Real-World Evaluation of Response to Hepatitis B Vaccination in Cirrhosis: A Brief Report

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Response to hepatitis B vaccination in cirrhosis

Cirrhosis (N=678)

Excluded
165 antiHBs + 72 Hepatitis B + 277: Lost to follow-up or incomplete vaccination

Analyzed (n=164)

Usual Schedule (N=152)
20 mcg 0, 1 and 6 months

Response: 91 (59.9%)

Double dose for previously vaccinated (N=12)
40 mcg 0, 1 and 6 months

Response: 12 (100%)

Older age predicted non-response
MELD Score did not predict response
Introduction

All patients with chronic liver disease who do not have evidence of hepatitis B virus (HBV) infection, hepatitis B surface antigen (HBsAg-), anti-HBc, and anti-HBs-negative are advised HBV vaccination. However, this is seldom followed in clinical practice, and data regarding response rates to vaccination in India is scarce. Despite the wide availability of the HBV vaccine, a majority of these patients are not immunized due to ignorance and fear of side effects associated with the vaccine. Health-care professionals are often busy managing complications of cirrhosis and forget about the preventive aspect. We conducted this study to determine response to HBV vaccination and its determinants in adult patients with cirrhosis.

Methods

This prospective study was conducted over a period of 3 years from 2019 to 2021. Cirrhosis was diagnosed based on clinical and radiological parameters. Endoscopic screening was done to confirm the presence of varices. All adult patients (> 18 years) with cirrhosis of the liver were screened for HBsAg, total anti-HBc, and anti-HBs. Those who were negative for all three markers were advised vaccination. For vaccine-naïve patients, a dose of 20 µg intramuscular in the deltoid region was administered at 0, 1, and 6 months. For those with prior history of vaccination but negative anti-HBs titers, a dose of 40 µg was used at 0, 1, and 6 months. Patients who were known HBsAg positive, on oral antiviral drugs, who did not complete the vaccination schedule, or were lost to follow-up were excluded. Anti-HBs titers were measured 2 months after completion of vaccination. Patients with anti-HBs titers more than 10 IU/L were considered as responders and those with titers less than 10 IU/L were labeled as nonresponders. The two groups were compared for demographic parameters, anthropometry, model of end-stage liver disease score, and history of prior vaccination. The study cohort included 164 patients (median age: 43, range: 18–68 years, and 67% males). On follow-up at 2 months after vaccination, 103 (62.8%) patients had anti-HBs titer more than 10 IU/L. Of these, 54 (52.4%) had titers more than 100 and 49 (47.6%) had titers ranging from 10 to 99. Nonresponders were significantly older than responders (48 vs. 41 years, p = 0.01). Seroresponse to HBV vaccination in adult patients with cirrhosis was 62.8%. Older age predicted nonresponse to HBV vaccination.

Results

A total of 678 patients with cirrhosis were seen over the study period. Seventy-two patients were newly detected to be HBsAg+/anti-HBc+ and 165 were detected to be anti-HBs+. A total of 277 cases did not complete the vaccination schedule or were lost to follow-up. The study cohort included 164 patients—median age 43 (18–68) years and 67% males (110). Patients were followed up at 2 months after completion of vaccination. One-hundred and three (62.8%) patients had anti-HBs titer more than 10 IU/L. Of these, 54 (52.4%) had titers more than 100 IU/L and 49 (47.6%) had titers ranging from 10 to 99 IU/L. Twelve patients had a history of prior vaccination but low anti-HBs titers. After double dose vaccination, 10 patients had anti-HBs titers more than 100 IU/L, while 2 had anti-HBs titer between 10 and 99 IU/L. Therefore, all nonresponders had a serological response after the double dose of vaccination.

Nonresponders were significantly older than responders (48 vs. 41 years, p = 0.01) (Table 1). A majority of the patients had MELD score ranging from 10 to 15. The response rates for the different MELD groups were as follows: MELD
less than 10 (12/24, 50%), MELD 10 to 15 (82/124, 66%), and MELD more than or equal to 16 (9/16, 56.25%). Response rates were not significantly different among different MELD groups ($p = 0.28$).

**Discussion**

This study highlights a low response rate (62.8%) in cirrhotics for HBV vaccination. Nonresponse was likely in older patients. Previous studies have shown that low rates of anti-HBs seroconversion are related to alcohol use, male gender, nonalcoholic fatty liver disease, HCV infection, presence of cirrhosis, and older age.$^{6-9}$ Patients with cirrhosis have low anti-HBs seroconversion rates. Despite this, HBV vaccination is recommended in these patients as it provides protection via clonal expansion of specific memory cells. Vaccination of all cases waiting for liver transplantation is likely to prevent de novo HBV infection in pre- and post-transplant periods.$^{10-12}$

This study has a few shortcomings like being a single-center study with a limited sample size and only patients with end-stage liver disease were included. The waning of anti-HBs titers is a known phenomenon over the long term. Several patients may be nonresponders or may have low titers that respond to even a single booster dose that enhances the antibody titers. We included patients with a history of vaccination but low anti-HBs titers and administered them a double dose of vaccine as per the study protocol. However, it is debatable if all these cases were nonresponders to initial vaccination or lost titers over time. Other factors like malnutrition, hypoalbuminemia, and sarcopenia may affect the response rates. Unfortunately, these were not evaluated in this study. More Indian data are needed to ascertain the efficacy of HBV vaccination in this special patient population.

**Ethical Statement**

Written informed consent was obtained from the patients. Ethical Clearance was obtained from Ethics committee, Arihant Hospital and Research Centre, Indore, India.

**Author Contributions**

M.J. conceptualised, collected data, analyses, wrote the draft and approved the work.

**Data Availability statement**

The corresponding author will provide anonymized data on a reasonable request.

**Funding**

None.

**Conflict of Interest**

None declared.

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None

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