Journal of Epidemiology

Letter to the Editor

J Epidemiol 2023;33(1):62-62

Seropositivity for SARS-CoV-2 in a General Population: How Specific Is the Diagnostic?

Zhaoqing Lyu, Tomoko Fujitani, and Kouji H. Harada

Department of Health Environmental Sciences, Kyoto University Graduate School of Medicine, Kyoto, Japan

Received May 20, 2022; accepted May 25, 2022; released online July 30, 2022

Key words: seroprevalence; SARS-CoV-2; specificity; IgG; immunological response

We read the article by Sanada et al in the Journal of Epidemiology[1] with great interest. The authors surveyed the seroprevalence of immunoglobulin G (IgG) against SARS-CoV-2 among hospital visitors from September 2020 to March 2021 and found an estimate of 3.40% seropositivity in the Tokyo area. This was 3.9-fold higher than polymerase chain reaction (PCR)-based cases of novel coronavirus disease 2019 (COVID-19).

We have comments on this study regarding the specificity of testing and target proteins. The authors employed two chemiluminescence immunoassay kits (iFlash–SARS-CoV-2 IgG kit and iFlash–SARS-CoV-2 IgG-S1 kit). They are validated better than previous point-of-care testing.[2] In the methods section, the authors claimed that the diagnostics showed 100% specificity that was calculated in limited sample numbers (around 100) in the cited literature.[3] The authors also conducted the test by YHLO S1-IgG in PCR-negative subjects ($n = 163$) and found no positive sample. The point estimate of false positive rate (1-specificity) is 0% but the 95% confidence interval is 0–2.3%. The confidence interval should be considered for a low prevalence situation.

The authors used two test kits and found a number of single positive samples (Figure 2 of the article).[1] The authors stated that "although the iFlash–SARSCoV-2 IgG kit detects anti-N and anti-S antibodies (YHLO IgG), it primarily detects anti-N antibodies".[1] If this is correct, the samples with a single positive result only contained either anti-S1 or anti-N antibody. Is this possible? Immunological responses in COVID-19 patients showed elevated IgG antibodies against the N protein, the S1 subunit of the spike protein, and the receptor-binding domain of the spike protein of SARS-CoV-2.[4] It is possible that they were false positives. The specificity of anti-N antibody is less than that of anti-S antibody because of cross-reactivity with other coronaviruses.[5] Validation in pre-COVID-19 samples would help the estimation of non-specific cross-reactions.[6] In addition, the authors conducted the survey from September 1, 2020, to March 31, 2021, and vaccination for COVID-19, which induces anti-S antibodies, began in Japan in 2021. The vaccination status of the participants was not confirmed. It may contaminate the seroprevalence rate.

This is a minor point, but the method to detect anti-N protein antibody titer was not provided in eFigure 1 of the article.[1]

ACKNOWLEDGEMENTS

Data availability: There are no new data associated with this article.

Author contributions: ZL, TF, and KHH drafted the manuscript. All the authors read and approved the final manuscript.

Funding: There was no funding support for this letter.

Conflicts of interest: None declared.

REFERENCES

1. Sanada T, Honda T, Yasui F, et al. Serologic survey of IgG against SARS-CoV-2 among hospital visitors without a history of SARS-CoV-2 infection in Tokyo, 2020–2021. *J Epidemiol*. 2022 Feb 5;32(2):105–111.
2. Takita M, Matsumura T, Yamamoto K, et al. Geographical profiles of COVID-19 outbreak in Tokyo: an analysis of the primary care clinic-based point-of-care antibody testing. *J Prim Care Community Health*. 2020;11:2150132720942695.
3. Parai D, Dash GC, Choudhary HR, et al. Diagnostic accuracy comparison of three fully automated chemiluminescent immunoassay platforms for the detection of SARS-CoV-2 antibodies. *J Virol Methods*. 2021 Jun;292:114121.
4. Kurano M, Morita Y, Nakano Y, et al. Response kinetics of different classes of antibodies to SARS-CoV2 infection in the Japanese population: the IgA and IgG titers increased earlier than the IgM titers. *Int Immunopharmacol*. 2022 Feb;103:108491.
5. Kontou PI, Braliou GG, Dimou NL, Nikolopoulos G, Bagos PG. Antibody tests in detecting SARS-CoV-2 infection: a meta-analysis. *Diagnostics (Basel)*. 2020 May 19;10(5):319.
6. Lyu Z, Harada Sassa M, Fujitani T, Harada KH. Serological tests for SARS-CoV-2 coronavirus by commercially available point-of-care and laboratory diagnostics in pre-COVID-19 samples in Japan. *Diseases*. 2020 Sep 23;8(4):36.

Address for correspondence. Kouji Harada, Department of Health and Environmental Sciences, Kyoto University Graduate School of Medicine, Kyoto 606-8501, Japan (e-mail: kharada-hes@umin.ac.jp).

DOI https://doi.org/10.2188/jea.JE20220151
HOMEPAGE http://jeaweb.jp/english/journal/index.html