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Letter to the editor

‘Post-COVID-19 syndrome and humoral response association after one year in vaccinated and unvaccinated patients’: authors’ response

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To the Editor,

We thank Drs Pathum Sookaromdee and Viroj Wiwanitkit for their thoughtful remarks on our study on the role of vaccination and humoral response in post-COVID-19 syndrome after one year. Their letter raises important issues, and we appreciate the opportunity to address these. Based on our data, the SARS-CoV-2 vaccination should be recommended for patients with a history of previous COVID-19 infection, regardless of age and severity of acute disease, because hybrid immunity may not worsen *sequelae* and may reduce their risk of reinfection to avoid a vicious immune circle.

We concur that one of the main limitations of our study is that rates of asymptomatic reinfection may be underestimated, since reinfections were not routinely checked [1]. Natural infection with SARS-CoV-2 has been shown to elicit strong protection against reinfection with the B.1.1.7 (Alpha), B.1.351 (Beta), and B.1.617.2 (Delta) variants, with a lower overall incidence rate of COVID-19 reinfections (range 0.15%–2.2%) [1,2]. The risk of reinfection with B.1.1.529 (Omicron) variant in individuals previously infected with other variants has been described to be higher ($\leq 10\%$) [2]. However, our study included patients cared for during the first wave of the

pandemic (March–May 2020) and the follow-up was performed up to May 2021, when the SARS-CoV-2 wild type and B.1.1.7 (alpha) variant were mainly circulating in Italy. Therefore, as many as 50% of people infected with COVID-19 have no symptoms, we estimate that we might have missed very few asymptomatic reinfections in our cohort (range 0–5 episodes) and that it might not impact our results.

We also agree that the role of asymptomatic infection is an important and interesting topic that may influence the immunological response and the development of post-COVID-19 syndrome and that should be further explored. Data regarding asymptomatic patients over time are still scarce. Serological response and kinetics are significantly different between symptomatic and asymptomatic patients, since asymptomatic individuals maintain low levels of IgG with rapid seroreversion [3]. We believe that the humoral response of asymptomatic patients provides interesting insights, since it could be the result of the complex balance between the individual immune state and the inflammatory response against SARS-CoV-2, manifesting itself in an asymptomatic acute infection and absence of development of post COVID-19 syndrome. Of note in our cohort we found that 5.4% (3 of 55) and 7.2% (4 of 55) asymptomatic patients at acute onset complained symptoms at 6- and 12-month follow-up respectively [4,5]. Interestingly, taking into consideration the limited size, two out of three and two out of four maintained serological response at 6- and 12-month postinfection follow-up respectively.

In conclusion, we concur with Drs Sookaromdee and Wiwanitkit that there are critical unmet needs for the study of clinical and immunological parameters in post-COVID-19 syndrome prediction after acute infection. Further studies are needed to better understand the pathophysiology and immune mechanisms linking acute viral injury to downstream post-COVID-19 syndrome in patients with different degrees of severity, including asymptomatic patients, to inform preventive policies and lines of treatment for prevention and treatment.

Transparency declaration

The authors declare that they have no conflict of interest.

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References

- [1] Peghin M, Bouza E, Fabris M, De Martino M, Palese A, Bontempo G, et al. Low risk of reinfections and relation with serological response after recovery from the first wave of COVID-19. *Eur J Clin Microbiol Infect Dis* 2021;40:2597–604.
- [2] Altarawneh HN, Chemaitelly H, Hasan MR, Ayoub HH, Qassim S, AlMukdad S, et al. Protection against the omicron variant from previous SARS-CoV-2 infection. *N Engl J Med* 2022;386:1288–90.
- [3] Peghin M, De Martino M, Fabris M, Palese E, Graziano E, Gerussi V, et al. The fall in antibody response to SARS-CoV-2: a longitudinal study of asymptomatic to critically ill patients up to 10 months after recovery. *J Clin Microbiol* 2021;59:e0113821.
- [4] Peghin M, Palese A, Venturini M, De Martino M, Gerussi V, Graziano E, et al. Post-COVID-19 symptoms 6 months after acute infection among hospitalized and non-hospitalized patients. *Clin Microbiol Infect* 2021;27:1507–13.
- [5] Peghin M, De Martino M, Palese A, Gerussi V, Bontempo G, Graziano E, et al. Post-COVID-19 syndrome and humoral response association after 1 year in vaccinated and unvaccinated patients. *Clin Microbiol Infect* 2022;28:1140–8.