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Research note

Outbreak of SARS-CoV-2 B.1.617.2 (delta) variant in a nursing home 28 weeks after two doses of mRNA anti-COVID-19 vaccines: evidence of a waning immunity

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ABSTRACT

Objectives: To describe a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.617.2 (Delta) variant outbreak among residents ($n = 69$) and health workers ($n = 69$) of a small nursing home in northeastern Italy, with full vaccination coverage of 91% and 82%, respectively. Evaluation of the anti-Spike IgG titres 28 weeks after the mRNA vaccine booster dose against SARS-CoV-2 infection and severe coronavirus disease 2019 (COVID-19).

Materials and methods: Sera were collected within 48 hours from the index case; anti-Spike IgG was determined (expressed as WHO binding antibody units (BAU)/mL) through a commercial quantitative assay; SARS-CoV-2 was diagnosed using RT-PCR, and full-genome sequencing was performed for lineage characterization. Residents were grouped according to anti-Spike IgG titres ($\leq$50, 51–1000 and > 1000 BAU/mL) and the resulting protection against infection and severe disease was measured.

Results: None of the health workers and 14 of the 59 (24%) residents fully vaccinated and without a previous SARS-CoV-2 infection showed anti-Spike IgG $\leq$50 BAU/mL (one-sided Fisher exact test, p 0.011). Among these residents, a level of anti-Spike IgG $\leq$50 BAU/mL resulted in a higher risk of SARS-CoV-2 infection (relative risk 1.55, 95% CI 1.17–2.05) and severe COVID-19 (relative risk 5.33, 95% CI 1.83–15.57).

Conclusion: Low levels of SARS-CoV-2 neutralizing anti-Spike IgG in serum 28 weeks after the administration of the second dose parallel the waning of vaccine protection. **Alice Pierobon, Clin Microbiol Infect 2022;28:614.e5–614.e7**

Introduction

Outbreaks in long-term care facilities are considered sentinel events for re-infection after full vaccination, as the result of a sub-optimal antibody response due to the age of residents, underlying comorbidities and ongoing corticosteroid therapies [1]. In this regard, the recent spread of B.1.617.2 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Variant of Concern (VOC Delta) is of particular concern [2–4].

In this paper, we report an outbreak in a small nursing home in northeastern Italy that started on 25 August 2021, along with extensive and timely serological measurements of the SARS-CoV-2 anti-Spike IgG among residents. The aim is to shed some light on how a decrease in anti-Spike IgG titre parallels the waning of mRNA vaccine protection against the VOC Delta.

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Materials and methods

On 25 August 2021, a healthcare worker (HCW) tested positive to routine checks performed using a microfluidic immunofluorescence assay for the qualitative detection of nucleocapsid antigens (LumiraDX SARS-CoV-2 Ag).

Immediately, all residents and the nursery staff were screened with the same assay, and 12 additional residents and five HCWs tested positive. Within the next 48 hours, confirmatory molecular RT-PCR tests of nasopharyngeal swabs were carried out among all residents and HCW and ten swabs were sent to the accredited laboratory of Istituto Zooprofilattico Sperimentale delle Venezie for SARS-CoV-2 B.1.617.2 lineage characterization via Illumina MiSec platform. At the same time, blood samples were drawn from residents and a sample of HCWs, for the determination of both the anti-Spike IgM and IgG in sera (Abbott SARS-CoV-2 IgG II Quant Assay). IgG results were expressed in WHO binding antibody units (BAU) per mL, using the manufacturer's conversion factors, based on the WHO International Standard Anti-SARS-CoV-2 Immunoglobulin (NIBSC code 20-136) [5]. Testing was carried out at the Local Health Unit (ULSS 7 Pedemontana) analytical laboratory, under quality assurance/quality control. The following two conventional threshold levels of anti-Spike IgG were adopted: $\leq$50 BAU/mL and >1000 BAU/mL.

The outbreak lasted from 25 August to 6 October 2021, 10 days after the last SARS-CoV-2 infection. Affected residents were grouped as follows: (a) Asymptomatic: including <38°C fever or headache; (b) Symptomatic: >38°C fever, cough, diarrhoea, anorexia, lethargy, psychomotor retardation, mental confusion; and (c) Severe: dyspnoea, desaturation <92% leading to fatal outcomes. Previous immune stimuli were considered: doses of mRNA coronavirus disease 2019 (COVID-19) vaccination received within 8 August 2021 and SARS-CoV-2 RT-PCR-confirmed infection before 25 May 2021.

The relationship between anti-Spike IgG titres and COVID-19 status among fully vaccinated residents without a previous SARS-CoV-2 infection was described through a tabular and graphical bivariate analysis. Cumulative risk ratios (RR) and vaccine effectiveness (VE) against infection and severe COVID-19 were calculated according to the formula: $1 - RR$, where RR represents the cumulative risks of an adverse outcome comparing individuals with anti-Spike IgG $\leq$50 BAU/mL with individuals anti-Spike IgG >50 BAU/mL.

The study was approved by the competent Ethics Committee on 26 August 2021.

Results

On the index-case incidence date, among the 69 residents (80% female, 84% $\geq$ 80 years old, 88% completely dependent) and 69 HCWs present, three and five individuals, respectively, had a previous SARS-CoV-2 RT-PCR-confirmed infection (March 2020–April 2021). The full vaccination coverage was 83% among HCWs and 91% among residents, mainly via BNT162B2 mRNA vaccine (98%), with the booster dose received on average 196 ± 36 days before the outbreak. Among residents, two had received only the priming dose and four were unvaccinated; among HCWs, six had received only the priming dose and six were unvaccinated.

Within 30 days, 46 and 14 new cases were found among residents and HCWs, respectively (cumulative incidences: 67% and 20%), with 75% of cases within the first week from the Index case. Spike sequencing Of swabs from seven residents and three HCWs confirmed the VOC Delta lineage.

Among residents, 13 individuals were asymptomatic, 21 were symptomatic and 12 had severe COVID-19 (eight deaths). Two deaths (aspiration pneumonia and cachexia), occurring 11 days from the last negative PCR test, were not recorded as fatal COVID-19 cases.

The anti-Spike IgG geometric mean was 161 BAU/mL (95% CI 98–268 BAU/mL) and 625 BAU/mL (95% CI 289–1353 BAU/mL) among tested residents (66/69) and HCWs (23/66), respectively; comparison of residents aged $\leq$80 years with those aged >80 years showed a geometric mean of 585 BAU/mL (95% CI 263–1300 BAU/mL) and 103 BAU/mL (95% CI 58–186 BAU/mL), respectively.

Among tested fully vaccinated individuals without previous SARS-CoV-2 infection, 0/20 HCWs, but 14/59 (24%) tested residents had anti-Spike IgG $\leq$50 BAU/mL (one-sided Fisher exact p 0.011).

For these residents, the elapsed time since the booster dose at the onset of the outbreak was 199 days (interdecile range 154–209 days), and an anti-Spike IgG titre $\leq$50 BAU/mL resulted in a higher risk of SARS-CoV-2 infection (RR 1.55, 95% CI 1.17–2.05) and severe COVID-19 (RR 5.33, 95% CI 1.83–15.57) (Table 1, Fig. 1). In terms of VE, the corresponding figures against SARS-CoV-2 infection and severe COVID-19 were 35% (95% CI 15%–51%) and 79% (95% CI 37%–93%), respectively; similar results were obtained when including the unvaccinated ($n = 2$) and partially vaccinated ($n = 3$) residents into the comparison group (data not reported).

Discussion

One-quarter of the 59 fully vaccinated nursing home residents with no previous SARS-CoV-2 infection had anti-Spike IgG $\leq$50 BAU/mL about 28 weeks after the booster dose. This translates to a VE of 35% (95% CI 15%–51%) against infection and 79% (95% CI 37%–93%) against severe COVID-19, suggesting that the protection conferred from an anti-Spike IgG titre $\leq$50 BAU/mL is very low, if any.

Table 1
SARS-CoV-2 infection and COVID-19 incidence, according to the threshold anti-Spike IgG level ($\leq$50 versus >50 BAU/mL) in 59 fully mRNA vaccinated residents

Anti-Spike IgG	SARS-CoV-2	COVID-19			Total
>50 BAU/mL	Negative	Asymptomatic	Symptomatic	Severe	
No	1 (7%)	3 (21%)	4 (29%)	6 (43%)	14 (100%)
Yes	18 (40%)	9 (20%)	14 (31%)	4 (9%)	45 (100%)
Total	19 (32%)	12 (20%)	18 (31%)	10 (17%)	59 (100%)

Abbreviations: BAU, WHO binding antibody units; COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
Fisher exact test: p 0.012.

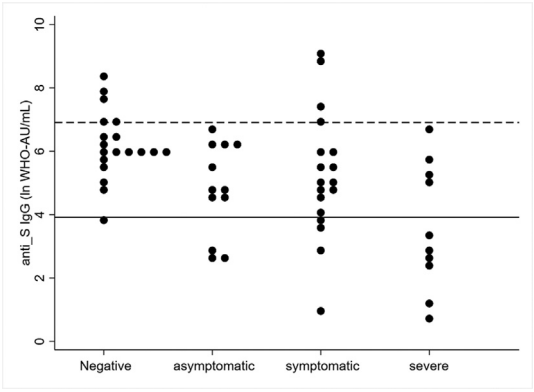

Fig. 1. Cumulative incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and coronavirus disease 2019 (COVID-19) among 59 residents fully vaccinated with mRNA vaccine 28 weeks before, and with no previous SARS-CoV-2 PCR-confirmed infection, by anti-S IgG level (WHO binding antibody units (BAU)/mL) measured at the beginning of the outbreak. Full and dotted red lines represent two conventional threshold levels of 50 and 1000 BAU/mL.

A large US CDC study carried out among 3862 nursing home residents fully vaccinated with mRNA vaccines reports a VE against SARS-CoV-2 infection of 53% (95% CI 49%–57%) comparing post-Delta (2 June to 1 August 2021) with pre-Delta period [6]. Otherwise, a nationwide UK study computed a VE of 71% (95% CI 41%–86%) against hospitalization with Delta infection among clinically extremely vulnerable ≥65-year-old individuals 20+ weeks after the BNT162B2 boost [7].

In its Rapid Risk Assessment on COVID-19 outbreaks in long-term care facilities, the European Center for Disease Prevention and Control reported 2/18 VOC Delta outbreaks until July 2021, with 63 fully vaccinated and 12 partially vaccinated or unvaccinated residents. The reported attack rate among fully vaccinated residents is 31/63 (49%), with 5/63 (8%) COVID-19 hospitalizations [4]. These figures are somewhat lower in comparison with our study, which also shows a higher vaccination coverage among residents and HCWs; which is probably the result of differences in time elapsed since the booster dose.

To this purpose, a recent study evaluated anti-Spike immunoglobulin titre among 472 long-term care facility residents with Elecsys Anti-SARS-CoV-2 S Assay (April–May 2021), 64 days (interquartile range 63–65 days) from the BNT162b2 booster dose. The high, medium, low and null titre groups (>1000, 101–1000, 1–100 and < 1 BAU/mL) showed frequencies of 62%, 22%, 16% and 4%, respectively. The risk of being a non-responder was eight times higher in individuals with no previous SARS-CoV-2 infection (about 30% of the tested residents) [1]. In the present case study, only 5 (7%) residents had a previous SARS-CoV-2 infection in the pre-Delta period; none of them became infected during the outbreak described in this study.

To conclude, this study first reports a VOC Delta outbreak in an Italian Nursing Home [8,9]; the extensive and timely measurement of anti-Spike IgG among residents provides valuable immunological information. As a result of the small size of the study and the limits of our observations, further research is needed to define appropriate threshold anti-Spike IgG levels to identify and best protect those residents at higher risk of severe COVID-19 from VOC Delta lineages.

Transparency declaration

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Author contributions

AA, FR, LV, ADC and MS conceptualized the study; AA, AP, MEDA, MG and ADZ performed the investigations; formal analysis was by AP, ADZ and MS; the manuscript was written by GB; and MS supervised the study.

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