

# Is it the Right Time to Introduce the Hepatitis B Booster Vaccine in National Immunization Schedule? An Analysis from the Available Evidence

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## Abstract

Hepatitis B virus (HBV) infection is a global health concern, and it is considered one of the deadliest infections in the world, having nearly 1.2 million deaths annually. Around 75% of all global HBV carriers live in the Asia-Pacific region. In this regard, India has a prevalence ranging between 2% and 7% with exposure rates of 10%–60%. Hepatitis B is a vaccine-preventable disease. In India, the World Health Organization protocol for hepatitis B vaccination has been followed, and it is given free of cost in public health facilities under the National Immunization Schedule. Despite the free hepatitis vaccination program in India, coverage and awareness are low. Low awareness, followed by low coverage of hepatitis vaccination, can prove dangerous for the Indian population in the long run. A majority of chronic hepatitis cases progress silently to end-stage liver disease without having many signs and symptoms. Once occurred, a complete cure is not possible with currently available drugs. The studies from neighboring countries such as China and Taiwan documented that the impact of single-dose booster for children of 10 years has made a significant difference from the cost-effectiveness perspective. They have also included the booster dose in their national vaccination program. Considering the low level of vaccination awareness, small coverage, high disease burden, and high treatment cost, now, it is high time for India to introduce hepatitis B booster vaccine.

**Keywords:** Booster dose, hepatitis B, vaccine

## INTRODUCTION

Hepatitis B virus (HBV) infection is a global health problem, and it is considered one of the deadliest infections in the world, having nearly 1.2 million deaths annually.<sup>[1]</sup> As per the recent estimates published by the World Health Organization (WHO), 257 million people are living with HBV infection;<sup>[2]</sup> around one-third of people infected with HBV globally.<sup>[3]</sup> The prevalence of positive HBV infection differs in different groups of people and different regions.<sup>[4,5]</sup> Around 75% of all global HBV carriers live in the Asia-Pacific region. In this regard, India is a region among intermediate HBV endemic having a prevalence ranging between 2% and 7% with exposure rates of 10%–60%.<sup>[6]</sup> Hepatitis B is a vaccine-preventable disease. The transmission occurs majorly through horizontal route. Compared to the perinatal transmission being an important mode of transmission, horizontal transmission of hepatitis

B infection in early childhood is more common in India as stated.

## MATERIALS AND METHODS

The current article aimed at comparing the various hepatitis B vaccination strategies around the globe. The literature search was done using PubMed, Google Scholar, and Scopus databases for the following key terms “Hepatitis B vaccine,” “Booster dose of hepatitis-B vaccine,” “Hepatitis-B,” and HB vaccination. All the relevant articles were included to support the argument for this narrative review.

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## RESULTS

As per the WHO recommended schedule, complete hepatitis B vaccination consists of three doses of vaccine administration. The birth dose is given within 24 h of birth, followed by the first, second, and third doses with an interval of at least 4 weeks (birth, 6<sup>th</sup>, 10<sup>th</sup>, and 14<sup>th</sup>) of the doses.

In India, the same protocol has been followed, and it is given free of cost in public health facilities under the National Immunization Schedule. Despite free hepatitis vaccination in India, the coverage is low. A recent study from Gujarat reported that less than one-fifth of people had been vaccinated. Besides the increasing prevalence of HBV infections, disease awareness among the Indian population is dismally low.<sup>[7]</sup> Low awareness, followed by low coverage of hepatitis vaccination, can prove dangerous for the Indian population in the long run. A majority of chronic hepatitis cases progress silently to end-stage liver disease without having many signs and symptoms. This will exert tremendous pressure on family and the existing overburdened Indian health-care system. Once occurred, a complete cure is not possible with currently available drugs; long-term antiviral therapy being a current solution itself leads to poor treatment compliance along with the costly treatment.<sup>[8]</sup> The course of infection with HBV is a significant predictor of disease outcome; the earlier the age, the higher the risk of chronicity. In highly endemic areas, hepatitis B is most commonly spread from mother to child at birth (perinatal transmission). Parenteral transmission is another important mode of transmission which can occur at any age. More than 90% of HBV-infected infants and 25%–50% of children infected between the ages of 1 and 5 years usually develop chronic hepatitis. More than 25% of HBV-infected infants and children older than 6 years will develop HBV-related cirrhosis and hepatocellular carcinoma (HCC).<sup>[9,10]</sup> It is suggested that the full primary course of hepatitis B vaccine provides complete protection against disease of hepatitis B infection for an extended period of time, although in some cases of vaccinated individuals, anti-HBs decrease and become undetectable over a period of time.<sup>[11]</sup> In regard to these findings, the WHO does not recommend booster vaccination to immunized individuals (however, countries such as the USA recommend for boosters of HBV<sup>[12]</sup>).

## DISCUSSION

Evidence from the national immunization program in Taiwan suggests that there is a warning in HBV carrier rates and long-term consequences of HBV infection (like HCC).<sup>[13]</sup> Coverage evaluation survey revealed that compared to the DPT vaccine, the coverage of the HBV vaccine is lower.<sup>[14]</sup> The poor coverage issues were due to lack of staff training, poor record-keeping, poor management of vaccine stocks, and the use of multidose vials.<sup>[15,16]</sup> The impact of single-dose booster among 10-year children will make a significant difference from the cost-effectiveness perspective. Costs associated with the treatment of chronic hepatitis and utility assumptions

for patients with chronic hepatitis have emerged as the most influential parameters in the sensitivity analysis. However, it was observed that cost-effectiveness ratios remained below the GDP per capita for China in the “worst-case” scenario, which was explored in the sensitivity analysis. Increasing cost recurred for HBV infections such as HCC, chronic hepatitis, and liver cirrhosis in chronic HBV patients is continuing due to a more significant number of cases which goes unobservable and silent.<sup>[17]</sup>

According to the study of Salama *et al.*, 88.6% of the children <5 years had a seroprotective level of HBs antibody, where five cluster areas were randomly chosen (two urban and three rural areas) in Egypt from July 2010 to June 2013.<sup>[18]</sup> This is the success of the immunization programs and the implementation of blood donor screening.

Findings from Wang *et al.* study suggest that booster dose is protective among both children born to mothers of hepatitis B surface antigen (HBsAg) (+Ve) and HBsAg (–Ve) (comparatively less protection).<sup>[19]</sup> As the risk of developing chronic HBV infection is much more in children born to HBsAg (+Ve) mothers compared to HBsAg (–Ve) mothers, the adult booster vaccination would be appropriate for HBsAg serum-positive mothers.<sup>[19]</sup>

Compared to a single dose, a three-dose booster is required for most of the individuals to reach an anti-HBs level >100 mIU/mL, to achieve memory immunity in a large portion of individuals.<sup>[20]</sup> However, results from meta-analysis revealed that immunity provided by three-dose HBV continues for a minimum of 20 years in the majority of immunocompetent persons if they are adequately vaccinated.<sup>[21]</sup>

Contrary to the findings stated in anti-HBs level, China already implemented the booster doses to children aged 10 years from evidence generated to support the efficacy and cost-effectiveness from studies reported.<sup>[22–24]</sup> Considering the cost-effectiveness of the providing booster dose to 10-year children as proposed by China, the advantage of it outweighs other facts, and this suggests that booster doses to children aged 10 years would be highly recommended and high time to follow on this initiative.

In some carriers, it is observed that treatment provided with antiviral therapy to chronic hepatitis B infection resulted in clearance of HBsAg and hepatitis B e-antigen. However, the long-term benefit of antiviral treatment is unclear.<sup>[25]</sup> Regarding prevention and control of disease, vaccination programs is an effective approach. Antiviral therapy has cost-effectiveness issues.<sup>[26]</sup> The recent data from neighboring countries strongly suggest that there is a need for initiating booster dose program to prevent the silent hepatitis B epidemic.<sup>[7]</sup>

Bruce *et al.* have demonstrated that protection out to 22 years among persons vaccinated as children or adults among Alaska native people. They have also conducted a cohort study, 30 years after primary vaccination due to the following up original cohort. This research suggests that

“children vaccinated through catch-up programs or young adults vaccinated for occupational safety reasons have a high likelihood of being protected for multiple decades”.<sup>[27]</sup>

Lu *et al.* have suggested that when the vaccination protocol is completed at childhood, and after 20 years, negative results for HBsAg and anti-HBs levels have reported, a booster dose of HBV vaccine would be enough to regain positive postbooster anti-HBs status ( $\geq 10$  mIU/mL). To complete the vaccination, protocols are essential for not only population but also cost-effectiveness.<sup>[28]</sup>

The other perspectives are the differences among different HBV genotypes with respect to their transmission route. East Asia is a high prevalence area of genotypes B and C due to the vertical transmission, whereas horizontal transmission is more relevant in sub-Saharan Africa and the Mediterranean area where genotypes A and D are the dominating HBV strains. In Turkey, horizontal transmission is the main route.<sup>[4]</sup> For countries such as Turkey, tourism, migration, or refugees could be a risk of transmission. Vaccination is essential. To complete the vaccination, protocols are essential for not only population but also cost-effectiveness.<sup>[29]</sup>

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### Conflicts of interest

There are no conflicts of interest.

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