Monitoring of the immune response to SARS-CoV-2 in vulnerable population: the COVICO study

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Conclusion: The immune response remains stable over time, with slight declines in KTP, HP and WAP. LTR display comparatively weaker humoral response. These findings underscore the importance of ongoing monitoring and potentially additional booster doses, particularly for vulnerable populations, to maintain protection against emerging variants of SARS-CoV-2.

Vulnerable populations have been extensively characterized to exhibit attenuated immune responses to SARS-CoV-2 compared to the general population. Hence, it is imperative to monitor the magnitude and dynamics of their immune responses over time.

Methods

- This 4-years Belgian multicenter prospective cohort study encompasses 106 working age individuals (WAP) and 139 vulnerable subjects, including 39 nursing home residents (NHR), 28 hemodialyzed patients (HP), 48 kidney- (KTR), and 30 lung- transplant recipients (LTR).
- Participants undergo thrice-yearly follow-ups involving blood sampling and surveys in February (v1), June (v2), and October (v3).
- Over 2023, SARS-CoV-2 anti-receptor binding domain (RBD) specific IgG concentrations (v1, v2, v3) and neutralizing antibody titres (nAb) against SARS-CoV-2 Wuhan, Delta, XBB.1.5 (v1,v2) and BA.5 (v1) were assessed. NAb responses against Delta, XBB.1.5 and BA.5 were evaluated only when nAb against Wuhan >300 IU/ml.
- Participants receive COVID-19 vaccinations through the regular standard of care.
- Data regarding vaccination status, COVID-19 infections, and flu-like symptoms are collected via surveys at each time point.
- Within-and-between group comparisons were conducted on paired cohorts using non-parametric ANOVA with random effect.

Results

Anti-RBD binding IgG levels (Fig. 2A)

- They exhibit considerable stability over the year across all five groups, with a slight decline observed between v1 and v3 for KTR (p=0.005) and HP (p=0.004).
- LTR demonstrate significantly lower anti-RBD IgG titres compared to the other groups, with ~10% exhibiting an undetectable response.

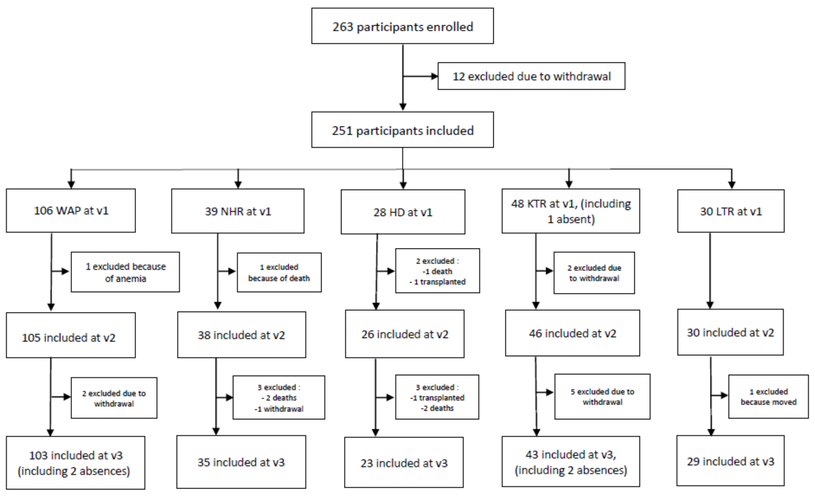
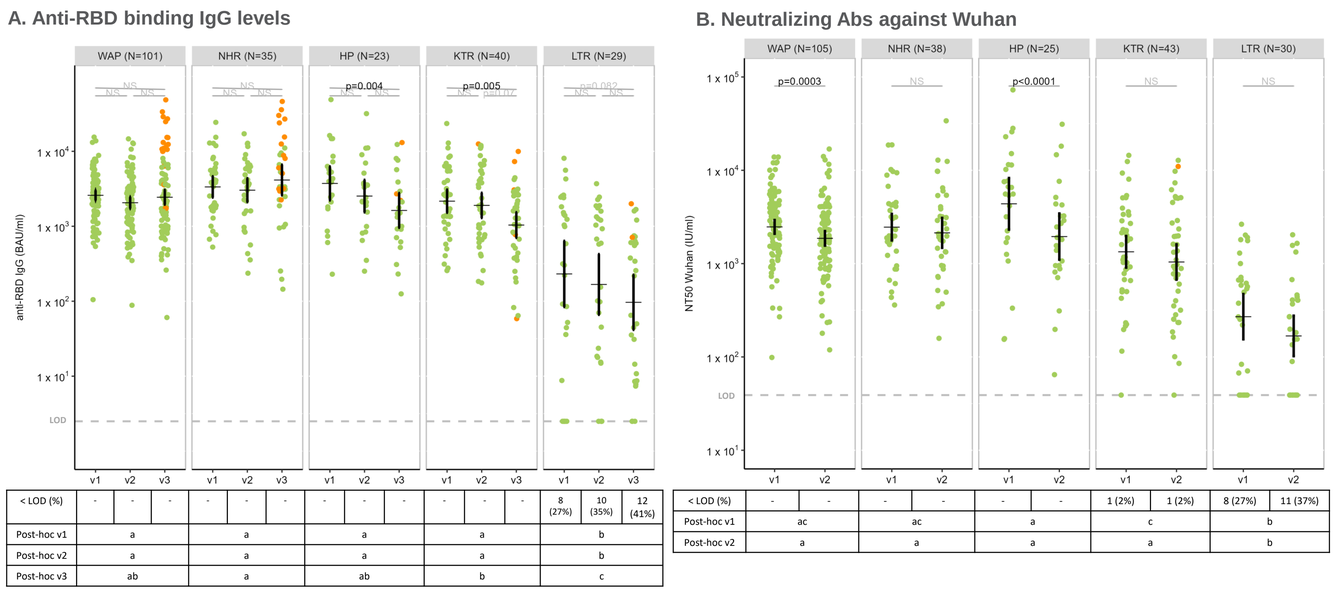


Figure 1. Study flow-chart

Table 1. Demographics, characteristics by study groups

		Working age population (WAP, N=106)	Nursing home residents (NHR, N=39)	Hemodialyzed patients (HD, N=28)	Kidney transplant recipients (KTR, N=48)	Lung transplant recipients (LTR, N=30)
Characteristics						
Age (years, mean ± SD)		49.4 ± 9.7	83.4 ± 10.5	68.2 ± 15.6	59.7 ± 13.2	52.7 ± 14.0
Sex	**Female**	83 (78.3%)	20 (51.3%)	13 (46.4%)	19 (39.6%)	17 (56.7%)
Ethnicity	**European**	103 (97.2%)	39 (100%)	14 (50.0%)	39 (81.2%)	28 (93.3%)
BMI (mean ± SD)		26.1 ± 4.4	25.3 ± 3.5	27.8 ± 6.8	25.6 ± 4.6	22.9 ± 4.0
Vaccination v1-v2						
	Number of people (%*)	0 (0%)	0 (0%)	0 (0%)	1 (2.1%)	0 (0%)
	Median time (days) between vaccine and v2 (min-max)	-	-	-	116	-
Vaccination v2-v3						
	Number of people (%)**	20 (18.9%)	16 (41.0%)	3 (10.7%)	6 (12.5%)	2 (6.7%)
	Median time (days) between vaccine and v3 (min-max)	25.5 (14-41)	28 (18-29)	17 (1-24)	13 (8-63)	5 (4-6)

* % calculated on cohort still followed at 2, ** or v3



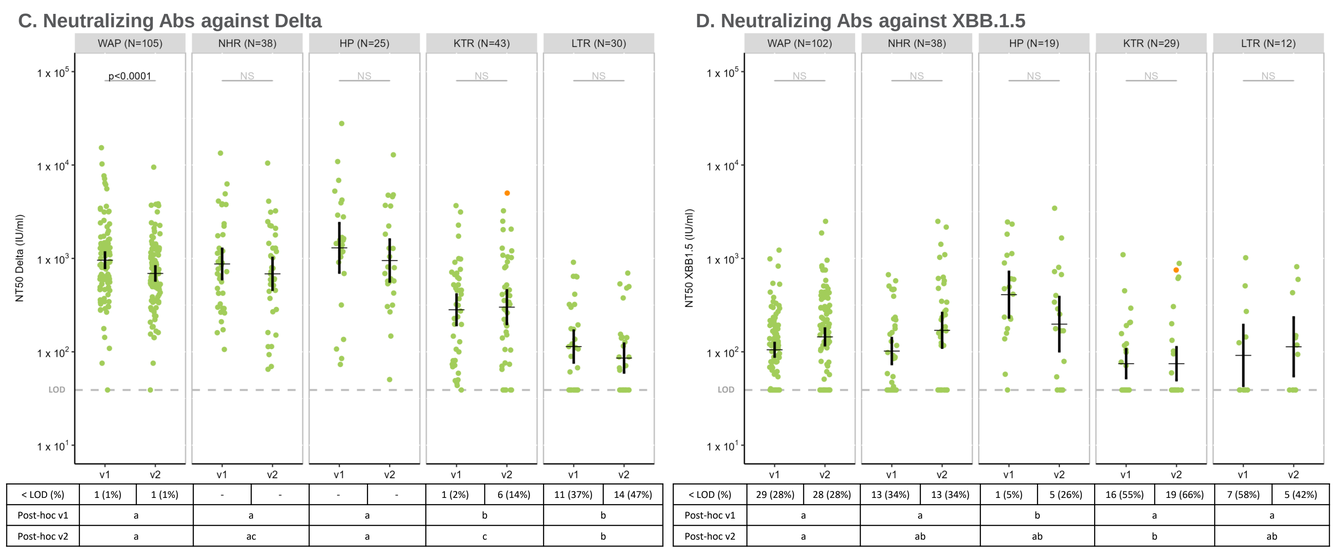


Figure 2. Anti-RBD binding antibody (A) and neutralizing antibody response against Wuhan (B), Delta (C) and XBB.1.5 (D) variants of concern according to the group (WAP, NHR, HDR, KTR and LTR) and the 3 time points (v1, v2, v3). Geometric mean titers (GMTs) with 95% CI are represented as a black cross. In orange, people having received a COVID-19 booster between two visits. Within and between groups comparisons were analyzed using an aligned ranks transformation ANOVA with random effect taking into account the repeated measures (N are given next to the group name). Post-hoc comparisons were calculated using bonferroni correction. *P*-values of the within group comparisons (analyses between time points inside a group) are represented at the top of each graph (NS: not significant). The between group comparisons at each time point are represented in the table at the bottom of each graph by letters: groups with a same letter are not significantly different at α=0.05 (Post-hoc v1, Post-hoc v2, Post-hoc v3: between group analysis results at v1, v2, v3 respectively). Number (%) of undetectable response for each group at each time point are given in the table (LOD: limit of detection).

Neutralizing Abs (Fig. 2B-C-D)

- NAb responses against Delta, BA.5 and XBB.1.5 exhibit a ~3-fold, ~5-fold and ~14-fold decreased respectively compared to the response against Wuhan, with LTR and KTR standing out with lower titres compared to the 3 other groups.
- No significant evolution was observed in nAb response, except for WAP against Wuhan (p=0.0003) and Delta (p<0.0001), and HD against Wuhan (p<0.0001).
- Undetectable nAb responses against Wuhan and Delta were mainly observed in LTR (37% and 47% at v2 respectively). High rates of undetectable nAb against XBB.1.5 responses were exhibited across all the groups (range of 28-66% at v2).

Discussion

- The yearly SARS-CoV-2 vaccination spreads out from September to January and is reflected in v1 and v3. The strains used for vaccination were Wuhan, BA1 and BA4/5 in 2022 and XBB.1.5 in 2023.
- Re-infection were not actively monitored via testing. Possible re-infections were thus defined based on 4 criteria: i) a positive PCR test (but very few people got a PCR test in 2023), ii) detectable SARS-CoV-2 nucleocapsid specific antibodies whereas they were undetectable at the previous time point, iii) an increase of at least 30% of the nAb between two time points without being vaccinated, and iv) flu-like symptoms outside of the flu season. With at least one of the 4 criteria that should be positive to define a re-infection, 80 re-infections (33%) were observed between v1 and v2, and 55 (24%) between v2 and v3, distributed over all the groups.
- The immune response reflects boosting by infection and/or vaccination.
- Results for nAb at v3 and for cellular immunity are still under study.

REFERENCES

- Etienne, I. et al, Humoral and cellular immunity to SARS-CoV2 remain defective in lung transplant recipients, *Journal of Heart and Lung Transplantation* 2024, Submitted.

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