JAMDA xxx (2022) 1–2

JAMDA

journal homepage: www.jamda.com

Research Letter

Risk of SARS-CoV-2 Infection in Nursing Home Residents According to COVID History and IgG Anti-Spike Antibody Levels

To the Editor:

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 the history of COVID-19 provided a clear advantage in the magnitude and duration of high (IgG anti-spike antibody, [IgG(S)]) titers following the second dose of COVID-19 messenger RNA 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 3 doses of the BNT162b2 (mean age 87 ± 9 years; 76% women), with IgG(S) quantification 39 ± 9 days after the third dose. The follow-up of this cohort began the day of the third vaccination of each resident (September 15, 2021—October 28, 2021) and ended for all patients on May 15, 2022. Mean follow-up duration was 215 ± 8 days. History of COVID-19 (ie, positive real-time polymerase chain reaction RT-PCR) before the third 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 third dose (April 10, 2020—April 1, 2021) and 71 developed SARS-CoV-2 infection after the last IgG(S) quantification (November 5, 2021—April 24, 2022). At the end of the study, none of the individuals 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 of 180) were infected by SARS-CoV-2 after the third vaccine dose vs 6% (3 of 54) among those with history of COVID-19 ($P < .0001$). Time between the third vaccination and SARS-CoV-2 infection was 156 ± 29 days and 138 ± 79 days in residents with and without history of COVID-19, respectively ($P = .75$).

Logistic regression analysis showed that the risk of SARS-CoV-2 infection was not associated with IgG(S) levels ($P = .45$) but was 90% lower in residents with history of COVID-19 ($P < .001$, 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 ($P = .03$).

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

Discussion

We previously reported that, in vaccinated NH residents, history of COVID-19 induces a more pronounced IgG(S) response and longer protection.[2] 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 (eg, anti-spike antibody levels and neutralization titers).[4] In addition, increased frequencies of pre-existing S-II specific CD41 T cells, following SARS-CoV-2 pre-exposure, were associated with the efficacy of anti-S1 IgG and S1 neutralizing vaccination responses in older individuals.[5] Protection associated with previous COVID-19 infection may depend on (1) 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]; and (2) T cell responses directed toward 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.

Because 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 NH residents, 6 months after vaccination.[7] In conclusion, in very old fully vaccinated NH residents, IgG(S) levels

Funded by the Agence Nationale de la Recherche, Grant/Award Number: ANR-15-IDEX-04-LUE.

The sponsor did not have any role in the design, methods, subject recruitment, data collection, analysis and interpretation of the results, or preparation of the article.

The authors declare no conflicts of interest.

https://doi.org/10.1016/j.jamda.2022.11.004

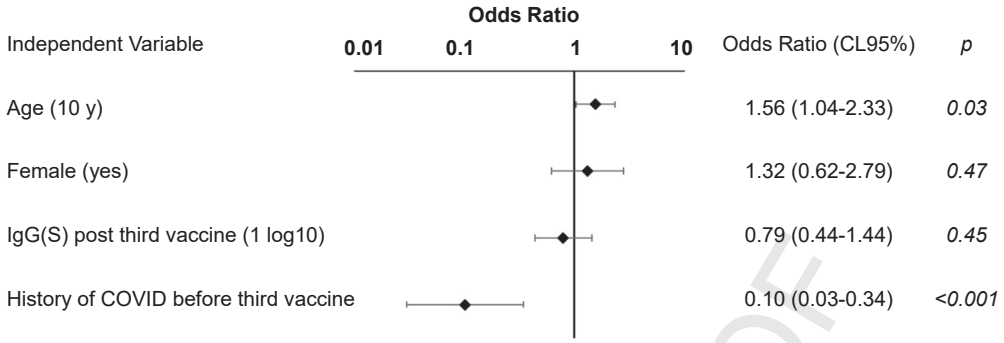

Fig. 1. Logistic regression of SARS-CoV-2 infection in NH residents after the third vaccination. Absence of history of prior COVID-19 was associated with a 10-fold increase in the risk of SARS-CoV-2 infection. Age also was a significant determinant of the risk of SARS-CoV-2 infection. Sex and IgG(S) levels following the third dose of COVID-19 messenger RNA vaccine BNT162b2 (BioNTech-Pfizer) were not associated with the risk of SARS-CoV-2 infection.

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.

Acknowledgments

We thank all the directors and the staff of the nursing homes of the Lorraine Region for contributing to the realization of this study. We thank Pierre Pothier for language review and stimulating discussions.

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