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Short Communication

First-generation BNT162b2 and AZD1222 vaccines protect from COVID-19 pneumonia during the Omicron variant emergence

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Objective: This study aimed to identify factors predicting pneumonia in adults with coronavirus disease 2019 (COVID-19) during the Omicron variant (B.1.1.529) emergence. We also evaluated, in fully vaccinated (BNT162b2 or AZD1222) individuals, if the time (< 6 or ≥ 6 months) elapsed since the last shot was received was associated with the risk of severe illness.

Study design: A retrospective cohort study was conducted in Mexico.

Methods: Data from 409,493 were analyzed, and risk ratios (RRs) and 95% confidence intervals (CIs) were computed through generalized linear models.

Results: We documented a total of 3513 COVID-19 pneumonia cases (69.5 per 100,000 person-days). In multiple analyses, a protective effect was observed in vaccinated adults (RR = 0.996, 95% CI 0.995−0.997). Male gender, increasing age, and smoking were associated with a greater risk of pneumonia. Individuals with chronic comorbidities (pulmonary obstructive disease, type 2 diabetes mellitus, arterial hypertension, kidney disease, and immunosuppression) were also at higher risk. Among fully vaccinated subjects (n = 166,869), those who had received the last shot at 6 more months were at increased risk for developing pneumonia (RR = 1.002, 95% CI 1.001−1.003).

Conclusions: Our results suggest that the first-generation BNT162b2 and AZD1222 vaccines reduce the risk of COVID-19 pneumonia during the Omicron emergence. We also found that adults with longer interval from the administration of the second shot to illness onset were at increased risk of severe manifestations.

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The main binary outcome (no/yes) was pneumonia due to COVID-19, and it was defined by clinical and radiographic findings that required hospital admission. Clinical and epidemiological data of interest, as well as the COVID-19 vaccination status and dates of their administration, were retrieved from the audited surveillance system.

We used generalized linear regression models to compute risk ratios (RRs) and 95% confidence intervals (CIs). Two multiple regression models were built. The first model was used to evaluate predictors of COVID-19 pneumonia during the Omicron emergence; the latter one evaluated the effect of the time elapsed since the last vaccine shot with the risk of pneumonia in fully immunized subjects.

## Results

Data from 409,493 laboratory-confirmed cases of COVID-19 were analyzed. The mean age (± standard deviation) of participants was aged 39.0 ± 13.3 years, and most of them were female (56.1%). The total follow-up was 5,052,192 person-days, and 3513 cases of COVID-19 pneumonia were registered (69.5 per 100,000 person-days). A fatal outcome was documented in one-third (33.8%) of patients with severe manifestations.

The vaccinated group was integrated by 166,869 participants (40.8%), and AZD1222 was administered in most of them (60.7%). Table 1 shows the characteristics of the study sample for the analyzed variables. Pneumonia patients were more likely to be

| Table 1 | Predictors of pneumonia in laboratory-confirmed cases of COVID-19 (n = 409,493) during the Omicron variant emergence, Mexico 2021–2022. |
|-------------------------------------------------|---------------------------------------------------------------------------------------------------|
| Characteristic                                   | Pneumonia (n)                                                                                     | Bivariate analysis | Multiple analysis |
| Sex                                              |                                                                                                   | RR (95% CI) | P          | RR (95% CI) | P          |
| Female                                           |                                                                                                   |               |            |               |            |
| Male                                             |                                                                                                   |               |            |               |            |
| Age group (years)                                |                                                                                                   |               |            |               |            |
| 18–39                                            |                                                                                                   |               |            |               |            |
| 40–59                                            |                                                                                                   |               |            |               |            |
| ≤60                                              |                                                                                                   |               |            |               |            |
| COVID-19 vaccination status                      |                                                                                                   |               |            |               |            |
| Unvaccinated                                     |                                                                                                   |               |            |               |            |
| Vaccinated                                       |                                                                                                   |               |            |               |            |
| Personal history of                              |                                                                                                   |               |            |               |            |
| Obesity                                          |                                                                                                   |               |            |               |            |
| No                                               |                                                                                                   |               |            |               |            |
| Yes                                              |                                                                                                   |               |            |               |            |
| Smoking (current)                                |                                                                                                   |               |            |               |            |
| No                                               |                                                                                                   |               |            |               |            |
| Yes                                              |                                                                                                   |               |            |               |            |
| Chronic pulmonary obstructive disease            |                                                                                                   |               |            |               |            |
| No                                               |                                                                                                   |               |            |               |            |
| Yes                                              |                                                                                                   |               |            |               |            |
| Type 2 diabetes mellitus                         |                                                                                                   |               |            |               |            |
| No                                               |                                                                                                   |               |            |               |            |
| Yes                                              |                                                                                                   |               |            |               |            |
| Arterial hypertension                            |                                                                                                   |               |            |               |            |
| No                                               |                                                                                                   |               |            |               |            |
| Yes                                              |                                                                                                   |               |            |               |            |
| Chronic kidney disease (any stage)               |                                                                                                   |               |            |               |            |
| No                                               |                                                                                                   |               |            |               |            |
| Yes                                              |                                                                                                   |               |            |               |            |
| Immunosuppression                                |                                                                                                   |               |            |               |            |
| No                                               |                                                                                                   |               |            |               |            |
| Yes                                              |                                                                                                   |               |            |               |            |

RR, risk ratios; CI, confidence interval.

(1) Generalized linear regression models were used to obtain the presented estimates; (2) RR and 95% CI from the multiple analysis were adjusted by the variables presented in the table.

a Vaccinated adults were those two shots of BNT162b2 (Pfizer, Inc./BioNTech) or AZD1222 Covishield (AstraZeneca); unvaccinated participants were those who had not received any COVID-19 vaccine dose from any pharmaceutical company.

b Any cause (excluding type 2 diabetes mellitus).
male and to be older than mild cases ($P < 0.001$). Patients with severe illness were also more likely to be unvaccinated or to present any comorbid condition ($P < 0.001$ in all of them).

In the first multiple regression model (Table 1), fully vaccinated subjects had a reduced risk of pneumonia (RR $= 0.996$, 95% CI 0.995–0.997). Male gender (RR $= 1.002$, 95% CI 1.001–1.003), increasing age (vs 18–39 years old: $40–59$, RR $= 1.002$, 95% CI 1.001–1.003; 60 or older, RR $= 1.065$, 95% CI 1.062–1.068), as well as all the analyzed comorbidities (except for obesity), were also associated with an increased risk of COVID-19-related pneumonia. The greatest risk was conferred by the personal history of chronic kidney disease (any state; RR $= 1.134$, 95% CI 1.108–1.160).

In fully vaccinated adults (please see the Supplementary data 1), we documented that participants with a longer interval from the last vaccine shot and illness onset (6 or more months) had a slight but significantly reduced risk for developing severe illness (vs <6 months: RR $= 1.002$, 95% CI 1.001–1.003). This estimate was adjusted by host factors. When compared with the rest of the estimates from the first model, no major changes were observed in the ratios from the latter one.

**Discussion**

We characterized factors predicting pneumonia due to laboratory-confirmed COVID-19 in a large subset of adults during the Omicron emergence in Mexico. Our results suggest that even though this variant can evade neutralizing antibodies, the first-generation BNT162b2 and AZD1222 vaccines reduce the risk of developing pneumonia in fully immunized adults. Otherwise, we observed that host factors, such as gender, age, and chronic medical conditions, are associated with an increased risk of severe illness. If later replicated, these findings would highlight the relevance of promoting healthy lifestyles and immunization in eligible subjects to reducing the pandemic burden.

In our study, patients who had received the last vaccine shot at 6 or more months were at greater risk of developing pneumonia (vs <6 months: 1.002, 95% CI 1.001–1.003). This is consistent with previously published data where a decrease in anti-spike IgG and neutralizing antibodies were evidenced after 6 months of the BNT162b2 vaccine administration.6

We analyzed the BNT162b2 and AZD1222 vaccines because they had been broadly administered in Mexico. By February 7, 2022, about 51.5 and 90.6 million doses of BNT162b2 and AZD1222 had been received in our country.14 When we evaluated de specific effect of each of these biological products on the risk of pneumonia, similar estimates were observed in both of them (BNT162b2, $n = 65,565$; AZD1222, $n = 101,304$). The same was documented when the interval between the last vaccine shot and illness onset was evaluated.

Another aspect that must be highlighted is that most of the identified COVID-19 cases during the study period had mild symptoms, and pneumonia was observed in around 8 out of 1000 laboratory-positive cases. This is related to the smaller virulence of Omicron when compared with previous variants.3 The pneumonia rate in our analysis is much lower than the observed during previous variant emergences in the same study setting, which was around 30%.3 A fatal outcome was documented in nearly one-third (33.8%) of the enrolled individuals. Therefore, the case fatality rate in the study sample was 29.0 per 10,000.

The potential limitations of this study must be discussed. First, according to normative standards, the genomic sequencing is not performed in all laboratory-positive COVID-19 cases. Therefore, we are unable to ensure that all the analyzed participants were infected by the Omicron variant. However, we consider that most of these infections correspond to the variant of interest given (1) the documented peak in the incidence of COVID-19 in Mexico during the study period (please see the Supplementary data 2) and (2) in the United States, and also during the end of 2021 of start of 2022, the Omicron variant was identified in nearly 99% of genomic sequences.36 Second, vaccines booster began to be applied to the general population during January 2022 in high-risk population, so a small fraction of participants may have had it at the time of symptoms onset. These data were not collected by the audited surveillance system at the time of recruitment.

**Conclusions**

Our results suggest that during the Omicron variant emergence, the first-generation BNT162b2 and AZD1222 COVID-19 vaccines are effective in reducing the risk of pneumonia. We also found that participants with a shorter interval between the second shot and illness onset were at reduced risk of severe manifestations. If later replicated, these findings may provide additional data to support the administration of a third vaccine shot to reduce the pandemic-related burden.

**Author statements**

**Ethical approval**

This study was reviewed and approved by the Committee of Ethics in Health Research (601) of the IMSS (approval R-2020-601-022).

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None.

**Competing interests**

None declared.

**Appendix A. Supplementary data**

Supplementary data to this article can be found online at https://doi.org/10.1016/j.puhe.2022.04.001.

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