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Short communication

## Independent risk factors of COVID-19 pneumonia in vaccinated Mexican adults

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## ABSTRACT

**Objectives:** To evaluate host factors associated with the risk of coronavirus disease 2019 (COVID-19) pneumonia in vaccinated adults.**Methods:** A cohort study was conducted in Mexico, and data from 1607 adults with confirmed illness, with a positive history of COVID-19 vaccination, were analyzed. Risk ratios (RR) and 95% confidence intervals (CI) were computed as a measure of the significance of the associations between putative risk factors and the prevalence of COVID-19 pneumonia in vaccinated subjects.**Results:** The overall risk of pneumonia was 1.98 per 1000 person-days. In the multiple regression analysis, older subjects, those with a history of smoking (current), obesity, and type 2 diabetes mellitus were at increased risk of pneumonia.**Conclusions:** Our results suggest that the effectiveness of COVID-19 vaccines may be reduced in a subset of adults who are older aged, smokers, obese, or have type 2 diabetes mellitus.

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## Introduction

## Background

The availability of vaccines against coronavirus disease 2019 (COVID-19) represent a significant step toward ending the pandemic, and most COVID-19 vaccines confer close to 100% reduction in the risk of serious illness or death (Sharma et al. 2021). In Mexico, vaccination of the general population started in mid-February 2021, and by June 2021, 7 COVID-19 vaccines have received approval by health authorities for their application in Mexico: BNT162b2 (Pfizer, Inc./BioNTech), AZD1222 Covishield (AstraZeneca), Gam-COVID-Vac (National Center Gamaleya), Coron-

aVac (Sinovac Research and Development Co.), Ad5-nCoV Covidecia (CanSino Biologics Inc.), BBV152 Covaxin (Bharat Biotech International Limited), and Ad26.COV2-S (Janssen-Cilag).

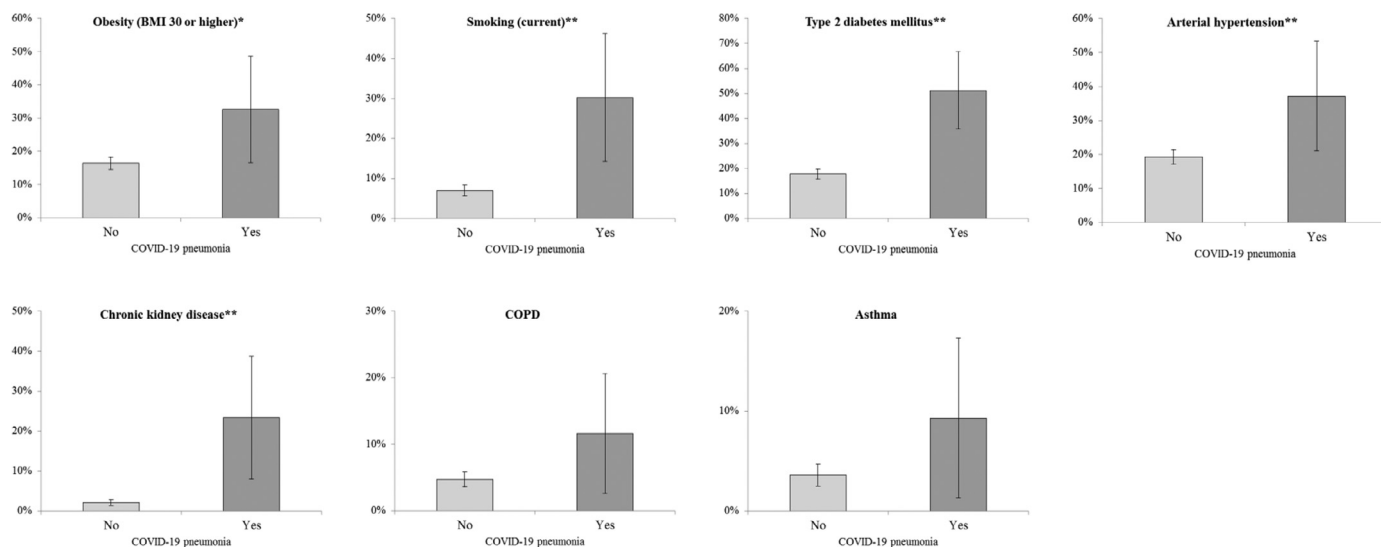
However, given that vaccine effectiveness may be affected by diverse factors that include host factors (such as age and comorbidities) and alignment of the vaccines with circulating strains, severe cases might still develop among fully vaccinated persons (Lopalco and DeStefano, 2015). This might be particularly relevant in Mexico, where the pandemic burden has been high. The aim of this study was to evaluate the host factors that could be used in predicting the risk of COVID-19 pneumonia in vaccinated adults.

## Methods

A nationwide retrospective cohort study was conducted in Mexico from August to October 2021, and a broader description of the research methods was previously published in a study evaluating

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**Figure 1.** Prevalence (%) and 95% confidence interval (CI) of chronic conditions according to the COVID-19 pneumonia status, Mexico 2021. Abbreviations: **BMI**, Body mass index; **COVID-19**, coronavirus disease 2019; **COPD**, chronic pulmonary obstructive disease.

\*  $p < 0.05$ ; \*\*  $p < 0.001$ .

predictors of COVID-19 pneumonia during the first semester of the pandemic (Murillo-Zamora et al., 2020). Adults aged 20 years or older with laboratory-confirmed (reverse transcription-polymerase chain reaction or rapid antigen test) disease, illness onset from March to July 2021, and history of COVID-19 vaccination before illness onset were extracted for this analysis. All subjects meeting the selection criteria were enrolled.

The vaccinated subjects were those with 2 shots of any COVID-19 vaccine ( $n = 426$ ; 26.5%) or a single shot ( $n = 1366$ ; 73.5%) at  $\geq 14$  days before illness onset. Clinical and radiographic findings defined COVID-19 pneumonia (Government of Mexico, 2021); factors associated with its risk were evaluated through risk ratios (RR), and 95% confidence intervals (CI) were computed through generalized linear regression models. The Local Health Research Committee (601) of the Mexican Institute of Social Security approved this study (R-2020-601-015).

## Results

Data from 1607 patients were analyzed for a total follow-up of 21,713 person-days. The overall risk of pneumonia was 1.98 per 1000 person-days (43/21,713), and the mortality in this group was 53.5% (23/43). Compared with patients without pneumonia, those with COVID-19 pneumonia were older (mean  $\pm$  standard deviation,  $65.5 \pm 12.0$  vs  $49.5 \pm 14.4$  years,  $p < 0.001$ ) and had a higher prevalence of chronic noncommunicable conditions (Figure 1). A broader description of the study sample is presented in Supplementary data 1.

In multiple regression analysis (Table 2), vaccinated individuals aged 65 years or older (RR = 1.04, 95% CI 1.02–1.07) and smokers (RR = 1.07, 95% CI 1.04–1.10) were at increased risk of pneumonia. Adults with obesity (RR = 1.02, 95% CI 1.01–1.04) or type 2 diabetes mellitus (RR = 1.03, 95% CI 1.01–1.05) also had a higher risk of developing COVID-19 pneumonia.

Table 1.

## Discussion

Our results suggest that the effectiveness of COVID-19 vaccines in preventing severe illness may be diminished by host characteristics, including age and conditions associated with unhealthy lifestyles (eg, smoking, obesity, and type 2 diabetes mellitus).

The older aged adults are at risk of a progressive decline in function of the immune system—immunosenescence—that could be associated with diminished humoral and cellular immune responses (Nikolich-Zugich, 2018). In our study, the risk of COVID-19 pneumonia increased an average of 0.2% (RR per year = 1.002, 95% CI 1.001–1.003) per year of age. Therefore even fully vaccinated older adults are at increased risk of serious illness, and other protective measures should be taken to reduce the risk of infection.

The prevalence of smoking among the patients with pneumonia was higher than among nonsevere COVID-19 cases (30.2% vs 7.0%; RR = 1.07, 95% CI 1.04–1.10). The prevalence among all those with COVID-19 infection was also higher than the general prevalence of smokers among Mexican adults aged 20 years or older (National Institute of Public Health of Mexico, Health and Nutrition Survey, 2018; 30.5% vs 11.4%). The differences are not unexpected given that smoking history has been associated with a poorer COVID-19 outcome (Zhao et al., 2020). Published data also suggest reduced effectiveness of influenza vaccine among smokers (Godoy et al., 2018).

We also observed a significant increase in the risk of pneumonia in vaccinated adults with type 2 diabetes mellitus (RR = 1.03, 95% CI 1.01–1.05) and obesity (RR = 1.02, 95% CI 1.01–1.04). Both conditions have also been associated with poor disease outcomes among unvaccinated patients in other populations (Zhou et al., 2021) as well as in Mexico (Barquera and Rivera, 2020).

Finally, according to the aim of our study, we clustered the vaccinated participants and no specific estimates (RR) were obtained for each of the received vaccines. As presented in Supplementary data 1, the AZD1222 Covishield (AstraZeneca) or BNT162b2 (Pfizer, Inc./BioNTech) vaccine were administered to most (82%) of enrolled subjects.

## Conclusions

The effectiveness of COVID-19 vaccines may be reduced in a subset of adults who are older aged, smokers, obese, or have type 2 diabetes mellitus.

## Authors' contributions

EMZ performed the experiments, analyzed the data, and wrote the first draft of the manuscript. XT made data analysis and data

**Table 1**  
Predictors of COVID-19 pneumonia in vaccinated adults, Mexico 2021

| Characteristic                    | RR (95% CI), <i>p</i><br>Bivariate analysis |             |         | Multiple analysis |             |         |
|-----------------------------------|---|-------------|---------|-------------------|-------------|---------|
|                                   |   |             |         |                   |             |         |
| <b>Gender</b>                     |   |             |         |                   |             |         |
| Female                            | 1.00  |             |         | 1.00              |             |         |
| Male                              | 0.99  | (0.98-1.02) | 0.898   | 0.99              | (0.98-1.01) | 0.244   |
| <b>Age (years)</b>                |   |             |         |                   |             |         |
| < 65                              | 1.00  |             |         | 1.00              |             |         |
| ≥ 65                              | 1.07  | (1.05-1.10) | < 0.001 | 1.04              | (1.02-1.07) | < 0.001 |
| <i>Personal history of:</i>       |   |             |         |                   |             |         |
| <b>Obesity (BMI 30 or higher)</b> |   |             |         |                   |             |         |
| No                                | 1.00  |             |         | 1.00              |             |         |
| Yes                               | 1.03  | (1.01-1.05) | 0.005   | 1.02              | (1.01-1.04) | 0.034   |
| <b>Smoking (current)</b>          |   |             |         |                   |             |         |
| No                                | 1.00  |             |         | 1.00              |             |         |
| Yes                               | 1.09  | (1.06-1.12) | < 0.001 | 1.07              | (1.04-1.10) | < 0.001 |
| <b>Asthma</b>                     |   |             |         |                   |             |         |
| No                                | 1.00  |             |         | 1.00              |             |         |
| Yes                               | 1.04  | (0.99-1.09) | 0.055   | 1.04              | (0.99-1.08) | 0.081   |
| <b>Type 2 diabetes mellitus</b>   |   |             |         |                   |             |         |
| No                                | 1.00  |             |         | 1.00              |             |         |
| Yes                               | 1.06  | (1.04-1.08) | < 0.001 | 1.03              | (1.01-1.05) | 0.007   |
| <b>Chronic kidney disease</b>     |   |             |         |                   |             |         |
| No                                | 1.00  |             |         | 1.00              |             |         |
| Yes                               | 1.24  | (1.18-1.30) | < 0.001 | 1.02              | (0.99-1.14) | 0.059   |

Abbreviations: **BMI**, Body mass index; **CI**, Confidence interval; **RR**, Risk ratio

Notes: 1) Generalized linear regression models were used to obtain RR and 95% CI; 2) Multiple regression coefficients were adjusted by variables listed in the table.

collection. RASP and MH contributed with the methodology and writing—review and editing. MRS contributed with revisions and data analysis. OMC conceived and designed the experiments and is responsible for the final version of the manuscript that has been read and approved by all authors.

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### Availability of data and materials

All data generated or analyzed during this study are included in this published article.

### Ethics approval and consent to participate

The Local Health Research Committee approved this study of the IMSS (approval R-2020-601-015).

### Competing interests

None declared under financial, general, and institutional competing interests.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.ijid.2022.02.003](https://doi.org/10.1016/j.ijid.2022.02.003).

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