SARS-CoV-2 Natural Antibody Response Persists for at Least 12 Months in a Nationwide Study From the Faroe Islands

Dear Editor,

Only a few studies have assessed the long-term duration of the humoral immune response against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Recently, an American study found that immunoglobulin G (IgG) titers were durable, with modest declines in titers 6 to 8 months after symptom onset [1], while a Canadian study showed a reduction in circulating antibodies over time but increasing and persisting levels of receptor-binding domain (RBD)–specific B cells up to 8 months after symptom onset [2]. Here, we report the results of natural IgG response to SARS-CoV-2 infection up to 12 months after symptom onset in a longitudinal nationwide study from the Faroe Islands [3] with participation of >80% of all individuals with polymerase chain reaction (PCR)–confirmed COVID-19 during 2 waves of infections (March to April and August to December 2020). Samples were drawn at 3 longitudinal time points for each wave: wave 1 at a median of 89, 210, and 363 days (range, 29–380 days) and wave 2 at a median of 27, 125, and 210 days (range, 27–231 days) after symptom onset, respectively (wave 1: n = 172; 54% women; median age, 42 years; range, 1–93 years; wave 2: n = 233; 53% women; median age, 35 years; range, 0–83 years). There was no observed overlap among the 2 waves, indicating that wave 1 participants were not reinfected in wave 2. The disease course ranged from asymptomatic to critically ill, with only 6 and 8 individuals hospitalized, respectively (Supplementary Table 1). All participants provided written informed consent.

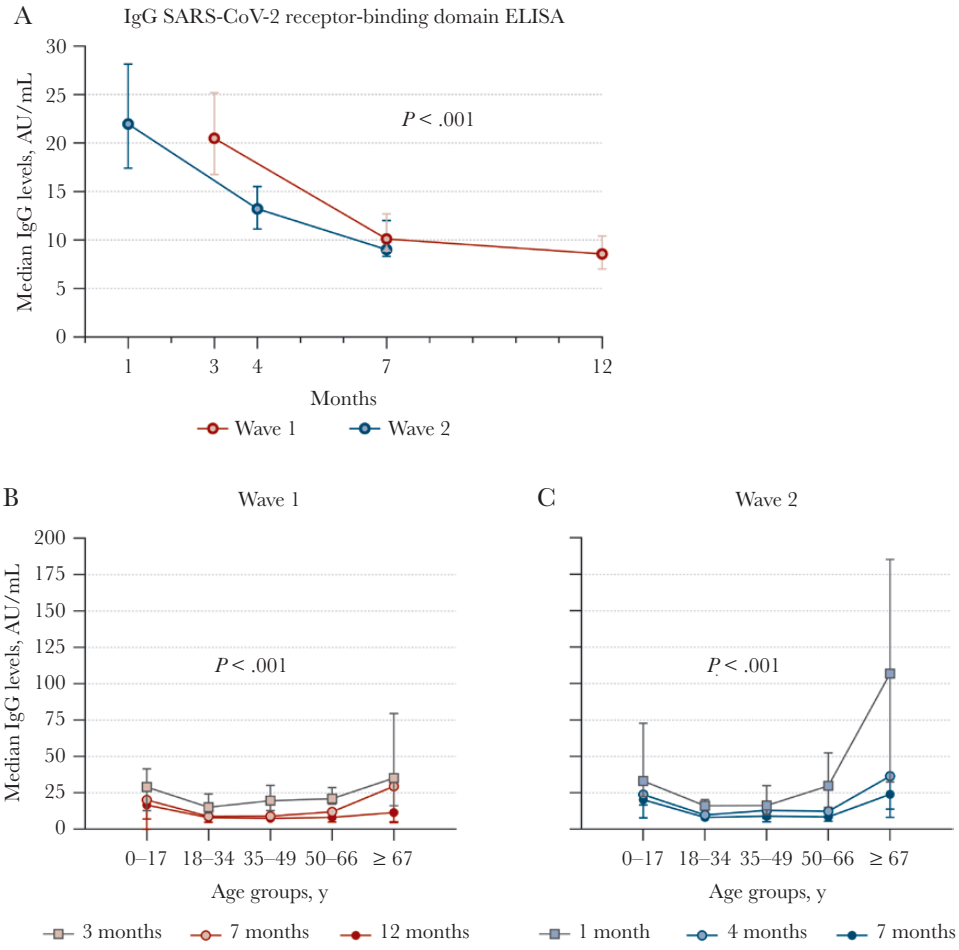

Figure 1. IgG titers against SARS-CoV-2 over time (A) and by age group (B and C). A, IgG levels plotted against median time from symptom onset to sampling (Friedman test). B and C, IgG levels plotted against age groups (Kruskal-Wallis test). Data are expressed as medians with 95% CIs. Abbreviations: CIs, confidence interval; ELISA, enzyme-linked immunosorbent assay; IgG, immunoglobulin G; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

The study was approved by the Faroese Bioethics Committee and the Data Protection Agency.

Serum was analyzed with a direct quantitative IgG antibody binding enzyme-linked immunosorbent assay (ELISA) to detect anti-SARS-CoV-2 spike RBD antibodies [4].

The seropositive rate in the convalescent individuals was above 95% at all sampling time points for both assays and remained stable over time; that is, almost all convalescent individuals developed antibodies. There was an overall decline in IgG titers over time in both waves (Friedman test: $\chi^2(2) = 133.273$; $P < .001$; and $\chi^2(2) = 112.407$; $P < .001$) (Figure 1A). Wilcoxon signed-rank pairwise comparison showed that IgG declined significantly from the first sample until ~7 months in both waves ($P < .001$) (Figure 1A). After that, the antibody level continued to decline significantly, but decelerated with an altered slope, remaining fairly stable from 7 months to 12 months after infection ($P < .001$). Antibody levels did not differ significantly between women and men over time ($P = .09$–$.7$). Interestingly, the IgG titers followed a U-shaped curve, with higher antibody levels among the oldest (67+) and youngest (0–17) age groups compared with intermediate groups (Kruskal-Wallis test: $\chi^2(4) = 15.132$; $P = .004$; and $\chi^2(4) = 52.582$; $P < .001$) (Figure 1B and C). One limitation of the study is that we did not measure neutralizing antibodies. However, the neutralizing antibody and ELISA results generally correlate with each other [5], and RBD is the target of most neutralizing antibodies against SARS-CoV-2 [6].

Although the protective role of antibodies is currently unknown, our results show that SARS-CoV-2 antibodies persisted at least 12 months after symptom onset and maybe even longer, indicating that COVID-19-convalescent individuals may be protected from reinfection. Our results represent SARS-CoV-2 antibody immunity in nationwide cohorts in a setting with few undetected cases [7], and we believe that our results add to the understanding of natural immunity and the expected durability of SARS-CoV-2 vaccine immune responses. Moreover, they can help with public health policy and ongoing strategies for vaccine delivery.

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Patient consent. All participants provided written informed consent. The study was approved by the Faroese Bioethics Committee and the Data Protection Agency.

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References

1. Dan JM, Mateus J, Kato Y, et al. Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection. Science. **2021**; 371:eabf4063.
2. Anand SP, Prévost J, Nayrac M, et al. Longitudinal analysis of humoral immunity against SARS-CoV-2 spike in convalescent individuals up to eight months post-symptom onset. Cell Rep Med. **2021**; 2(6):100290.
3. Strøm M, Kristiansen MF, Christiansen DH, et al. Elimination of COVID-19 in the Faroe Islands: effectiveness of massive testing and intensive case and contact tracing. Lancet Reg Health Eur **2021**; 1:100011.
4. Hansen CB, Jarlhelt I, Pérez-Alós L, et al. SARS-CoV-2 antibody responses are correlated to disease severity in COVID-19 convalescent individuals. J Immunol **2021**; 206:109–17.
5. Iyer AS, Jones FK, Nodoushani A, et al. Persistence and decay of human antibody responses to the receptor binding domain of SARS-CoV-2 spike protein in COVID-19 patients. Sci Immunol. **In press**.
6. Ju B, Zhang Q, Ge J, et al. Human neutralizing antibodies elicited by SARS-CoV-2 infection. Nature **2020**; 584:115–9.
7. Petersen MS, Strøm M, Christiansen DH, et al. Seroprevalence of SARS-CoV-2-specific antibodies, Faroe Islands. Emerg Infect Dis **2020**; 26:2761–3.

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