Cost-Utility Analysis of Expanding Hepatitis B Vaccination Among Healthcare Workforce in Ethiopia

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Abstract

Objective Ethiopia is one of the countries with high endemicity of hepatitis B infection. In Ethiopia, the current vaccine coverage among health care workers accounts for around 14%. Most health workforce (241,250) of Ethiopia was first considered as susceptible with a probability of getting Hepatitis B Virus acutely and 5–10% chance of progressing to chronic Hepatitis B. Hence, examining cost-utility analysis of hepatitis B vaccination coverage among healthcare workers in Ethiopia was found the most essential work.

Method Markov model for expanding vaccination coverage (3 doses of hepatitis B vaccine) was simulated based on the data obtained both primary and secondary data. A secondary data particularly cost and effectiveness data were obtained from published articles, World Health Organization (WHO) guidelines and Ethiopian Federal Ministry of Health (FMOH) documents. Moreover, cost related data for vaccination and chronic hepatitis B treatment were also gathered by interviewing expertise from Tikur Anbesa Specialized Hospital (TASH). This study was conducted from a healthcare payer perspective, with 3% discount rate of cost and health outcome as WHO recommendation. Primarily health outcome was measured by Quality Adjusted Life Year (QALY) gain and Incremental Cost-Effectiveness Ratio (ICER). Deterministic analysis and tornado diagrams were employed to manage parameter uncertainty and show a plausible range of cost and effectiveness of variables.

Result Current vaccination program is more expensive (USD 29.99) with a positive incremental cost of USD 1.32 and less effective that have negative incremental effectiveness of -0.08 and total life year gains of 28.54 than Expanded Hepatitis B vaccination strategy which costs USD 28.67 and gives relatively high total life-year gain of 28.62. The resulting ICER was USD 16.23 per QALY gained. However, the ICER was a negative for the current vaccination strategy that could show, it was dominated by the Expanded Hepatitis B vaccination strategy. One-way sensitivity analysis also provided that the current vaccine coverage was dominated for an increase in the risk of infection among unvaccinated individuals.

Conclusion Increasing current vaccine coverage from 14% to no less than 80% across Ethiopian healthcare workforces would be the most cost-effective strategy.

Introduction

Hepatitis B Virus (HBV) is one of the serious global health burdens that affect the lives of more than two billion peoples. Hepatitis B (HepB) is primarily transmitted by percutaneous or mucosal contact of infected blood and body fluids, and occupationally exposure of healthcare workers during dental, medical and surgical procedures¹. HepB virus could be acute or chronic based on the persistence of HepB surface antigen (HBsAg) for less or more than six months. Most of the acute HepB infections were self-limiting that doesn't require specific treatment. However, 0.5-1% of individuals may develop fulminant hepatitis with a mortality rate of 70–80%. Meanwhile, 3–5% of adults with acute HepB have a chance of progressing into chronic HepB². Chronic HepB could be treated by highly effective antiviral therapy like

Tenofovir, lamivudine, etc. Despite that only 5% of Chronic Hepatitis B (CHB) patients have access to treatment for various reasons³. Patients with chronic HepB may have a 40% risk of developing sequelae like cirrhosis, liver failure, and Hepatocellular Carcinoma. Consequently, 15–25% of peoples with chronic HepB infection die every year due to liver complications³.

Recently it was estimated that around 350 million peoples all over the world live as chronic carriers of the virus with a prevalence of 3.5%⁴. However, the endemicity of HBV varies across the world with the highest prevalence occurring in Asia and Africa⁵. Particularly healthcare workers have 10 times more risk of acquiring HBV infection than the general population⁶. Globally, the annual incidences of hepatitis B infection in healthcare professionals reach about 6%⁴. Likewise, in Ethiopia, the high risk of exposure was also reported among physicians, clinical nurses, midwives, laboratory technicians, and anesthetists consecutively⁷.

Currently, three doses of monovalent HepB vaccinations which are given for six months were the most effective and safe way to prevent HepB infection⁸. Both WHO and Ethiopian FMOH recommends that all health professionals should be vaccinated against HBV. Those institutions indorsed to reach the HBV vaccination coverage at least 90% among highly susceptible health professionals such as midwifery, surgeons, dialysis workers, and laboratory reach⁹.

However, across several countries, HBV vaccination coverage among all healthcare workforce who directly or indirectly participate in the healthcare service delivery including health extension workers, medical waste handlers, janitors remained low (< 20%)¹⁰. In Ethiopia, the minimal (14%)^{11,12} coverage of HepB vaccination among healthcare professionals was also reported. Different studies stated several reasons such as lack of vaccine availability at healthcare centers, higher cost of vaccine at private health facilities, lack of knowledge about the severity of HBV infection, and low attitude towards risk factors and efficacy of the vaccine^{11,12} for the low coverage in the country. Hence, this cost-utility analysis determined the cost of increasing HepB vaccine coverage among all healthcare workforces such as nurses, laboratory, pharmacy, medical doctors, midwives, janitor workers, supportive staff and its effectiveness on disease prevention, QALY gained in comparison to current HepB vaccination coverage.

Method

Cost-utility analysis of expanding HepB vaccination was conducted in comparison to current Ethiopian HepB coverage among healthcare workers in Ethiopia. Ethiopian FMOH is the main public healthcare deliverer which is responsible for policy formulation, planning, development, and management of all health issues. The minster office has above 241,250 health workforces under various categories such as health extension workers (15%), paramedical professionals (35%), medical doctor professionals (3%), supportive and administrative staff (30%) and others⁹. The average age of individuals was estimated at 32 years. All healthcare workforces in Ethiopia were included in this study. It is because these peoples have a relatively high occupational exposure to the HepB virus as compared to the general population⁷.

Accordingly, this study was implemented across all health facilities in the country i.e., 16,243 health posts, 3,743 health centers, 220 primary hospitals, 64 general hospitals, 27 referral hospitals, and other administrative offices like the regional health bureau, district health offices, and FMOH⁹.

The study was conducted from the healthcare payer perspective i.e., Ethiopian FMOH, though vaccines are financed by international donors (Table 1). Finally, the cost of increasing vaccination coverage, effect on the life year gains, quality of life, ICER, and disease prevention of HepB vaccine was evaluated over the lifetime of healthcare workers i.e., 65 years since it was assumed that vaccines provide lifetime protection. The cost and QALY were adjusted to a 3% discount rate as of WHO recommendation (Table 1). Synthesis based estimate of data was used accordingly, several studies conducted in China, USA, and Ethiopia were referred, and mean value was taken to overcome misleading data findings from a single study.

Table 1
Method summary of economic evaluations of cost-utility analysis of expanding hepatitisB vaccination among healthcare workforce in Ethiopia

Disease	Hepatitis B
Population	Healthcare workforce
Intervention	Increasing vaccination
Comparators	Current vaccination
Outcome	Disease prevented, QALY gained, Cost
Perspective	Health care payer
Time Horizon	Lifetime
Discounting	3%
Sensitivity Analysis	Deterministic Sensitivity analysis
Type of Model	Markov modeling

All necessary pharmaceuticals including the HepB vaccine were procured and supplied primarily by the Ethiopian pharmaceutical supply agency (EPSA). Antiviral drugs like Tenofovir 300mg, Lamivudine 150mg alone which are used for the treatment of chronic HepB are not included in the pharmaceutical procurement list of Ethiopia ¹³. However, they are assumed to be supplied by EPSA and currently available at a TASH. Cost related data were gathered by interviewing expertise from TASH (Nurses, Physicians, and Pharmacists), WHO HBV guideline. Furthermore, effectiveness related information were also gathered from distinctive pieces of literature review. All costs were expressed in USD at an exchange rate of 28 Ethiopian Birr to USD 1 on June, 11, 2019.

Model structure

As the model of HepB virus disease progress depicted in (Fig. 1) indicates any susceptible individual may stay at “susceptible state” without acquiring an infection. Otherwise, get infected by HBV first acutely with a 5–10% chance of progressing to chronic HepB and 0.5-1% case fatality rate. The other chance of susceptible individuals is either develop self-immunity or get vaccinated from prior infection. Any person who has immunity could stay an “immune” health state. The other health state is the “Chronic hepatitis” state. In this health state, an infected person may live as a chronic carrier or get treatment then progress to a healthy (“immune”) state. On the other hand, when any abnormality following or resulting from a chronic HepB infection such as liver permanent damage (cirrhosis), the individual enters to “Sequelae” health state. Despite this, any health state has a probability of entering into an absorbing state i.e., death.

Assumptions

Hepatitis B vaccines are available in different formulations for an infant in combination with other vaccines, like diphtheria–tetanus–pertussis (DTP), Haemophilus influenzae type b (Hib), and Inactivated Poliovirus (IPV). However, in this economic evaluation, only the monovalent HepB vaccine was considered since it is presently implemented with an effectiveness/protection rate of 90% in Ethiopia^{4,9}. The term immunized is considered as healthcare workers receive a complete series of 3 doses of HepB vaccine within a six-month duration. All Healthcare workers who didn't receive the vaccination before were assumed to be eligible for vaccination without being screened for HBV. Utility value for chronic HepB, sequelae, immune and susceptible was adopted from a study conducted in the USA. The transmission of HepB virus infection at health facilities and healthcare workers was not considered in our model. In this economic evaluation treatment cost of acute hepatitis is not included because it is essentially self-limiting infection. For patients with liver complications such as hepatocellular carcinoma and cirrhosis only supportive care like resuscitation, symptomatic treatment was taken into consideration. Vaccination results in life long (up to 65 ELY) immunization of healthcare workers.

Model Input

Effectiveness Data

In this study, the data regarding the chronic HepB disease progression, the natural history of the disease, vaccine effectiveness in infection prevention, treatment effectiveness in reducing disease progression towards sequelae, and the health outcome was taken from various kinds of literature and guidelines^{2,3,14} as indicated in Table 2.

Table 2

Various probability estimation of Hepatitis B disease progression obtained from published follow-up studies.

Health event incidence/transition	Probability	Range	Data source
Incidence of hepatitis B infection without vaccination among healthcare workers	0.05	0.4–0.8	16
The transition of acute hepatitis B to chronic hepatitis B	0.05	0.05–0.1	2
Progression of Untreated hepatitis B to sequelae (cirrhosis, HCC)	0.05	0.02–0.054	1
Death due to hepatitis B infection	0.0106	0–0.0106	
Incidence of sequelae chronic following hepatitis B treatment	0.0175	0.017–0.022	2,4
Death due to Hepatitis B complication	0.2	0.15–0.25	17
Utility of chronic hepatitis B	0.87	–	15
Utility of sequelae hepatitis B	0.57	–	
Utility of acute hepatitis B	0.43	–	
<i>HCC: Hepato-Cellular Carcinoma;</i>			

Cost Data

Cost of three series doses of HepB vaccine (Table 3) for every unvaccinated susceptible health workforce which accounts around 86% of the currently active healthcare workforce was determined and the price of one dose monovalent HepB vaccine is USD 17.8 and costs related to vaccine administration were also considered (total cost of the vaccine and its administration per cycle length/1 year was estimated at USD 57). For HepB treatment generic TDF 300 mg tablet was given as once-daily dose also optionally Propranolol 1 Omg, Furosemide 20mg tablet may be given as prophylaxis to sequelae and its cost was estimated USD 57 per length cycle (1 year) ².

Table 3

Estimated individual annual hepatitis B vaccination cost vs hepatitis B disease management cost

Service	List of items consumed/ service provided	Total cost per year
Vaccination	Hepatitis B, glove, syringe	USD 57
Hepatitis B treatment	TDF 300mg daily +/- diuretics	USD 57
Laboratory investigation	HBsAg ALT, AST, INR, BUN, Albumin, Creatinine	USD 88.56
Hospitalization cost	Symptomatic treatment and bed admission	USD 189
<i>ALT: Alanine Amino Transferase; AST: Aspartate Amino Transferase; HBsAg: Hepatitis B Surface Antigen; INR: International Normalized Ratio; TDF: Tenofovir</i>		

Laboratory monitoring and investigation for a patient with chronic HepB was estimated to cost ~ USD 57. This cost covers most of necessary laboratory tests like liver function tests (ALT, AST), HBsAg, Albumin, BIR, and BUN except HBV DNA test which is the most expensive and inaccessible test. For patients who develop sequelae like cirrhosis, Ascites, portal hypertension, and hepatocellular carcinoma cost of hospitalization and symptomatic treatment (USD 189) were also added to laboratory cost and treatment cost. Liver transplant cost for patients with liver failure was not estimated since it is not applicable in Ethiopia.

Most of the information regarding the cost of HepB vaccination and chronic HepB disease management was obtained from pharmacists, nurses, and physicians who actively work in TASH at the department of Gastroenterology, pharmacy, and internal medicine. Indirect cost, transportation cost, capital item costs like cold chain storage, deep freezer vans or vehicles, and other operational costs related to logistics were not included. Finally, the upfront cost for (e.g., flyers/advertisement) to increase vaccine coverage was not considered due to a lack of data (Table 3). The cost of the three series of vaccine doses and its administration costs (one-time costs) were considered at the beginning cycle of the simulation. Whereas the other costs were considered over the life time of health care work forces i.e., 65 years (33 cycles).

Model Output

An output of this economic evaluation were incremental cost, incremental effectiveness, and quality-adjusted life years gains of expanding HepB vaccination (from 14–80%) among all health workforce; and finally, its ICER per QALY was calculated.

Sensitivity Analysis

Deterministic sensitivity analysis was employed to manage some uncertainty relating to methodological assumption (such as time, cost, and effectiveness) variation of distinctive parameters and heterogeneity among healthcare workforce. Additionally, tornado diagram was also used to illustrate the plausible ranges of parameters obtained from published literature and guidelines of the country.

Results

The current vaccination coverage (14%) program is more expensive (USD 29.99) with a positive incremental cost of USD 1.32. It was also less effective having a negative incremental effectiveness of -0.08 and total life year gains of 28.54 than Expanded Hepatitis B vaccination strategy (80%). Expanding Hepatitis B vaccination costs USD 28.67 that gives relatively high total life-year gain of 28.62. The resulting ICER was USD 16.23 per QALY gained. Overall current vaccination strategy was dominated by increasing vaccination coverage to 80% (Table 4). The final average costs of the two alternatives were less than the estimated costs at the beginning of the cycle. This is for the reason that all healthcare workers might not get treatment as it could determine by the probability of getting the treatments such as, Tenofovir (due to unavailability and/or expensiveness issues).

Table 4

Base case results from cost-effectiveness analysis of Expanding Hepatitis B vaccination coverage versus Current vaccination coverage (June 2019)

Strategy	Cost	Life Years	ICER	NMB	C/E
Expanding Hep B vaccination coverage	28.67	28.62	—	24,954.85	1
Current He B vaccination coverage	29.99	28.54	-16.23	24,882.53	1.05
<i>ICER: Incremental Cost-Effectiveness Ratio; NMB: Net Monetary Benefits; C/E: Cost Per Effectiveness</i>					

Since Ethiopia does not have a standardized cost-effectiveness threshold (CET), the World Bank report of Ethiopia's GDP per capita (USD 783) was used to determine CET. Accordingly, GDP was multiplied by three to obtain an estimated CET of USD 2,349 per QALY gains. Despite ICER showed negative, the current vaccination strategy was dominated by increasing vaccination strategy (Fig. 2). Since an increasing in vaccination coverage on cost-effectiveness plane lies on quadrant two. Which made it a less expensive and more effective quadrant.

One-way sensitivity analysis provides that the current vaccine coverage was dominated for an increase in the risk of infection among unvaccinated individuals. For instance, when the probability of infection is increased among unvaccinated individuals; the outcome of ICER has increased from - 0.9 to -0.81. Accordingly, the cost has increased from 1.54 to 2.04 while the effectiveness had decreased from - 0.09 to -0.13 as the chance of infection is raised with the current vaccine coverage. The additional incurred cost was related to treatment costs after infection. Similarly, tornado result revealed that the probability of die due to sequelae, death due to hepatitis B infection, the progression of untreated chronic hepatitis B to sequelae, cost of lab investigation, probability of treating chronic hepatitis B is the main parameter which possibly affects the ICER value (Fig. 3). Varying cost parameters in the allowable range could increase the ICER value and the rest of the parameters might reduce or increase the ICER value base on the range.

From the two-way sensitivity analysis (Fig. 4), it was found that irrespective of probability of death occurrence in chronic hepatitis B and the probability of HBV infection in unvaccinated individuals increasing vaccine coverage improve total QALY gain.

Discussion

The foremost aim of this economic evaluation was to compare cost-utility analysis of increasing vaccination by 80% versus keeping current coverage (14%). By doing these costs required per every healthcare worker in either strategy was determined, welfare obtained in kind of life year gains, utility increment and infection prevention were also calculated. Several secondary data were used to conduct this analysis that obtained from published articles particularly effectiveness data. Moreover, estimated cost data for vaccination and chronic hepatitis B treatment was also collected from TASH^{1,3,15}.

The new expanded coverage (80%) strategy reduces the cost by USD 16.23 that was expended by the current vaccination program for every QALY gains in lifetime horizon. Besides this promoting vaccination coverage was necessary as it is a less expensive and highly effective strategy to combat hepatitis B infection among healthcare workers. Alongside in Ethiopian health care system economic evaluations was not common practice, hence conducting such analysis would help policymakers, public healthcare payers to invest scarce healthcare resource cost-effectively.

Deterministic sensitivity analyses showed that varying the probability of different variables of cost and effectiveness as the new strategy significantly dominates the current program (Fig. 2). While tornado result indicates that some variables impact on ICER value (Fig. 3). Cost-effectiveness threshold of USD 2,349 i.e., three times of Ethiopia GDP was used to check the affordability of the new strategy. Therefore, since the ICER has a negative value implementation of the new program could not be affected by the cost of the program.

In general, increasing vaccination coverage by 80% among healthcare work forces was found cost-effective in Ethiopia compared to the current coverage (14%) alternative. Furthermore, the Hep B monovalent vaccine highly effective in preventing the infection which gives a 90% effectiveness on the life time protection of the healthcare workers⁸. Hence; with a high risk of infection and burden of Hep B among healthcare workers and minimal reduction of the prevalence with the current coverage (from 7.4–6%)¹⁶, the new strategy is highly recommended in Ethiopia as it was more effective and saves additional cost that would be consumed by the current coverage (14%) strategy. Existing evidences also supports the high prevalence of Hep B among healthcare workers in Ethiopia. For instance, the seroprevalence of Hepatitis-B viral infection among the sample healthcare workers was 4.52% (95% CI: 2.4, 6.5) and 2.6% at Gondar and Addis Ababa referral hospitals respectively^{7,12}. Moreover, the pooled estimation of prevalence among healthcare workers presented a 5% prevalence in Ethiopia. When compared with other studies from African countries, the burden of Hep B viral infection is somewhat lesser. Healthcare workers are at high risk for viral infection compared to other ordinary people. Predisposing factors such as contamination due to medical procedures, workover load, and other factors are claimed to be responsible^{11,12,14,16}. Moreover,

regarding the accessibility of vaccines for health work remind a challenge particularly unavailability and cost are reported^{11,12,14}. This implies the burden of this viral infection is being an additional challenge for the health system of Ethiopia since the government is facing other diseases such as infectious and non-communicable diseases.

Study limitation

This economic evaluation has some limitations especially regarding costing variables. We did not include viral transmission rates among study participants, this might underestimate the benefit. Indirect cost related to increasing vaccination coverage such as vaccine transport and cold chain equipment cost was not included even though the expansion of vaccination coverage to around 80% over all the country health facility requires a high investment of capital items. This might cause an underestimation cost of the expanded vaccination program and might result in the absolute dominance of the current vaccination strategy. So, we recommend for future studies to include those costs.

On the other hand, the cost of a liver transplant for patients with liver failure and the cost of acute hepatitis B treatment was not explicitly determined. Also, direct non-medical cost like transport cost, loss of work due to the disease of every healthcare workforce was also not included. Although this study gives high emphasis to reduce healthcare worker occupational exposure to hepatitis B infection by providing vaccines, it does not determine the cost of screening before vaccination it uses a methodological assumption of all healthcare workers are susceptible and eligible to vaccination. Of despite all these limitations efforts have been made to use reliability data by gathering cost data from active physicians and other health professionals in TASH. In addition, a sensitivity analysis was conducted to test the robustness of the model to check whether it is consistent with the base-case analysis or not.

Conclusion

From this economic evaluation, it is possible to conclude that increasing current vaccine coverage from 14% to at least 80% among all Ethiopian all healthcare workforces was the most cost-effective strategy. As long as expanding hepatitis B vaccine coverage does not incur additional costs and in the meantime, it improves the healthy life of susceptible healthcare workers Ethiopian FMOH should work on its implementation.

Abbreviations

ALT: Alanine Amino Transferase; AST: Aspartate Amino Transferase; BIR: Bilirubin; BUN: Blood Urea Nitrogen; CHB: Chronic Hepatitis B; DNA: Deoxyribo-Nucleic Acid; ELY: Expected Life Year; EPSA: Ethiopian Pharmaceutical Supply Agency; FMOH: Federal Ministry of Health; GDP: Gross Domestic Product; HBsAg: Hepatitis B Surface Antigen; HBV: Hepatitis B Virus; HCC: Hepato-Cellular Carcinoma; HepB: Hepatitis B; ICER: Incremental Cost-Effectiveness Ratio; INR: International Normalized Ratio; QALY: Quality Adjusted Life Year; USD: United States Dollar; USA: United States of America; WHO: World Health Organization.

Declarations

Acknowledgment

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Authors' contributions

DT and MG, conceived of research problem and collected the dataset. DT, MG, and GA did a literature review and performed data analysis. GA and DT critically drafted and reviewed the manuscript. The manuscript has read and approved by all authors in this study.

Competing Interests

None

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None

Availability of Data and Materials

All data generated and analyzed during this during study are included in this published article and publicly available.

Ethics Approval and Consent to Participate

Not Applicable

Consent for Publication

All authors agreed to publish this research article

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Figures

Figure 1

Model of Hepatitis B virus disease progress and consequence

Cost-Effectiveness Analysis

Figure 2

Cost-effectiveness analysis of increasing Hepatitis B vaccination coverage

Figure 3

Tornado diagram of current hepatitis coverage versus increasing current hepatitis coverage
(Net Benefit, WTP=873.0)

Figure 4

Two-way sensitivity analysis of infection among unvaccinated and death due CHB infection