

SYNOPSIS

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Review of “Humoral immune response to SARS-CoV-2 in Iceland”

Article citation: Gudbjartsson DF, Norddahl GL, Melsted P, Gunnarsdottir K, Holm H, Eythorsson E, et al. Humoral immune response to SARS-CoV-2 in Iceland. *New Engl J Med*. 2020 Sep 01 [Epub ahead of print]. Available from: <https://doi.org/10.1056/NEJMoa2026116>

One-minute summary

- The authors assessed Coronavirus Disease 2019 (COVID-19) seroprevalence among 30,576 Iceland residents.
- Using positivity data by quantitative polymerase chain reaction (qPCR) and serological status, the authors **estimate that 0.9% (95% CI: 0.8%–0.9%) of Iceland residents have been infected with COVID-19.**
- At 25 days after diagnosis, 91.2% (1,152/1,263) tested positive with two pan-Ig antibody assays. Among 487 qPCR-positive persons with repeat serum samples:
 - **Antibody levels plateaued for 120 days after diagnosis.**
 - **IgM anti-N antibody level rose and fell rapidly shortly after diagnosis to undetectable levels after 2 months.**
 - **IgA anti-S1 antibody level dropped 1 month after diagnosis and remained detectable thereafter.**
 - **IgG anti-N and anti-S1 antibody levels rose for 6 weeks after diagnosis before dropping slightly.**
- **Higher antibody levels** were associated with older age, hospitalization, clinical severity and higher body-mass index; **lower antibody levels** were associated with smoking, being female and the use of anti-inflammatory medication.
- **Among 22 qPCR-positive persons who tested negative with both pan-Ig antibody assays, 19 tested negative again at least a month later.** The authors propose this could either be due to prior false-positive qPCR results or that some persons produce no or undetectable levels of antibodies even 3 months after infection.
- **Household exposure** was **more likely** than other types of exposure to **result in infection with COVID-19.**

Additional information

- To estimate the prevalence of COVID-19 infection in Iceland, serum samples were obtained from:
 - 1,237 hospitalized and recovered COVID-19 patients
 - 4,222 persons in quarantine

- 23,452 persons outside quarantine and never been tested for COVID-19 with qPCR
- To assess changes in antibody levels, 487 recovered qPCR-positive persons provided multiple serum samples, with first serum samples were collected at least 3 weeks after qPCR diagnosis and final serum samples were taken at least one month after the first sample.
- In view of the low prevalence of COVID-19 infection in Iceland, seropositivity in this study required testing positive for both pan-Ig anti-N assay and pan-Ig anti-S1-RBD assay.
- **Higher antibody levels were associated with:**
 - **Increasing age** ($P < .000001$ for both pan-Ig antibody assays)
 - **hospitalization** ($P < .00013$ for pan-Ig anti-S1-RBD)
 - **clinical severity** ($P < .00013$ for pan-Ig anti-N; $P < .000001$ for pan-Ig anti-S1-RBD); clinical severity was categorized into 3 stages:
 - low: with mild symptoms
 - moderate: with mild dyspnea, cough or fever for less than 5 days
 - high: with severe dyspnea, worsening cough, high or persistent fever for 5 days or more, or severe fatigue
 - **higher body-mass index** ($P < .00013$ for pan-Ig anti-N; $P < .05$ for pan-Ig anti-S1-RBD); categorization of body-mass index scale was not reported
- **Lower antibody levels were associated with:**
 - **smoking** ($P < .00013$ for both pan-Ig antibody assays)
 - **being female** ($P < .00013$ for pan-Ig anti-S1-RBD)
 - **use of anti-inflammatory medication** ($P < .05$ for both pan-Ig antibody assays); medication use was based on patient self-report to the question: “Do you take anti-inflammatory medication weekly or more often?”
- Proposed explanations for the longer persistence of antibodies than other studies include difference in sensitivity and specificity in the antibody assays used and the likelihood of healthier qPCR-positive persons in Iceland due to widespread testing (15% of the Iceland population had been tested with qPCR by June 15, 2020).
- **Among the infected, the authors estimate that:**
 - **56% had been diagnosed previously with qPCR**
 - 14% had been in quarantine but either not tested or tested negative with qPCR
 - 30% had never been quarantined or tested with qPCR
- **Household members** of someone infected with COVID-19 were **more likely to test positive by qPCR (odds ratio: 5.2; 95% CI 4.5–6.1) and more likely to seroconvert (odds ratio: 5.2; 95% CI 3.3–8.0)**. The authors suggest that for persons sharing a household with an infected person, they should refrain from contact with the infected person during their quarantine; also, contacts of household members should be quarantined.

PHO reviewer’s comments

- In estimating the prevalence of COVID-19 infection among Iceland residents, the authors obtained data from an inclusive set of samples embracing hospitalized and recovered patients with COVID-19, contacts under quarantine, as well as the general public. However, as demographic details on the sample and population are not reported, one should be cautious in generalizing the information to populations beyond Iceland residents.
- Cautions should also be exercised in extrapolating the information on the nature and durability of humoral immune response to COVID-19 infection, which may present different characteristics

depending on the sensitivity and specificity of the antibody assays used and the health status of the patient population.

Citation

Ontario Agency for Health Protection and Promotion (Public Health Ontario). Review of “Humoral immune response to SARS-CoV-2 in Iceland”. Toronto, ON: Queen’s Printer for Ontario; 2020.

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