PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Seroprevalence of anti-SARS-CoV-2 IgG among health-care workers of a large university Hospital in Milan, Lombardy, Italy
AUTHORS	Lombardi, Andrea; Mangioni, Davide; Consonni, Dario; Cariani, Lisa; Bono, Patrizia; Cantù, Anna; Tiso, Basilio; Carugno, Michele; Muscatello, Antonio; Lunghi, Giovanna; Pesatori, Angela; Riboldi, Luciano; Ceriotti, Ferruccio; Bandera, Alessandra; Gori, Andrea

VERSION 1 – REVIEW

REVIEWER	Edison J. Cano, MD Mayo Clinic, USA.
REVIEW RETURNED	06-Jan-2021

GENERAL COMMENTS	In this work, the authors present a sample of healthcare workers (HCWs) that were tested for anti-SARS-CoV-2 IgG during the COVID-19 pandemic in Italy. This is an overall well thought out and relevant work encompassing more than 4000 HCWs and confirms previous findings in a different setting. I would recommend the following changes/edits if possible: 1. Would be useful for the reader to have a few lines on how this particular serologic test behaves and losses sensitivity for confirmed cases over time if there is any data available. If there is no data available for this assay, then add info on how serologies decline over time 2. For this reason, it would be useful to add the date of the 1st COVID-19 case reported in the community and in the hospital where this study was carried, preferably right after describing the study timeline (it is vaguely reported in the discussion) 3. The prevalence of reported symptoms in this sample is of limited value without the date of serologic testing, particularly symptoms such as headache, myalgias, asthenia during a pandemic with overwhelmed HCWs. If the date of reported symptom is available, stratification of seropositivity by symptoms only in a subset of HCWs tested within 30 days (for example) of reported symptoms would be useful 4. Lastly, this study includes HCWs who were asked to respond to a questionnaire, yet HCWs victims to COVID-19 are well known in Italy and worldwide. Is it possible for the authors to draw any data on how many of those 517 HCWs who did not respond to the questionnaire had SARS-CoV-2 infection? Perhaps within their own IRB to look up and contrast known cases in their hospital to avoid selection bias

	Great work!

REVIEWER	Vidya Menon New York City Health +Hospitals/Lincoln Unites States of America
REVIEW RETURNED	08-Jan-2021

GENERAL COMMENTS	The serology assay being a quantitative assay, have you reviewed the data with respect to the titers of the Spike antibody and its correlation to clinical/baseline characteristics.

VERSION 1 – AUTHOR RESPONSE

1- Would be useful for the reader to have a few lines on how this particular serologic test behaves and losses sensitivity for confirmed cases over time if there is any data available. If there is no data available for this assay, then add info on how serologies decline over time.
We have added the following sentence: "No data are available about the performance over time of this specific test. Nonetheless, evidence is suggesting that, 6 months after reaching their maximum levels, anti-spike IgG are still detectable in almost all (94%) those infected". We are citing the results provided by Lumley et al. The duration, dynamics and determinants of SARS-CoV-2 antibody responses in individual healthcare workers. Clin Infect Dis (2021) 0:1–14. Moreover, we have cited also the following papers assessing the dynamics of anti-SARS-COV-2 antibodies:
1. Ward H, Cooke G, Atchison C, Whitaker M, Elliott J, Moshe M, Brown JC, Flower B, Daunt A, Ainslie K, et al. Declining prevalence of antibody positivity to SARS-CoV-2: a community study of 365,000 adults. medXriv (2020) doi:10.1101/2020.10.26.20219725
2. L'Huillier AG, Meyer B, Andrey DO, Arm-Vernez I, Baggio S, Didierlaurent A, Eberhardt CS, Eckerle I, Grasset-Salomon C, Huttner A, et al. Antibody persistence in the first six months following SARS-CoV-2 infection among hospital workers: a prospective longitudinal study. Clin Microbiol Infect (2021) doi:10.1016/j.cmi.2021.01.005
3. Wajnberg A, Amanat F, Firpo A, Altman DR, Bailey MJ, Mansour M, McMahon M, Meade P, Mendu DR, Muellers K, et al. Robust neutralizing antibodies to SARS-CoV-2 infection persist for months. Science (80-) (2020) 370:1227–1230. doi:10.1126/science.abd7728
4. Gudbjartsson DF, Norddahl GL, Melsted P, Gunnarsdottir K, Holm H, Eythorsson E, Arnthorsson AO, Helgason D, Bjarnadottir K, Ingvarsson RF, et al. Humoral Immune Response to SARS-CoV-2 in Iceland. N Engl J Med (2020) 383:1724–1734. doi:10.1056/nejmoa2026116
5. Seow J, Graham C, Merrick B, Acors S, Pickering S, Steel KJA, Hemmings O, O'Byrne A, Kouphou N, Galao RP, et al. Longitudinal observation and decline of neutralizing antibody responses in the three months following SARS-CoV-2 infection in humans. Nat Microbiol (2020) 5:1598–1607. doi:10.1038/s41564-020-00813-8

2- For this reason, it would be useful to add the date of the 1st COVID-19 case reported in the community and in the hospital where this study was carried, preferably right after describing the study timeline (it is vaguely reported in the discussion).
We have specified in the Methods section when the first case of COVID-19 was documented in our hospital (February 23, 2020).

3- The prevalence of reported symptoms in this sample is of limited value without the date of serologic testing, particularly symptoms such as headache, myalgias, asthenia during a pandemic with overwhelmed HCWs. If the date of reported symptom is available, stratification of seropositivity by symptoms only in a subset of HCWs tested within 30 days (for example) of reported symptoms would be useful.

Unfortunately, we do not have the date of symptoms appearance and therefore we can not perform the suggested analysis.

4- Lastly, this study includes HCWs who were asked to respond to a questionnaire, yet HCWs victims to COVID-19 are well known in Italy and worldwide. Is it possible for the authors to draw any data on how many of those 517 HCWs who did not respond to the questionnaire had SARS-CoV-2 infection? Perhaps within their own IRB to look up and contrast known cases in their hospital to avoid selection bias.
Personal data protection policies of our institution do not allow us to have access to individual data of those who did not answered to our questionnaire. Therefore, we cannot correctly estimate the proportion of positives among those who did not respond to the questionnaire.

5- The serology assay being a quantitative assay, have you reviewed the data with respect to the titers of the Spike antibody and its correlation to clinical/baseline characteristics.
Unfortunately, we have not performed the suggested analysis.

VERSION 2 – REVIEW

REVIEWER	Edison Cano Mayo Clinic, USA
REVIEW RETURNED	03-Feb-2021

GENERAL COMMENTS	No additional comments