SARS-CoV-2 natural antibody response persists up to 12 months in a nationwide study from the Faroe Islands.

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Abstract

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).

In this nationwide longitudinal study from the Faroe Islands with close to full participation of all individuals on the Islands with PCR confirmed COVID-19 during the two waves of infections in the spring and autumn 2020 (n=172 & n=233), samples were drawn at three longitudinal time points (3, 7 and 12 months and 1, 3 and 7 months after disease onset, respectively).

Serum was analyzed with a direct quantitative IgG antibody binding ELISA to detect anti–SARS-CoV-2 spike RBD antibodies and a commercially available qualitative sandwich RBD ELISA kit measuring total antibody binding.

The seropositive rate in the convalescent individuals was above 95 % at all sampling time points for both assays. There was an overall decline in IgG titers over time in both waves ($p < 0.001$). Pairwise comparison showed that IgG declined significantly from the first sample until approximately 7 months in both waves ($p < 0.001$). After that, the antibody level still declined significantly ($p < 0.001$), but decelerated with an altered slope remaining fairly stable from 7 months to 12 months after infection. Interestingly, the IgG titers followed a U-shaped curve with higher antibody levels among the oldest (67+) and the youngest (0–17) age groups compared to intermediate groups ($p < 0.001$).

Our results indicate that COVID-19 convalescent individuals are likely to be protected from reinfection at least 12 months after symptom onset and maybe even longer. We believe our results can add to the understanding of natural immunity and the expected durability of SARS-CoV-2 vaccine immune responses.

Research letter

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 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 results of natural IgG response to SARS-CoV-2 infection up to 12 months from symptom onset in a longitudinal nationwide study from the Faroe Islands[3] with close to full participation of all individuals with polymerase chain reaction (PCR) confirmed COVID-19 during two waves of infections (March to April and August to December 2020). Samples were drawn at three longitudinal time points for each wave: wave 1 at median 89, 210 and 363 days (range 29–380 days), and wave 2 at median 27, 125 and 210 days (range 27–231 days) after symptom onset, respectively (wave 1: n = 172, 54% women, median age 42, range 1–93 years; wave 2: n = 233, 53% women, median age 35, range 0–83 years). There was no observed overlap among the two 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 (table 1 for study characteristics).

Serum was analyzed with a direct quantitative IgG antibody binding ELISA to detect anti–SARS-CoV-2 spike RBD antibodies[4] and a commercially available qualitative sandwich RBD ELISA kit measuring total antibody binding (Beijing Wantai Biological Pharmacy Enterprise Co., Ltd., China).

The seropositive rate in the convalescent individuals was above 95 % at all sampling time points for both assays and remained stable over time, i.e. almost all convalescent individuals developed antibodies. There was an overall decline in IgG titers over time in both waves (Friedman test: $\chi^2(2) = 134.684$, $p < 0.001$ and $\chi^2(2) = 112.407$, $p < 0.001$) (figure 1a). Wilcox Signed-Ranks pairwise comparison showed that IgG declined significantly from the first sample until approximately 7 months in both waves ($p < 0.001$; figure 1a). After that, the antibody level still declined significantly, but decelerated with an altered slope remaining fairly stable from 7 months to 12 months after infection ($p < 0.001$). Antibody levels did not differ significantly between women and men over time ($p = 0.09 – p = 0.8$). Interestingly, the IgG titers followed a U-shaped curve with higher antibody levels among the oldest (67+) and the youngest (0–17) age groups compared to intermediate groups (figure 1b and 1c) (Kruskal-Wallis test: $\chi^2(2) = 17.943$, $p = 0.001$ and $\chi^2(2) = 52.048$, $p < 0.001$).

Albeit the protective role of antibodies is currently unknown, our results indicate that COVID-19 convalescent individuals are likely to be protected from reinfection at least 12 months after symptom onset and maybe even longer. Our results represent SARS-CoV-2 antibody immunity in nationwide cohorts in a setting with few undetected cases[5] and we believe our results can add to the understanding of natural immunity and the expected durability of SARS-CoV-2 vaccine immune responses. Moreover, they can help in public health policies and ongoing strategies for vaccine delivery.

Funding

The project is funded by the special COVID-19 funding from the Faroese Research Council, The Carlsberg Foundation (CF20-0045) and the Novo Nordisk Foundation (NNF20SA0063180 and NFF205A0063505) and the cooperations: Nótaskip, Krúnborg og Borgartún.

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Table 1. Characteristics of the COVID-19 patients in the Faroe Islands from March 2020 to December 2020, stratified in two waves (n = 172 and n = 233)

	Wave 1 (n = 172)		Wave 2 (n = 233)	
Sex, n (%)				
Female	92	53.5	123	52.8
Age				
Age (years), median (range)	42.3	1.2–92.9	34.7	0.27–82.6
Age distribution, n (%)				
0-17	17	9.8	27	11.6
18-34	54	31.2	90	38.6
35-49	39	22.5	56	24.0
50-66	45	26	41	17.6
67+	18	10.4	19	8.2
Symptoms during the acute phase[b], n (%)				
Asymptomatic[a]	33	19.2	32	15.9
Cough *	78	45.3	116	57.4
Fever*	110	64.0	107	53.2
Sore throat*	53	30.8	77	38.3
Headache*	84	48.8	112	60.7
Dyspnea*	19	11.0	32	15.9
Days from symptoms onset to blood sampling, median (range)				
First blood sample	89	29–163	27	10–79
Second blood sample	210	171–294	125	45–191
Third blood sample	363	302–380	210	94–231
Number of samples delivered, n				
First sample	168		221	
Two sample	139		221	
Three samples	158		153	
Disease groups, n (%)[c]				
Hospitalized	8	4.7	6	3.0
Asymptomatic[a]	33	18.6	31	15.3
Symptomatic	132	76.7	165	81.7

[a]Asymptomatic for the five symptoms which were asked about directly, not necessarily other symptoms; [b]n = 32 missing in wave 2; [c]n = 31 missing in wave 2.

Figure 1

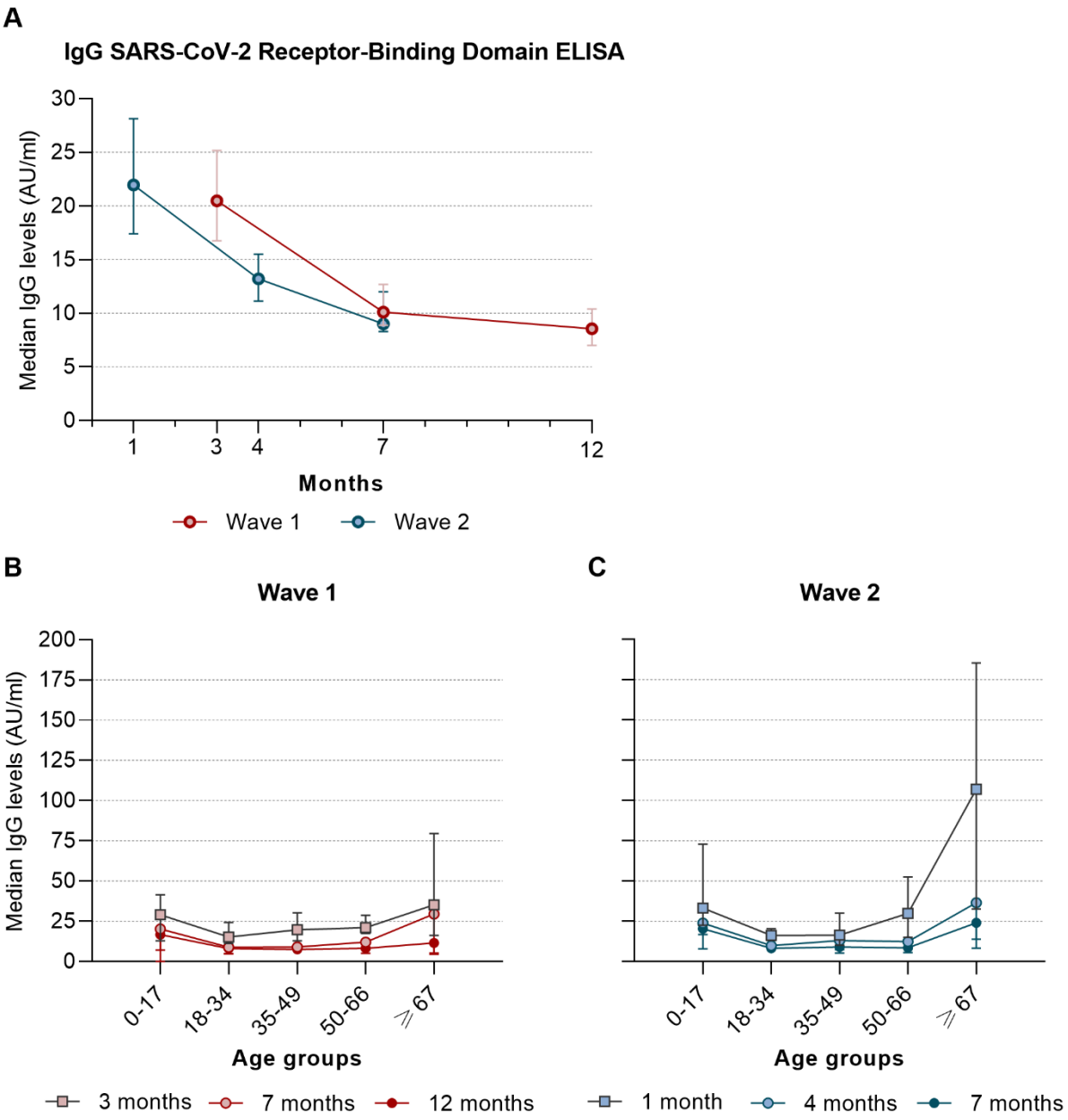

Figure 1. Longitudinal analyses of serum samples from COVID-19 patients in the Faroe Islands from March 2020 to December 2020, stratified in two waves.

a) Median IgG antibody titers plotted against median time from symptom onset to sampling. Data is expressed as median with 95 % confidence intervals. Median antibody titers were 22.7 AU/ml ((range:3.8–584.3 AU/ml), 11.8 AU/ml (0.1–200 AU/ml) and 9.1 AU/ml (1.7–104.7 AU/ml) respectively from 3 to up to 12 months in wave 1 (red line), and 24.6 AU/ml (2.9–842.5 AU/ml), 13.9 AU/ml (2.0–719.4 AU/ml) and 9.3 AU/ml (1.8–388.4 AU/ml) from 1 to 7 months (blue line). Friedman test showed an overall

decline in IgG titers over time in both waves ($\chi^2(2) = 134.684$, $p < 0.001$ and $\chi^2(2) = 112.407$, $p < 0.001$). Wilcox Signed-Ranks test pairwise comparison showed a significant decline between all time points (p<0.001).

b) Median IgG titers in wave 1 plotted against age group. Kruskal-Wallis test showed significant difference in antibody levels in age groups ($\chi2(2) = 17.943$, $p = 0.001$ and $\chi2(2) = 52.048$, $p < 0.001$). Pairwise comparisons (Mann-Whitney U test) indicated that the oldest age group had higher median IgG titers compared with the age groups 18-49 years, albeit only significantly in the first sample (p=0.01 and p=0.04) while age group 17+ had significantly higher IgG levels compared with the age group 18-34 ($p = 0.03$ in all samples.

c) Median IgG titers in wave 2 plotted against on age group. Kruskal-Wallis test showed significant difference in antibody levels in age groups ($\chi2(2) = 17.943$, $p = 0.001$ and $\chi2(2) = 52.048$, $p < 0.001$). Pairwise comparisons (Mann-Whitney U test) indicated that the oldest age group had significantly higher median IgG titers compared with all age groups ($p \leq 0.005$) in first sample while in the second and third sample, IgG levels were higher compared with all age groups ($p \leq 0.003$) except the youngest age group ($p = 0.2$ and $p = 0.6$). Age group 17+ had significantly higher IgG levels compared with age groups 18–66 years in second sample and third sample ($p < 0.001$ to $p = 0.04$).