Liver cirrhosis is associated with a lower immune response to COVID-19 vaccines but not with reduced vaccine efficacy

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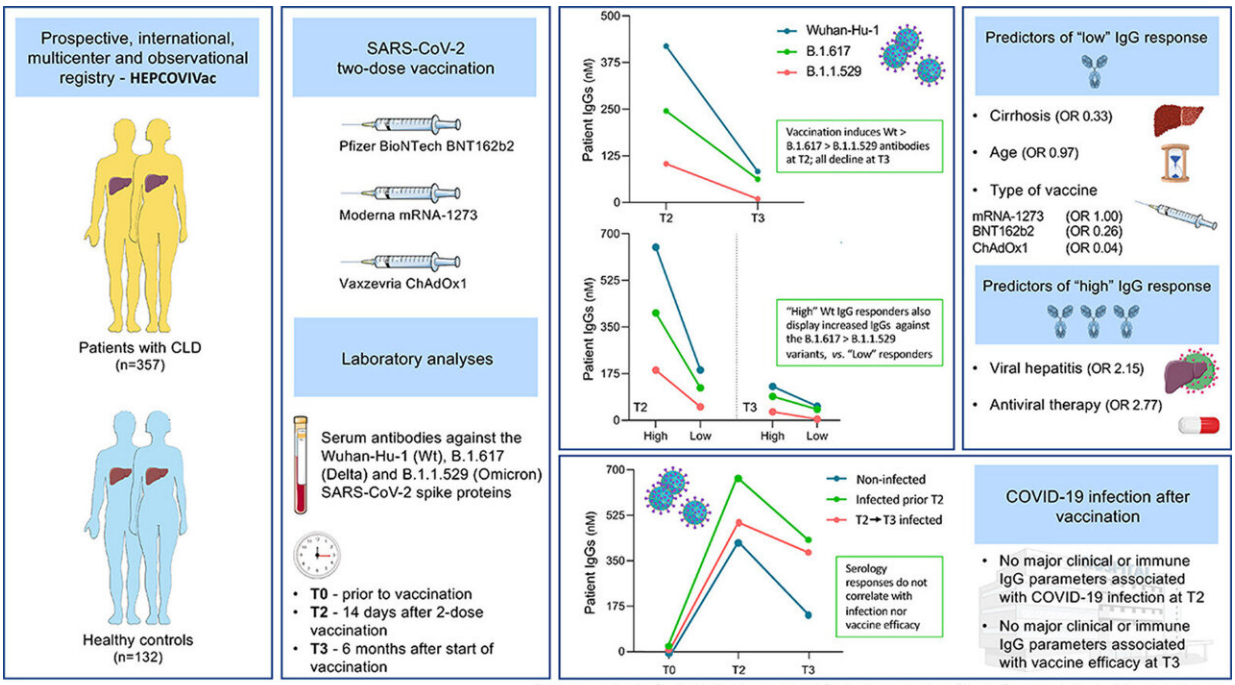

Graphical Abstract. Credit: *JHEP Reports* (2023). DOI: 10.1016/j.jhepr.2023.100697

The overall responsiveness of patients with chronic liver disease (CLD) to COVID-19 vaccines has been shown to be decreased in patients with cirrhosis. A new prospective study in *JHEP Reports* shows that this lower

response is observed up to six months following two-dose COVID-19 mRNA vaccination, but it does not reduce vaccine efficacy.

In this prospective study, more than 350 patients with CLD were recruited in clinical centers from Austria, Belgium, Italy, Portugal, Romania, and Spain. Cirrhosis, alongside age and vaccine type, is associated with lower immunoglobulin G (IgG) responses, while the presence of viral hepatitis or antiviral therapy is associated with higher IgG responses. Noteworthy, these differences did not correlate with vaccine efficacy at six months.

Rui Castro, MD, Ph.D., from the Research Institute for Medicines (iMed.ULisboa), Faculty of Pharmacy, Universidade de Lisboa, Portugal, explained that the consortium behind this study, HEPCOVIVac, "was brought together to create a prospective clinical registry of patients with CLD vaccinated for COVID-19, allowing for comprehensive studies on vaccination safety and efficacy." The consortium is co-led by Helena Cortez-Pinto, MD, Ph.D., Centro Hospitalar Universitário Lisboa Norte and Faculty of Medicine, Universidade de Lisboa, Portugal.

Results showed that, among patients with CLD, age, cirrhosis, and type of vaccine were identified as independent predictors of lower immune response, while viral hepatitis, and antiviral therapy stood as independent predictors of higher immune response.

"While the lower response in patients with cirrhosis could relate with cirrhosis-associated immune dysfunction (CAID), and age is already a well-established factor affecting vaccine-mediated immunity, the link between viral hepatitis and higher IgG titers was interesting and warrants further study," noted Dr. Castro.

When comparing patients who developed COVID-19 between two

weeks and six months following vaccination, vaccine efficacy appeared to be slightly lower in patients with higher weight and height. Of note, no correlation was found between the type of vaccine and SARS-CoV-2 infection rates; and no association was found between IgG titers at two weeks and vaccine efficacy.

In fact, Wuhan-Hu-1, B.1.617 and B.1.1.529 IgG levels were very similar between SARS-CoV-2 infected and non-infected patients. Results also showed no significant associations between clinical variables and COVID-19 infection rates or infection severity.

"We were surprised by these results, as they suggest that the distinct levels of antibodies induced by the distinct vaccine types, or associated with distinct disease etiology or severity, may not translate into lower vaccine efficacy (COVID-19 infection), at least within the first six months following two-dose vaccination," noted Dr. Castro.

"Although additional studies should ideally be performed, I think this message can already be communicated to patients. That is, that different two-dose mRNA COVID-19 vaccines are effective in a diverse group of patients with CLD. This will help to boost confidence in the vaccination plans put in place by different governments."

Notwithstanding, results also showed that patient IgG levels against the B.1.617 and, further, the B.1.1.529 variant, were decreased compared with Wuhan-Hu-1, at two weeks following vaccination. This differential pattern was maintained after six months, but with significantly lower antibody titers for all variants, particularly in patients with cirrhosis, in contrast to the results of healthy volunteers.

"These results highlight the need for patients with CLD, particularly those older and with cirrhosis, to receive booster shots" noted Dr. Castro. "Ideally, patients should be prioritized for adapted vaccines against

recent omicron variants, although studies on the efficacy of adapted vaccines in patients with CLD are still lacking."

More information: André Lopes Simão et al, Cirrhosis is associated with lower serological responses to COVID-19 vaccines in patients with chronic liver disease, *JHEP Reports* (2023). DOI: 10.1016/j.jhepr.2023.100697

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