Estimated half-life of SARS-CoV-2 anti-spike antibodies more than double the half-life of anti-nucleocapsid antibodies in healthcare workers

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Dear editor:

Lumley et al. studied the duration, and dynamics of SARS-CoV-2 antibody responses in 452 individual healthcare workers (HCW) over a 6-month period [1]. SARS-CoV-2 IgG anti-nucleocapsid (N) antibodies started to decline within one month after first positive PCR with an estimated half-life of 85 days and an estimated 50% of HCW becoming seronegative after 7 months. Confirming these results, we recently reported that 61.1% of mild SARS-CoV-2 infected patients became seronegative within 6 months after first positive PCR [2]. Anti-spike (S) antibodies, in contrast, remained positive up to 7 months in an estimated 94% of participants. The authors were unable to determine whether the longer anti-spike response was due to slower waning or higher initial antibody levels since most results were above the upper limit of quantification of their assay [1].

We report antibody levels for anti-S and anti-N in 118 individual HCW with a previous SARS-CoV-2 infection. Participants were sampled 1-3 months (28-103 days) and 7-10 months (209-315 days) after positive PCR. Seroconversion for anti-S and anti-N typically occurs within 28 days after positive PCR [3]. Antibodies were measured on Abbott Architect with the SARS-CoV-2 IgG (anti-N) and IgG II Quant (anti-S) assays using the manufacturer's cut-offs for positivity of 1.4 S/CO and 50 AU/mL, respectively. The median age was 48 years old (range 20-62), with 88.1% women. Most participants experienced mild disease and only six participants were briefly hospitalized.

At 1-3 months, 98.3% were positive for anti-S compared to 85.6% for anti-N ($p<0.01$ with Fisher's exact test). At 7-10 months, 92.4% of patients were still positive for anti-S compared to only 17.8% for anti-N ($p<0.01$). To estimate the antibody half-life, we used a simple linear regression model (RStudio version 1.3.1093) correlating the $\log_{10}$ antibody level to days after positive PCR. Only patients who tested positive for anti-N (n=101) or anti-S (n=116) 1-3 months after PCR were included to estimate half-life. The computed mean half-life was 76.4 days for anti-N [95% confidence interval (CI): 68.3-86.7] compared to 198.8 days for anti-S [CI: 143.6-323.0] with an estimated 50% of patients becoming seronegative for anti-N 201.2 [CI:179.9-228.3] days after positive PCR compared to 803.2 [CI: 580.2-1305.0] days for anti-S. We also calculated the half-life by dividing the $\log_{10}$ antibody level difference between the paired samples by the number of days between the

two samples for each patient. The results were normally distributed for anti-S and anti-N (Shapiro-Wilk test) and the estimated mean half-life was 74.8 days [CI: 70.1-80.1] for anti-N and 197.2 days [CI: 172.4-230.4] for anti-S.

Our results confirm a recent study that reported more than 90% anti-S seropositivity up to 8 months after positive PCR [4]. This could have implications on the estimated duration of the antibody response after vaccination which appears to be similar to the antibody response after infection during the first 8 weeks [5]. Of note, anti-N antibodies wane significantly slower in moderate to critical COVID-19 patients [2]. Further studies are needed to determine the dynamics of anti-S antibodies in these patients.

NOTES

Author contributions

PV conceived the study. JVE, LGr, PV, conducted experiments and drafted the manuscript. LGo aided in collecting data and all authors critically reviewed the manuscript.

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Conflicts of interest

The authors report no conflicts of interest.

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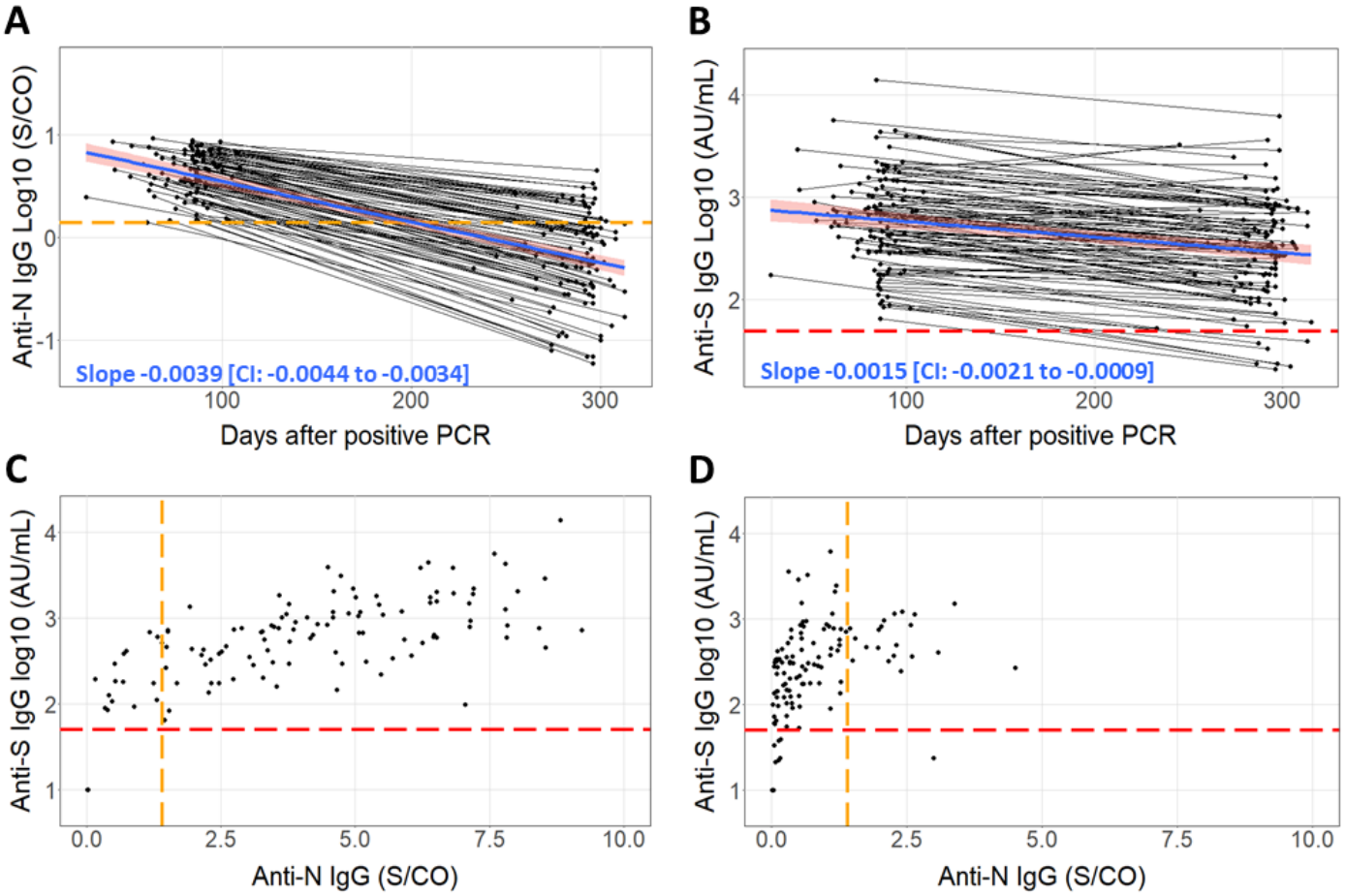
Figure legend:

Figure 1: **Longitudinal evolution of SARS-CoV-2 antibody titers against nucleocapsid (panel A) and spike (panel B) and correlation between both antibody levels 1-3 months (panel C) and 7-10 months (panel D) after positive PCR in 118 health care workers.** S: spike, N: nucleocapsid, S/CO: signal-to-cut-off, AU: arbitrary units. Thick blue line represents line of best fit (red: 95% confidence interval). Dashed orange and red lines represent the manufacturer's cut-offs for positivity for anti-N (1.4 S/CO) and anti-S (50 AU/mL), respectively.

Figure 1


A
Anti-N IgG Log10 (S/CO)
Slope -0.0039 [CI: -0.0044 to -0.0034]
Days after positive PCR
B
Anti-S IgG Log10 (AU/mL)
Slope -0.0015 [CI: -0.0021 to -0.0009]
Days after positive PCR
C
Anti-S IgG log10 (AU/mL)
Anti-N IgG (S/CO)
D
Anti-S IgG log10 (AU/mL)
Anti-N IgG (S/CO)