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EDITORIAL

Viral Vector Vaccines Are Victorious Against COVID-19 in Patients with Cirrhosis

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To the Editor,

The vaccines against coronavirus disease of 2019 (COVID-19) infection that were developed at astonishing speed have reduced the severity and rates of hospitalization and mortality of COVID-19-associated illness. Although patients with cirrhosis have higher mortality from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection compared to those without liver disease, vaccination is effective in this population, albeit at rates lower than the general population [1, 2]. The vast majority of published studies on COVID-19 vaccination in cirrhosis have explored the two mRNA vaccines—the Pfizer BNT162b2 and the Moderna mRNA-1273, respectively. In a study published early in the pandemic, the receipt of two doses of an mRNA-based COVID-19 vaccine was associated with a 78.6% reduction in COVID-19 infection among participants with cirrhosis [2]. Additionally, in patients with cirrhosis, vaccine-induced immunity offered from two doses of an mRNA vaccine was superior to the infection-induced immunity acquired from prior COVID-19 infection [3]. Although breakthrough infections were observed in participants with cirrhosis, post-vaccination COVID-19 was associated with a 79% reduction in death compared to unvaccinated COVID-19 [4]. Furthermore, studies that have examined the immunogenicity of mRNA vaccines in patients with chronic liver disease and cirrhosis have observed adequate antibody levels in a significant proportion of participants [5, 6]. All of these studies support the high efficacy of mRNA vaccination in cirrhosis.

Although most developed high GDP countries have adopted an mRNA vaccine as their primary tool to fight COVID-19, the majority of vaccines administered worldwide have been viral vector vaccines [7]. Viral vector vaccines utilize replication-deficient viral vectors such as adenovirus to induce transient expression of the immunogenic SARS-CoV-2 spike protein. Viral vector vaccines against COVID-19 are less expensive to develop, can be stored at room temperature, and are therefore more affordable and accessible to low and mid GDP countries. COVID-19 viral vector vaccines that have been authorized include the Janssen Ad.26.COV2.S vaccine, the Oxford/Astra Zeneca AZD1222 (also called the ChAdOx1-nCOV), the Sputnik V Gam-COVID-Vac, and the Can Sino Ad5-nCoV vaccines, with the latter three currently unavailable in the United States [8]. A recent test-negative case–control study in the Veterans Outcomes and Cost Analysis in Cirrhosis (VOCAL) cohort found that a single dose of the viral vector Ad.26.COV2.S vaccine was modestly effective (64%) against overall COVID-19 infection and 72% effective against severe/critical COVID-19-associated illness among participants with cirrhosis, comparable with the effectiveness of mRNA vaccines against both overall COVID-19 (73%) as well as severe/critical COVID-19 (82%) during the same phase of the pandemic [9].

In this month's *Digestive Diseases and Sciences*, Singh et al. describe the results of a retrospective cross-sectional study in an Indian patient population with cirrhosis who had completed 2 doses of a viral vector Oxford Astra Zeneca ChAdOx1-nCOV vaccine [10]. Participants who completed 2 doses of the ChAdOx1-nCOV vaccine, and without documented COVID-19 (pre or post vaccination) were queried about side effects related to vaccination during their tele-hepatology appointment, and were tested for antibodies against the spike protein. The authors found that of their roughly 1037 patient cohort, 231 patients had received at least one dose of ChAdOx1-nCOV. One hundred and thirty-four (58%) of these 231 patients were

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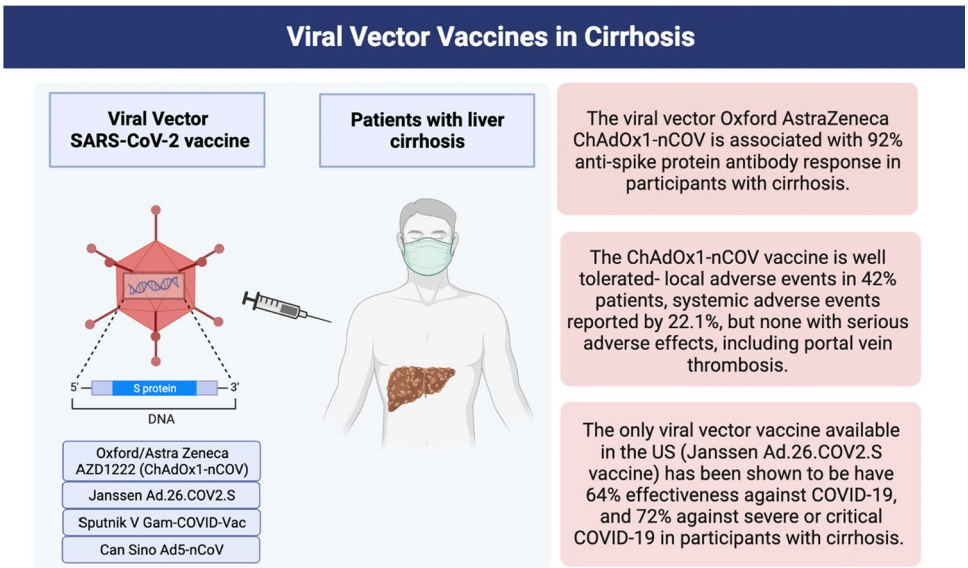
fully vaccinated with two doses of ChAdOx1-nCOV with an interval of 35 (28–50) days between the two doses. Importantly, a high proportion of seroconversion (92.1%) in patients with cirrhosis following 2 doses of ChAdOx1-nCOV vaccine was observed, comparable with the high seroconversion rate of 98% reported in the published pan-India coronavirus vaccine-induced antibody titer (COVAT) study in health care workers following two doses of ChAdOx1-nCOV and by numerous studies using two doses of mRNA vaccines in patients with cirrhosis.

In a safety assessment of the ChAdOx1-nCOV vaccine, Singh et al. found that among patients who had received at least one dose of the vaccine, local adverse events were reported by 42% patients, whereas systemic adverse events were reported by 22.1% patients, with fever the most common symptom (15.2%). All adverse events were self-limited, occurring without hospitalization and resolving within 72 h of vaccination. None of the patients developed acute hepatic decompensation or acute liver failure (ACLF) post-vaccination. In early 2021, the European Medicines Agency (EMA) concluded that the ChAdOx1-nCOV vaccine was associated with cerebral and mesenteric venous thrombosis and thrombocytopenia, observed most commonly ~ two weeks after vaccination. The sample size of the current study is likely too low to detect this infrequent side effect. It is reassuring that despite the baseline risk of portal vein thrombosis in participants with cirrhosis, no specific signal was observed in this study population.

The data presented here differ from the immunogenicity studies reported from the United States by Thuluvath et al., who found that in their cohort of 79 patients with cirrhosis, three had undetectable antibody levels and 15 had suboptimal antibody responses [5]. This indicates a higher rate of suboptimal immunogenicity of 24%, compared with 8% observed by Singh et al. Some of these differences may be attributed to immunosuppression (all three participants with undetectable antibodies were being treated with immunosuppressants for autoimmune hepatitis), and differences in antibody assays and cut-offs used between the studies. The data by Thuluvath et al. also observed high rates of suboptimal antibody response after a single dose of the Janssen Ad.26.COV2.S vaccine. On the other hand, another study from Europe observed that a negative or weak anti-SARS-CoV-2 response was observed in only 2% (using anti-S RBD antibodies), and 6% (using anti-S trimer antibodies) of patients with cirrhosis [6]. These different findings highlight challenges in comparing immunogenicity between studies that use different antibody assays that have not been standardized. Yet, the high rates of immunogenicity observed in this and the study by Reuther et al. [6] are consistent with the clinical effectiveness of viral vector vaccines observed in participants with cirrhosis.

Ultimately, there are many ways to crack an egg. Patients with cirrhosis should be encouraged to receive whatever vaccine is readily available to them—whether mRNA or viral vector vaccines—since all confer a reasonable level of protection. Future studies should focus on need for booster doses in cirrhosis, and whether the currently available vaccines maintain efficacy against the newer variants such as the Omicron subvariant BA.5.



Declarations

Conflict of interest None of the authors have personal or financial conflicts of interests to declare concerning this publication.

Ethical approval The authors prepared this work in their personal capacity. The opinions expressed in this article are the author's own and do not reflect the view of the Department of Veterans Affairs or the United States government.

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