Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

The Omicron wave and the waning of COVID-19 vaccine effectiveness. Influence of vaccine booster and age on confirmed infection incidence

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Dear Editor,

The high coverage rate of vaccination against coronavirus disease 2019 (COVID-19) in our area was envisaged to end the pandemic, or at least to control it. However, in the last months of 2021 and the firsts of 2022 there has been a rapid increase in COVID-19 cases. This change has been driven by the emergence of the new World Health Organization (WHO) Omicron variant.

Due to the increase of cases of COVID-19 in highly vaccinated populations, there is a growing concern about the effectiveness of the vaccines against this new variant. A national survey carried out in the United Kingdom [1] and a systematic review[2] have confirmed that primary immunization provided limited protection against symptomatic disease caused by the Omicron variant. The administration of a booster increased the protection against severe forms of the disease but waned after 3 months[1,3].

VACCICOVAO cohort study was intended to analyze the evolution of the COVID-19 pandemic in vaccinated health professionals. The methodology of the cohort was previously described[4]. In summary, the Hospital Universitario Rio Hortega (HURH) conducted a vaccination campaign of all health care workers between January and March 2021. Individuals were invited to participate in a prospective cohort after they were scheduled for a second dose of vaccine. Serologic testing was performed 2, 8 and 12 months after the first dose (March-April 2021, September-October 2021, February-March 2022 respectively) (eFig. 1, supplementary). A new SARS-CoV-2 infection was defined as a positive polymerase chain reaction (PCR) or positive antigen test on nasopharyngeal swab, and/or anti-nuclei capsid. The study was performed in accordance with the institutional review board of HURH. Written informed consent was obtained.

A total of 617 volunteers from the initial 680 participants (lost at of follow-up: 9.3%) completed the third survey and had their blood drawn for testing. New cases of COVID-19 were diagnosed in 162 patients (26.3%) (eFigure 2, supplementary material). Four out of ten new COVID-19 cases were asymptomatic and all the rest but one (hospitalized with symptomatic treatment) were mild. The most common symptoms were cough, sore throat, or muscular aches (eFigure 3, supplementary material). One-hundred-twelve were diagnosed with polymerase chain reaction (PCR) or antigens and 40 with antibodies (Ag) antiN1 with neither PCR nor Ag. Five hundred and eighty-nine patients (95%) received a vaccination booster. The booster was administered a mean of 305 ± 18 days after the first vaccine dose.

In Fig. 1, we show the effect of different population characteristics and vaccination schedules on the incidence of new COVID-19 cases. Only the administration of a booster and older age were associated with a decrease in new cases. Among the health professionals who did not receive a booster, there were 57% (CI 95%; 39-75%) of new COVID-19 cases compared to 25% (CI 95% 21-29%) in the population of health professionals who had received a booster with the same vaccine brand and 19% (CI 95% 2-36%) of the ones who were administered a booster with a different brand of vaccine (p=0.001). Among health professionals aged 36 or less the incidence of new cases nearly doubled that of cases in participants older than 50 years (38% [CI 95%; 28-47%] vs 19% [CI 95% 14-24%]) with participants aged between 35 to 50 years showing an incidence of new cases equal to that of the cohort (28% [CI 23-34%]) (p=0.001).

Antibodies titers against titers S1 SARS CoV-2 and survival curves are shown as supplementary material (eFigures 4a, 4b, 5a, 5b, supplementary material).

The emergence of the WHO Omicron variant has dramatically changed the strength of association against the SARS-CoV-2 infection of some factors, such as a previous infection with another SARS-CoV-2 variant. In our cohort, the risk of having a new SARS-CoV-2 infection during follow-up was not affected by a previous history of SARS-CoV-2 infection (before 2021), the type of mRNA vaccine administered, the days between first and second dose or the title of antiS1 antibodies achieved 3 months after vaccination. Only age (younger people) and the lack of booster vaccinations were associated with a higher risk of a new SARS-CoV-2 infection. The protection after a booster vaccination has been proved in other studies [1,3] but, to the best of our knowledge, the increase of confirmed infections in younger health professionals has not been shown before. This high prevalence could not be justified with medical causes or with vaccination coverage. Only the different lifestyle and the different way of facing the COVID-19 risk between younger and older health professionals seems to be a likely explanation for this

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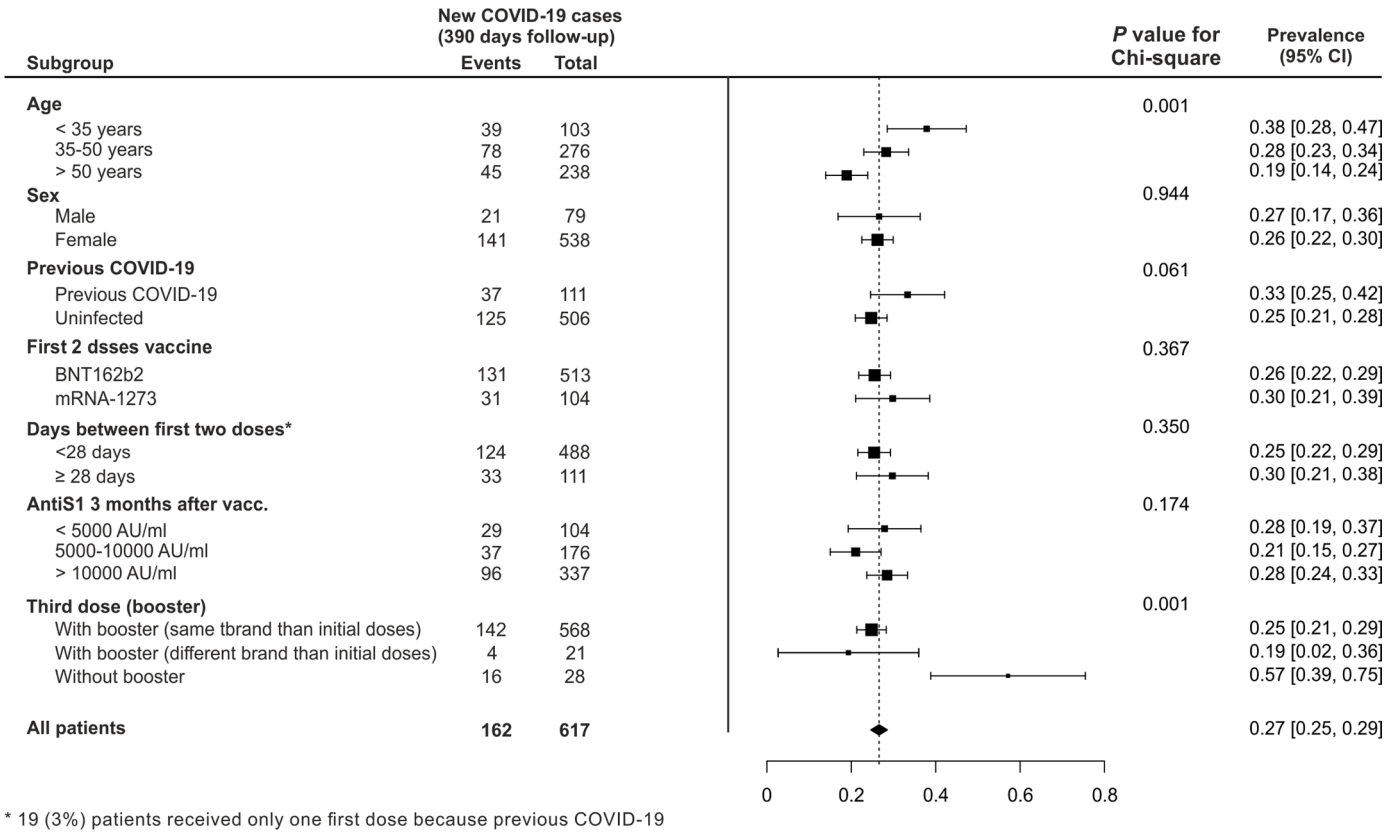

Fig. 1. Factors associated with the incidence of new cases of COVID-19

difference. Age has been significantly related to coronavirus risk-taking, with younger adults taking more risk[5].

The study has several limitations. First, the use of a convenience sample of health care professionals, which means that the results may not be generalizable. Second, the virus lineage was not directedly tested in the participants of our cohort. Instead, we used data from a surveillance of our own hospital that analyzed a random sample of SARS-CoV-2 every week. In addition, some of the diagnoses were made with an antigen test that makes it impossible to analyze lineage. Third, cellular immunity was not tested. Fourth, the small sample size hampers the possibility to draw conclusions in the analyzes of the subgroups of patients without a booster.

Evaluating vaccine efficacy or effectiveness with the emergence of new variants and the waning of vaccine effectiveness will be crucial for updating COVID-19 vaccine policy. The need of a fourth dose is widely discussed. A study from Israel suggests that this second booster could offer a protective effect against infection[6] when four doses were compared with three. However, the recommendation of a fourth dose is highly questionable. On one hand, the clinical presentation of COVID-19 is becoming milder, maybe due to vaccination programs, natural immunity achieved after infection[7], hybrid immunity[8] or the debatable less virulence on new variants[9]. On the other hand, the protection against severe illness did not wane as fast as the protection against a confirmed infection, and a third doses could be enough to avoid severe cases of COVID-19. Beyond the fourth dose[10], vaccination strategies are being optimized with heterologous vaccination schedules and optimal time interval between doses. The next logic step will be the development of variant-adapted vaccines. Finally, the age paradox in our study shows that keeping measures such as social distancing could continue to be a good tool to control the pandemic.

Author contributions

Dr Corral-Gudino had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: García-Cruces-Méndez, Domínguez-Gil-González and Corral-Gudino.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Del-Amo-Merino, Domínguez-Gil-González and Corral-Gudino.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Corral-Gudino.

Administrative, technical, or material support: García-Cruces-Méndez, Domínguez-Gil-González and Corral-Gudino.

Supervision: Eiros-Bouza.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ejim.2022.05.025.

References

[1] Andrews N, Stowe J, Kirsebom F, et al. Covid-19 Vaccine Effectiveness against the Omicron (B.1.1.529) Variant. N Engl J Med 2022;386(16):1532–46. https://doi.org/10.1056/NEJMoa2119451.

[2] Feikin DR, Higdon MM, Abu-Raddad LJ, et al. Duration of effectiveness of vaccines against SARS-CoV-2 infection and COVID-19 disease: results of a systematic review and meta-regression. Lancet 2022;399(10328):924–44. https://doi.org/10.1016/S0140-6736(22)00152-0.

[3] Tartof SY, Slezak JM, Puzniak L, et al. Durability of BNT162b2 vaccine against hospital and emergency department admissions due to the omicron and delta variants in a large health system in the USA: a test-negative case-control study. Lancet Respir Med 2022. https://doi.org/10.1016/S2213-2600(22)00101-1. Published online April 22S2213-2600(22)00101-1.

[4] García-Cruces-Méndez JF, Corral-Gudino L, Del-Amo-Merino MP, Eiros-Bouza JM, Domínguez-Gil González M. SARS-CoV-2 antibody response eight months after vaccination with mRNA vaccines. Influence of prior SARS-CoV-2 exposure. Eur J Intern Med 2022;97:113–5. https://doi.org/10.1016/j.ejim.2022.01.011.

[5] Wolfe K, Sirota M, Clarke ADF. Age differences in COVID-19 risk-taking, and the relationship with risk attitude and numerical ability. R Soc Open Sci 2021;8(9):201445. https://doi.org/10.1098/rsos.201445.

[6] Bar-On YM, Goldberg Y, Mandel M, et al. Protection by a Fourth Dose of BNT162b2 against Omicron in Israel. N Engl J Med April 5, 2022. https://doi.org/10.1056/NEJMoa2201570. Published online.

[7] Havervall S, Marking U, Greilert-Norin N, et al. Impact of SARS-CoV-2 infection on vaccine-induced immune responses over time. Clin Transl Immunology 2022;11(4):e1388. https://doi.org/10.1002/cti2.1388.

[8] Nordström P, Ballin M, Nordström A. Risk of SARS-CoV-2 reinfection and COVID-19 hospitalisation in individuals with natural and hybrid immunity: a retrospective, total population cohort study in Sweden. Lancet Infect Dis 2022. https://doi.org/10.1016/S1473-3099(22)00143-8. Published online March 31S1473-3099(22)00143-8.

[9] Malik JA, Ahmed S, Mir A, et al. The SARS-CoV-2 mutations versus vaccine effectiveness: New opportunities to new challenges. J Infect Public Health 2022;15(2):228–40. https://doi.org/10.1016/j.jiph.2021.12.014.

[10] Watson C. Three, four or more: what's the magic number for booster shots? Nature 2022;602(7895):17–8. https://doi.org/10.1038/d41586-022-00200-9.

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