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## Letter to the Editor

**Reply to letter to the editor by Lippi and Plebani: « The presence of anti-SARS-CoV-2 antibodies does not necessarily reflect efficient neutralization » (THEIJID-D-22-00085)**



We thank Lippi and Plebani for their comments on our article: “Evidence of SARS-CoV-2 Symptomatic Reinfection in Four Health Care Professionals from the Same Hospital Despite the Presence of Antibodies” (Gargouri *et al.*, 2022). Our study confirmed SARS-CoV-2 reinfection in 4 health care workers (HCW). Although anti-S1 immunoglobulin G (IgG) was detectable before reinfection in 3 patients, all of them developed symptomatic secondary infection after a symptom-free interval ranging between 45 and 141 days, with a more severe clinical presentation in 2 cases.

Lippi and Plebani pointed out that the presence of anti-SARS-CoV-2 antibodies does not necessarily reflect efficient neutralization. They suggested the following conclusion “reinfection occurred with the presence of low values of anti-S1 IgG antibodies” instead of “reinfection occurred despite the presence of antibodies”. Indeed, we would like to clarify this point. Lippi and Plebani mentioned the work carried out by Montesinos *et al.* (Montesinos *et al.*, 2021), who compared different serological tests, including the one used in our study (VIDAS SARS-CoV-2 IgG serologic test), and who support the use of this test to monitor neutralizing antibody response following natural SARS-CoV-2 infection. However, contrary to Lippi *et al.*, who mentioned negative predictive value (NPV) as a base to point out that several samples of patients with low values of these antibodies (and even samples of sero-reverted patients with a negative result) may retain significant neutralizing potential, in our study we chose to consider the specificity of the test and we will discuss the reason for that choice.

It is worth noting that predictive values (both positive and negative predictive values; PPV and NPV) depend upon the prevalence of the disease in a population. As the prevalence of the disease increases (that is, true positives are more common), the likelihood of a false positive decreases. Therefore, predictive values can change over time or in different places, whereas sensitivity and specificity do not change, as these are characteristics of the test itself. Therefore, both PPV and NPV are dependent on the proportion of the test population that has the disease (otherwise known as prevalence) Montesinos *et al.* (2021). carried out their work using samples collected between April 15, 2020, and December 7, 2020 (Belgium), whereas our samples were collected between August 2020 and October 2020. During this period, the prevalence of COVID-19 was very different between Tunisia and Belgium as well as within each country. For this reason, we rather considered the specificity of the test, which measures the proportion of negative test results out of all truly negative samples. The VIDAS test, used in our study, showed the best specificity (89% vs. 54.7%–79.7%).

Thus, it is clear that these results support our conclusion “Reinfection despite the presence of antibodies”, which means, based on the study of Montesinos *et al.*, “despite the presence of potentially neutralizing antibodies”. Second, according to Lumley *et al.* (Lumley *et al.*, 2021), the presence of anti-spike antibodies was associated with a substantially reduced risk of SARS-CoV-2 reinfection in the ensuing 6 months, and no symptomatic infections in HCWs with these antibodies were observed. Furthermore, Montesinos *et al.* (Montesinos *et al.*, 2021) showed that only a minority (16.9%) of the HCWs lost neutralizing antibodies within at least 6 months. Interestingly, in our study, all 4 reinfection cases occurred within a short period and all of them were symptomatic with a severe outcome in 2 patients.

Finally, we appreciate this comment on our findings and hope that our work contributes to the growing body of knowledge about SARS-CoV-2 reinfection.

#### Declaration of competing interest

All authors declare no competing interest.

#### Ethical approval

Not applicable

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