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Risk of SARS-CoV-2 infection in Nursing Home residents according to COVID history and IgG(S) levels

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**Brief summary:** History of past COVID-19 and age, but not IgG(S) levels, are a major determinant for risk of SARS-CoV-2 infection in old Nursing Home residents

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Introduction

From the onset of the pandemic, very old frail adults, such as Nursing Home (NH) residents, were among the populations most likely to develop severe forms of COVID-19. Mass vaccination of this population has resulted in an impressive decrease in COVID-19-related morbidity and mortality.\(^1\)

In a previous study in NH residents, we reported that history of COVID-19 provided a clear advantage in the magnitude and duration of high (immunoglobulin G anti-Spike antibody, IgG(S)) titers following the 2\(^{nd}\) dose of COVID-19 mRNA vaccine BNT162b2 (BioNTech-Pfizer).\(^2\) The question here is whether a higher IgG(S) level as well as history of prior COVID-19 offers protection against SARS-CoV-2 infection.

Methods

We assessed the risk of SARS-CoV-2 infection in 234 NH residents all vaccinated with three doses of the BNT162b2 (mean age=87±9 years; 76% women), with IgG(S) quantification 39±9 days after the 3\(^{rd}\) dose. The follow-up of this cohort began the day of the 3\(^{rd}\) vaccination of each resident (09/15/2021 – 10/28/2021) and ended for all patients on May 15, 2022. Mean follow-up duration was 215±8 days. History of COVID-19 (i.e., positive RT-PCR) before the 3\(^{rd}\) vaccination was investigated retrospectively at the onset of the pandemic in France (March 1, 2020). Among the 234 residents, 54 had a history of COVID-19 prior to the 3\(^{rd}\) dose (04/10/2020 - 04/01/2021) and 71 developed SARS-CoV-2 infection after the last IgG(S) quantification (11/05/2021 – 04/24/2022). At the end of the study, none of the subjects of this cohort had died from COVID-19.
This study was registered in ClinicalTrials.gov (NCT04964024) and received the approval of the Ethics Committee of the University Hospital.

Results

Among residents with no history of COVID-19, 38% (68/180) were infected by SARS-CoV-2 after the 3rd vaccine dose vs. 6% (3/54) among those with history of COVID-19 (p<0.0001). Time between the 3rd vaccination and SARS-CoV-2 infection was 156±29 days and 138±79 days in residents with and without history of COVID-19, respectively (p=0.75).

Logistic regression analysis showed that the risk of SARS-CoV-2 infection was not associated with IgG(S) levels (p=0.45), but was 90% lower in residents with history of COVID-19 (p<0.001, Figure 1). Age was the only other significant determinant with a 50% increase in SARS-CoV-2 infection for each increase in 10 years of age (p=0.03).

Interestingly, 51 out of 54 NH residents with history of COVID-19 were not re-infected at the time of the study, i.e., after a mean of 588 days (409 to 765 days).

Discussion

We previously reported that, in vaccinated NH residents, history of COVID-19 induces a more pronounced IgG(S) response and longer protection². Here we show that history of COVID-19 was a very strong protector against SARS-CoV-2 infection but that IgG(S) level was not associated with this protection. Similarly, it has been demonstrated that, in young individuals (< 53 years-old), the risk of SARS-CoV-2 infection remained low for a longer period when vaccine immunity was combined with previous infection.³ Several studies have supported the beneficial effects of pre-exposure to SARS-CoV-2 for immune protection. Data in older individuals underscored that SARS-CoV-2 infection prior to
vaccination resulted in the best immune humoral responses to vaccination (e.g., anti-spike antibody levels and neutralization titers)\(^4\). In addition, increased frequencies of pre-existing S-II specific CD4\(^+\) T cells, following SARS-COV-2 pre-exposure, were associated with the efficacy of anti-S1 IgG and S1 neutralizing vaccination responses in the elderly\(^5\). Protection associated with previous COVID-19 infection may depend on i) non-neutralizing antibodies, which bind to viral proteins but do not neutralize SARS-CoV-2 and are deemed to contribute to the immune control of infection, even when serum neutralizing activity has declined\(^6\); ii) T cell responses directed towards SARS-CoV-2 antigens that are present in convalescent individuals at sufficient levels to mount a recall response upon reinfection\(^6\) although cannot be assessed through serological methods.

Since all NH-resident presented high IgG(S) levels at the time of the study, it was not possible to ascertain whether effective protection against SARS-CoV-2 infection, associated with history of COVID-19, will persist after the decrease in IgG(S) levels; nevertheless, specific cellular immunity has been observed in 50% of seronegative NHR, six months after vaccination\(^7\). In conclusion, in very old fully vaccinated NH residents, IgG(S) levels were not associated with protection against SARS-CoV-2 infection whereas absence of history of COVID-19 as well as older age were associated with a higher risk of SARS-CoV-2 infection.

The confirmation of these results in larger clinical studies could lead to the conclusion that in vaccinated NH residents, history of SARS-COV-2 infection can be a strong factor for return to a normal social life.

**Conflict of interest statement**

Authors have no conflict of interest.
References


Figure 1. Logistic regression of SARS-CoV-2 infection in Nursing Home residents after the 3rd vaccination. Absence of history of prior COVID-19 was associated with a 10-fold increase in the risk of SARS-CoV-2 infection. Age also was a significant determinant of the risk of SARS-CoV-2 infection. Sex and IgG anti-spike antibody (IgG(S)) levels following the 3rd dose of COVID-19 mRNA vaccine BNT162b2 (BioNTech-Pfizer) were not associated with the risk of SARS-CoV-2 infection.
<table>
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<th>Independent Variable</th>
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<th>Odds Ratio (CL95%)</th>
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<tr>
<td>Female (yes)</td>
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<td>1.32 (0.62-2.79)</td>
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<td>IgG (S) post 3rd vaccine (1 log10)</td>
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<td>0.79 (0.44-1.44)</td>
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<tr>
<td>History of COVID before 3rd vaccine</td>
<td>0.10</td>
<td>0.10 (0.03-0.34)</td>
<td>&lt;0.001</td>
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