidence of HBV ( $n = 27$ ) or SARS-CoV-2 infection ( $n = 15$ ), refused vaccination ( $n = 11$ ) or had an incomplete HBV vaccination ( $n = 5$ ). Demographics, dialysis vintage, diabetes status, immunosuppressive treatment if applicable and time since last SARS-CoV-2 and HBV vaccine administrations were recorded. In each patient, a single sample was tested simultaneously with

five electro-chemiluminescent immunoassays (Roche Elecsys): SARS-CoV-2 recombinant nucleocapsid antigen antibody (anti-SARS-CoV-2 N), SARS-CoV-2 spike protein receptor-binding domain antibody (anti-SARS-CoV-2 RBD), hepatitis B surface antigen and antibody (HBsAg and anti-HBs Ab), and hepatitis B core antibody (anti-HBc Ab). Patients were divided into groups depending on their HBV and SARS-CoV-2 vaccine response status. Patients with an anti-HBs Ab titer  $>10$  IU/mL after three doses of Engerix-B<sup>®</sup> or Fendrix<sup>®</sup> and an anti-SARS-CoV-2 RBD Ab titer  $\geq 0.8$  U/ml after two doses of BNT162b2 SARS-CoV-2 vaccine were considered responders to the HBV and SARS-CoV-2 vaccines, respectively. Groups were compared using unpaired t-test, Mann–Whitney U test and Fisher's exact test, as appropriate. All tests were two-tailed and a P-value  $<0.05$  was considered significant.

Fifty-four patients (median age 72 years, 56% men, 91% Caucasians, on dialysis for a median of 47.0 months, 39% diabetics, 19% on immunosuppressive treatment) were included (Table 1). Serum samples were collected 4.1 months [interquartile range (IQR) 4.1–5.0] after the second dose of the SARS-CoV-2 vaccine. Responders to the SARS-CoV-2 vaccine did not differ from non-responders regarding demographics, dialysis vintage and diabetes. However, patients were less likely to respond to the SARS-CoV-2 vaccine if treated with immunosuppressive medications and in case of non-response to the HBV vaccine (Table 1,

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Table 1. Characteristics of the patients

Characteristics	All patients (N = 54)	SARS-CoV-2 vaccine responders (N = 49)	SARS-CoV-2 vaccine non-responders (N = 5)	P-value
Age, median (IQR), years	72 (62–81)	73 (63–81)	55 (55–67)	0.14
Gender: male, no. (%)	30 (56)	27 (55)	3 (60)	1.00
Race: Caucasian/African, no. (%)	49 (91)/5 (9)	45 (92)/4 (8)	4 (80)/1 (20)	0.40
Dialysis vintage, median (IQR), months	47.0 (23.6–78.8)	46.2 (23.7–76.6)	68.8 (20.6–110.1)	0.72
Diabetes, no. (%)	21 (39)	20 (41)	1 (20)	0.64
Immunosuppressive treatment, no. (%)	10 (19)	5 (10)	5 (100)	<0.001
HBV vaccine response, no. (%)	39 (72)	38 (78)	1 (20)	0.02

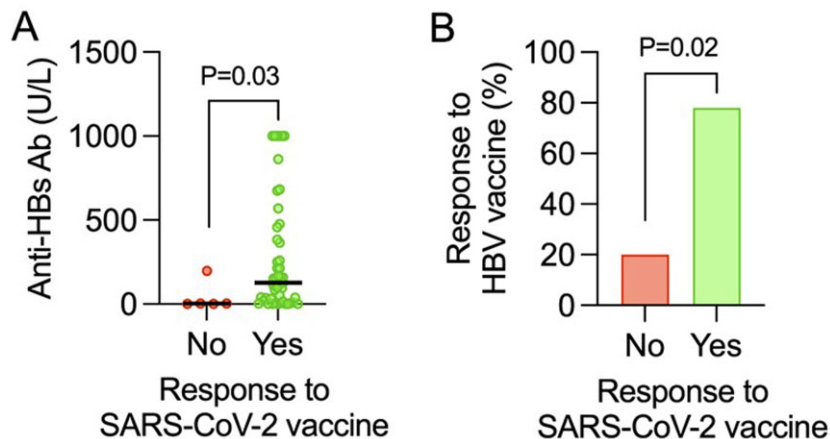


FIGURE 1: Level of anti-HBs Ab (A) and HBV vaccine response status (B) stratified for the presence vs absence of humoral response to SARS-CoV-2 vaccination.

Figure 1). Anti-HBs and anti-SARS-CoV-2 RBD Ab titers were correlated (Spearman,  $r = 0.34$ ,  $P = 0.01$ ). Out of the five patients who did not respond to the SARS-CoV-2 vaccine, one was on tacrolimus and mycophenolate mofetil, two were on maintenance rituximab and low-dose methylprednisolone, and two were on tacrolimus alone. Out of the five patients on immunosuppressive therapy who responded to the SARS-CoV-2 vaccine, three were on low-dose methylprednisolone and two on tacrolimus alone.

Our study shows a significant association between humoral responses after HBV and SARS-CoV-2 vaccines in a small cohort of patients on maintenance HD. HBV vaccine non-responders may therefore benefit from a systematic SARS-CoV-2 serological follow-up and potential intensification of the vaccine schedule. Furthermore, this study highlights the poor vaccine response of immunosuppressed patients, including those treated with rituximab, as recently reported [9].

A definite strength of this study is its novelty in assessing and correlating immunization responses to both HBV and SARS-CoV-2 vaccines among maintenance HD patients with a subgroup of patients on immunosuppressive therapy. The small sample size is a clear limitation.

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