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RESEARCH LETTER

Vaccination against COVID-19 decreases hospitalizations in patients with cirrhosis: Results from a nationwide analysis

1 | INTRODUCTION

Chile currently has the fifth-highest vaccination rate against COVID-19 in the world (up to 28 November 2021). Though several vaccines against COVID-19 have received regulatory approval from the Food and Drug Administration,[1] there is limited evidence supporting the protective effect of these vaccines in high-risk groups. We aimed to assess the impact of vaccination against COVID-19 in patients with cirrhosis.

2 | MATERIALS AND METHODS

We used comprehensive information obtained through the national SARS-CoV-2 surveillance program of the Chilean Ministry of Health. Under this program, all suspected cases of COVID-19 were notified to the ministry, including data on comorbidities and hospitalizations. We included both confirmed and probable cases of COVID-19 from 3 March 2020 to 30 May 2021. SARS-CoV-2 infection was confirmed by real-time polymerase chain reaction (qPCR) performed by the Chilean Institute of Public Health and certified laboratories. In addition, we updated twice a week the incidence rate and prevalence of comorbidities, including cirrhosis, diabetes, hypertension, chronic kidney disease, asthma and heart failure from the national SARS-CoV-2 surveillance program. Also, we collected the overall vaccination rate during the study period.

Using a quasi-experimental design, we assessed the effectiveness of COVID-19 vaccination in decreasing hospitalizations caused by COVID-19 infection. We used regression discontinuity (RD) models with a first-order polynomial and robust bias-corrected inference to estimate the impact of vaccinations as determined by hospitalization rates (recorded as a continuous variable). We estimated the hospitalization rate using a cut-off twice a week, considering the percentage of patients with determined comorbidity admitted during an established period. We defined the first vaccination dose as the date when the vaccination among the overall population began. The effect was estimated beyond 14 days after the first and second vaccination dose. There was a difference of 35 days between both assessments. In an RD design, assuming that there are no other contemporaneous changes, the temporal difference in the outcome could be attributable to the temporal change in the treatment.

3 | RESULTS

As of 30 May 2021, there were 1 648 680 COVID-19 cases in Chile (84% confirmed by qPCR), accounting for an incidence of 8472.9 cases per 100 000 inhabitants. The median age was 38 years old, 50.2% were female and 127 728 (7.7%) required hospitalization. A total of 10 526 028 (50.1%) individuals have been vaccinated (7 948 421 have received two doses and 2 577 607 received one dose); 18.7% received the BNT162b2 mRNA (Pfizer/BioNTech) vaccine, 1.9% the Vaxzevria (Oxford-AstraZeneca) vaccine and 79.4% the CoronaVac (Sinovac Life Sciences) vaccine. Sixty-three per cent of patients admitted to the intensive care unit (as a marker of severe disease) were not vaccinated, and 23% had not received the two vaccine doses.

A total of 2050 (0.1%) COVID-19 cases had underlying cirrhosis, and 881 (42.9%) required hospitalization. We observed a substantial decline in absolute hospitalization rates among patients with cirrhosis who were vaccinated versus those not vaccinated (−12.69, 95%CI -21.71 to −3.68; $p < .01$) beyond 2 weeks following administration of the second dose. This effect was also observed in patients with heart failure, diabetes, hypertension and asthma; however, the benefit of decreasing hospitalization rates was higher in patients with cirrhosis (Figure 1).

4 | DISCUSSION

Several comorbidities have been associated with hospitalization and death as a result of COVID-19.[2] Indeed, the mortality from COVID-19 is high among patients with advanced cirrhosis (Child-Pugh B or C) and those with alcohol-related liver disease (ALD).[3] In our study, patients with COVID-19 and underlying cirrhosis frequently required hospitalization during the infection (42.9% vs. 7.7% in the overall population). Among patients with cirrhosis, vaccination against COVID-19 was associated with a lower rate of hospitalization than individuals with no vaccination.

Several studies have demonstrated the impact of COVID-19 in patients with liver disease. Hepatic involvement has been associated with an increased risk of mortality (Odds ratio [OR] 3.46) and severe disease (OR 2.87) in the overall population.[4] A large cohort study demonstrated that individuals with COVID-19 and underlying cirrhosis have a mortality of 32% compared to 8% in those without cirrhosis.[3] This effect increases according to the severity of cirrhosis

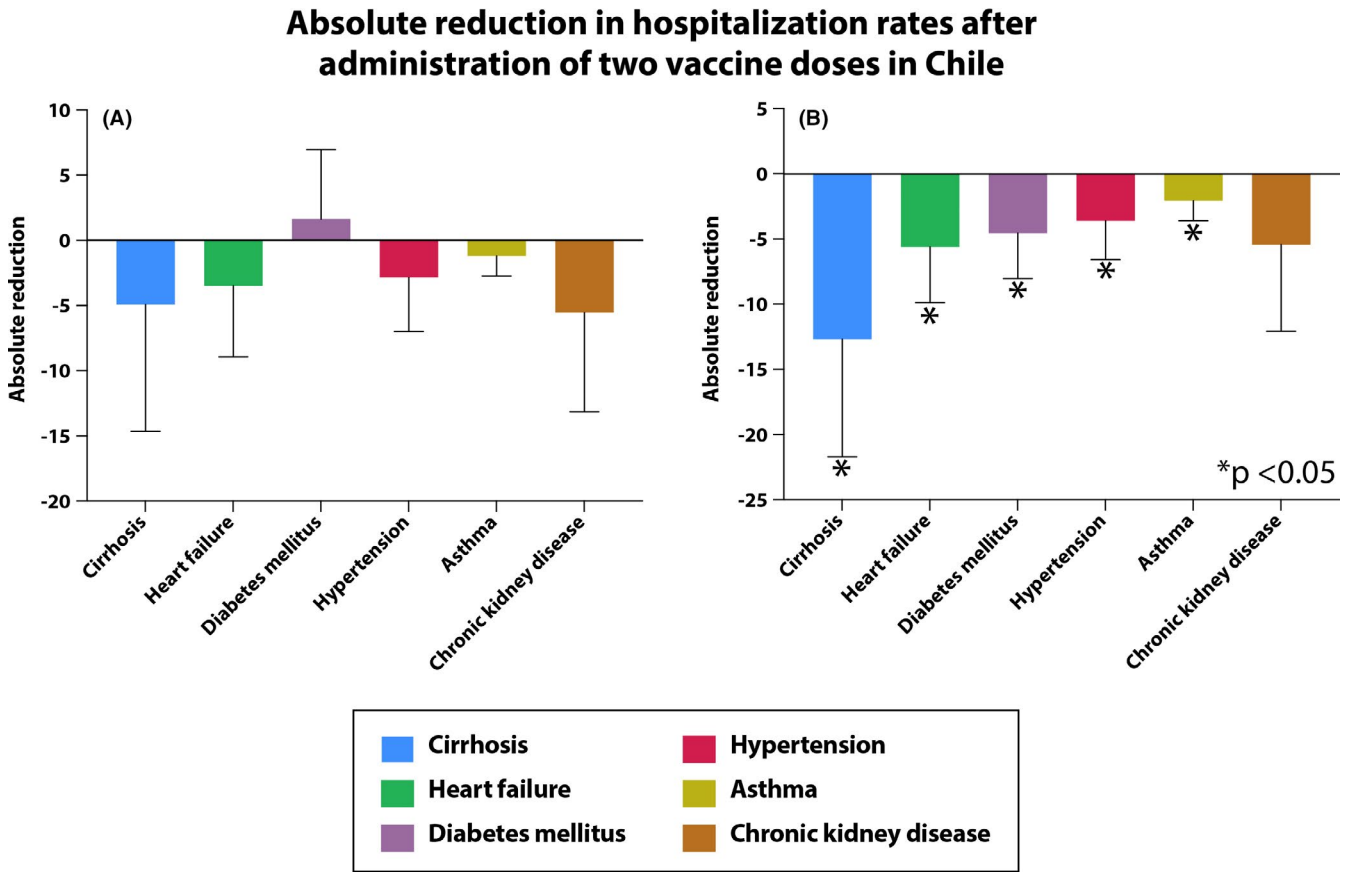

FIGURE 1 The absolute reduction in hospitalization rates after administration of one and two vaccine doses according to the presence of comorbidities in Chile

and contributes to acute hepatic decompensation in 46% of patients. Also, SARS-CoV-2 infection by itself can elevate the liver chemistries and affect liver function.[5] This evidence highlights the need to protect these populations from exposure to SARS-CoV-2 infection.[6]

Though prior nationwide studies using the BNT162b2 mRNA vaccine data demonstrated lower hospitalization rates in some high-risk groups,[7,8] the evidence of its impact on patients with cirrhosis is scarce because of the insufficient inclusion of participants with liver disease in the major trials.[8] The largest study, including 20037 cirrhotic patients, demonstrated a strong effect of BNT162b2 mRNA and Moderna (mRNA-1273) COVID-19 vaccines, with a 78.6% reduction in COVID-19 infections and 100% reduction in COVID-19–related hospitalization or death after 7 days of the second dose.[9] Therefore, our study demonstrates the protective efficacy of COVID-19 vaccination among patients with cirrhosis, supporting the use of the vaccine among high-risk populations.

The effectiveness of COVID-19 vaccines is also an important issue in managing patients post-liver transplantation (LT). Indeed, immunosuppression may reduce the response to vaccination, increasing the risk of COVID-19 infection even after second-dose administration.[10] A recent Italian study, including 61 patients post-LT, demonstrated a serological and cellular response after second-dose administration of COVID-19 mRNA vaccine.[11] However, this response was significantly lower than healthy controls. Recent data in solid organ transplant recipients showed that administration of a third dose of mRNA vaccine improved the immunogenicity of the vaccine, with no cases of COVID-19 reported in any of the patients.[12] All the accrued evidence could promote prioritization in the vaccination process among populations at risk (including cirrhosis and LT recipients) and potentially a third-dose administration.

As demonstrated by the COVID-19 vaccination experience in the USA, several barriers remain to universal acceptance of vaccines.[1,13] These and other concerns must be addressed during the massive vaccination campaigns planned in other countries if the adoption of vaccines against COVID-19, especially in high-risk groups, is not widely accepted.

Our study had some limitations. The absence of individualized data limits the statistical analysis in a quasi-experimental study and the ability to control for confounding factors. Also, the severity (Child-Pugh or MELD scores) and the aetiology of cirrhosis are not available. The impact of liver disease aetiology (i.e. ALD versus non-alcoholic fatty liver disease) on the risk of hospitalization and death could not be ascertained. Because of the nature of the database, there may have been patients with cirrhosis, especially those with compensated cirrhosis, who may not have been identified with this comorbidity. Finally, we did not assess the prevalence of SARS-CoV-2 variants in our country. It is an important point since some variants could decrease COVID-19 effectiveness. Further studies are necessary to assess the effects of virus variants on COVID-19 vaccines efficacy.

In conclusion, we observed in our nationwide study an association between vaccination against COVID-19 and a lower hospitalization

risk in patients with cirrhosis and other important comorbidities such as diabetes, hypertension, asthma and heart failure. Thus, our data support large-scale vaccination in high-risk groups.

AUTHORS' CONTRIBUTIONS

Juan Pablo Arab and Luis Antonio Díaz conceived and designed the study; Luis Antonio Díaz and Eduardo Fuentes-López collected the data, contributed to data analysis and interpretation, and performed final analysis and drafted the manuscript. All the authors participated in drafting the article and revising it critically for important intellectual content, and gave final approval of the submitted version.

KEYWORDS

2019-nCoV-2, coronavirus, COVID-19, immunization, or novel coronavirus, SARS-CoV-2, vaccine

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ETHICAL APPROVAL

This study was based on public data and an ethical approval was not required.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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