



Why the Hepatitis B Vaccine is not accomplishing its ultimate target?: A Systematic Review

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Abstract

Background: Hepatitis B remains a critical global health issue, affecting 296 million people with severe liver diseases and high mortality. Regional transmission patterns vary, with perinatal and childhood infections posing chronic risks. Despite expanded vaccination efforts, persistent barriers necessitate continued global initiatives for effective control. **Objective:** This study explores the underlying reasons hindering the full success of Hepatitis B vaccination programs. **Methodology:** A comprehensive search across multiple databases to identify relevant studies using specific keywords. Only English-language studies matching the review topic were included, while case reports and non-matching studies were excluded. After screening abstracts and full texts, 17 studies were selected for analysis, while 23 others were excluded for not meeting the inclusion criteria. **Results:** Of the 17 reviewed studies, 11 were cross-sectional surveys, 2 were qualitative studies, 1 was retrospective, 2 were case-control, and 1 was a randomized controlled trial. Sample sizes ranged from 48 to 1026, with diverse participants across occupations and age groups. Ten key barriers to effective hepatitis B vaccination were identified, varying by region. Around 24% of studies focused on high-risk populations, while three examined vaccine escape mutants, posing a significant challenge. Another three studies highlighted vaccine non-responders, which is estimated at 10% globally. More than 53.0% of studies linked inadequate immunization to low parental education and lack of vaccine awareness. Cultural barriers and needle phobia appeared in 26.0%, vaccine cost, and availability in 14.0%, and healthcare workers' insufficient knowledge in 9.0%, all contributing to vaccination challenges. **Conclusion:** Hepatitis B vaccination has reduced infection rates, but low coverage and incomplete dosing remain concerns. Addressing vaccination barriers is crucial for prevention. Despite challenges, global HBV eradication is possible with improved vaccination guidelines and enhanced efforts in screening and immunization.

Keywords: Hepatitis B Vaccination; vaccination barrier; hepatitis B elimination barrier

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Introduction

Hepatitis B virus (HBV) infection is one of the most urgent public health concerns in the world. Significant differences nevertheless exist even though hepatitis B infection has decreased globally, especially among children under five, thanks to national immunization

campaigns¹. The hepatitis B virus (HBV) continues to pose a serious threat to public health around the world in spite of the stringent vaccination campaigns. Globally, both acute and chronic liver illnesses significantly increase the burden of disease and mortality^{2,3}. According to the Centers for Disease Control and Prevention (CDC), HBV complications are the seventh most common cause of death worldwide³.

According to estimates from the World Health Organization (WHO), there were over 296 million chronic hepatitis B (CHB) sufferers globally in 2019⁴. In the same year, around 1.5 million new HBV

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infections occurred, and an estimated 820,000 deaths, were primarily due to the complications such as cirrhosis and hepatocellular carcinoma (HCC)^{1,4}. Transmission patterns of HBV infection vary by endemicity. In low-endemic regions, HBV spreads mainly through horizontal transmission among adolescents and young adults. On the other hand, infection is often acquired in early childhood, in highly endemic areas. Side by side, perinatal transmission is the most common route in Asia, Whereas in Africa, childhood horizontal transmission predominates⁵⁻⁷. The likelihood of becoming a chronic HBV carrier depends on the age of infection. Perinatal infection results in a 90% risk of chronicity, while infection in infants and children under five carries a 25.0% to 30.0% risk. In contrast, fewer than 10% of infected adults develop chronic HBV⁵⁻⁶.

In 1981, the United States authorized the first HBV vaccine, which was made from human carrier plasma. The WHO suggested in 1991 that all nations should have universal HBV immunization by 1997⁸. Since then, the majority of countries have included the HBV vaccine in their baby vaccination regimens. From less than 1% in 1990 to 30% in 2000, the global vaccination rate rose to almost 50.0% in 2004 and 69.0% in 2008⁹. Ninety-two percent (177 out of 193) of WHO member states have started HBV immunization campaigns by 2008¹⁰. Although widespread vaccination has significantly reduced chronic HBV infection rates¹¹ however, persistent barriers hinder complete HBV eradication, necessitating continued efforts to improve vaccine access and awareness globally. In this review, we evaluated the underlying reasons why the ultimate target for making a successful Hepatitis B vaccination program is not being fulfilled.

Methodology

Method of Selecting Articles: We utilized comprehensive search strategies for this review across multiple databases like PubMed, BanglaJOL, Scopus, Academia.edu, Web of Science, Google Scholar, ScienceDirect, and Embase. To gather the relevant literature, we searched using keywords such as “Hepatitis B infection”, “Hepatitis B vaccination”, “Hepatitis B elimination barrier”, and “Hepatitis B vaccination barrier”, and the best-matched papers were selected.

Inclusion Criteria: Those studies were only included which were written in the abovementioned keywords and also written in English.

Exclusion Criteria: Those studies were not included which were written in other than English language, and also based on case reports, comparative studies, or not matched with our review topic.

Overall Outcome of the Search: For this writing, we selected 17 studies that were the best match. Those published articles were evaluated to see whether they fulfilled our writing objectives. First of all, the papers were selected by overlooking the paper's abstract. Then, the full papers were looked at to understand whether they met our review's inclusion criteria. And finally, we included and analyzed the relevant papers. At the same time, another 23 (other than the finally selected 17) studies that did not meet the inclusion criteria were excluded from our review.

Results

Overall review results: Of the 17 studies, 11 used a cross-sectional survey design, 2 publications utilized a qualitative study approach, and just one study used a retrospective methodology. There were two case-control studies and only one randomized controlled trial. The number of samples in each study ranged from 48 to 1026, with the retrospective study having the fewest samples of any study. The cross-sectional survey studies' samples varied the most between working sectors (businesspeople, permanent and part-time job holders, health care workers, foreign immigrants, institutional students, and also injectable drug users) and age groups (all ages) in community settings.

Identified reasons that are hampering the Hepatitis B Vaccination: Ten reasons in all have been found that could prevent the global hepatitis B immunization campaign from being effective. Each region has its own set of obstacles. Of all the investigations, about 24% (n=4) focused on the general population with high risk. Our review's findings showed that three studies concentrated on the emergence of vaccination escape mutants. This problem presents a significant obstacle to the vaccine's effectiveness.

Another significant factor is vaccination non-responders which was focused by the other three trials. This group is thought to comprise 10% of vaccination recipients worldwide. In the remaining published papers, we also noted some of the most frequent reasons why an HBV vaccination fails, including low educational attainment, cultural and customary barriers, needle phobia, side effects of the vaccine, health worker's limited knowledge about timing and dosing, the unusual price of HBIG,

inappropriately maintaining of the cold chain, etc. More than 53% (9) of the studies pointed out that the primary cause of inadequate immunization was parents' negligence and a lack of appropriate information about the necessity of the Hepatitis B vaccine. Cultural difficulties and parental or infant needle phobia were also reported by 26% (4) of the research. The unusual price of vaccines in the private sector and their unavailability were the main topics of 14% (2) of the analyzed research. About 9% (2) of the studies cited inadequate vaccination knowledge among healthcare personnel, making it the fourth most highlighted factor.

Discussion

The WHO urges nations and regions to invest in eradicating hepatitis by integrating costing, budgeting, and financing elimination services into their universal health coverage plans. To achieve this goal, it is crucial to implement not only effective vaccination programs and treatment but also comprehensive policies for addressing and solving the reasons behind it¹².

This vaccination has been proven the safest and most effective for all age groups in several clinical trials¹³. Nearly 28% of medical professionals are currently interested in getting vaccinated, while other general populations were unwilling to get vaccinated because they were unsure of the vaccines' effectiveness and safety margin¹².

Out of the four doses of the Hepatitis B vaccination, more than 2763 students from different institutions (76.75%) had already received the vaccine, while the remaining students had never received it, per a study done in Bangladesh. About 20 individuals (0.56%) out of the 76.75% of participants did not receive the recommended vaccination, while 166 individuals (4.61%) received the four dosages of immunizations later than expected. The efficacy of the hepatitis B vaccine is negatively impacted by this kind of activity¹⁴.

In our review, we found that more than 17% of the studies gave top priority to the emergence of vaccination escape mutants¹⁵. Some studies highlight that mutations in the S gene of HBV, particularly in the α -determinant, can be selected under the immune pressure exerted via vaccination, especially when HBIG is administered^{3,4,15}. Another seventeen percent of the papers focused on vaccination non-responders¹⁶. This non-vaccine response is an immune reaction state. This blunted immune response, often attributed to impaired T cell activation or the recognition of the

HBsAg antigen, presents a significant challenge^{6,8,16} in the vaccine's efficacy.

A number of obstacles, including social and cultural hurdles, time constraints, a lack of awareness regarding HBV14, HBV infection among high-risk populations, and a lack of understanding about the need to take the vaccines timely¹⁴, made it challenging to complete appropriate vaccination¹⁷.

Among 53% of the study shown; lack of information regarding hepatitis B vaccination and vaccine-related negligence among parents were the main factors that hampered successful vaccination. At the same time, about 14% of the studies focused on the unavailability and unexpectedly high price of the vaccine in the private sector. In this review, we found nine percent of reviewed studies noted that low awareness among healthcare workers as well as Inadequate knowledge of HBV was considered a barrier that hampered effective vaccination.

Predictable probability: There is considerable potential to improve HBV vaccination and screening rates through government-backed mass education initiatives and increased awareness among high-risk populations. Implementing such proactive interventions could enhance the overall effectiveness of the immunization campaign.

Conclusion

The rates of HBV infection, chronicity, and associated consequences have been successfully decreased by the hepatitis B vaccine. Even if the vaccination rate for hepatitis B is low, a sizable portion of the population is not receiving the entire dose, which could be harmful to their health. In order to stop the spread of hepatitis B infection, it is important to address the several factors that influence hepatitis B screening and vaccination. A significant fraction of the population still carries the virus despite significant attempts to lower HBV infection by universal immunization of all newborns and school-age children. As humans are the only HBV reservoir, future HBV eradication all over the world is still feasible despite its challenges. A revised and improved guideline on vaccination management should be followed for all countries.

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Conflict of Interest

No conflicts of interest are involved in producing this manuscript for publication.

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Authors' contributions

Tanzila Rawnuck, Md. Selim Reza and Shaheen Ara Begum were involved in the study's design, interpretation, and discussion as well as the search for pertinent literature. The manuscript was edited and critically reviewed by Shaheen Ara Begum, Md. Shahin Bepari, and Nusrat Jahan. The final manuscript was read and approved by all writers.

Data Availability

Any inquiries regarding supporting data availability of this study should be directed to the corresponding author and are available from the corresponding author on reasonable request.

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