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The Estimation of Economic Burden of Hepatitis B Virus Infection in Iran

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Abstract

One of the most important public health concerns in both developing and developed countries is viral hepatitis B. It is an autoimmune liver disease, which imposes a high economic burden on individuals and the society. The aim of our study was to determine economic burden of hepatitis B virus (HBV) infection in Iran. To this end, 300 patients with HBV infection, who referred to hospitals in three cities of Iran during the year 2015, were randomly selected. To estimate the total burden of hepatitis, direct and indirect costs, costs of DALYs and social welfare were calculated which gave the costs of 7500.93 PPP$ and 96782 PPP$, respectively. Finally, our results showed that the total economic burden of HBV in Iran is dramatic which can lead to decreased quality of life of household members and damage the economy of the society. Therefore, the benefit of prevention and control measures will justify the costs from social perspective.

Keywords: Hepatitis B, Economic Burden of Disease, Direct and Indirect Costs, DALYs

1. Background

One of the most important public health concerns in both developing and developed countries is viral hepatitis. It is highest in developing countries such as those in Asia, Africa, the Pacific Islands, and the Arctic, and lowest in developed countries such as those in North America, Europe, and Australasia (1). Hepatitis B virus (HBV) is an autoimmune liver disease, which imposes a high economic burden on individuals and the society (2, 3). It is the most widespread cause of chronic hepatitis across the world. Many of inactive HBV infections would significantly transfer to chronic hepatitis (4). The annual death rate for chronic HBV infection is 500,000 - 700,000, making it the 10th leading cause of death in the world (5). Chronic HBV infection can progress to liver failure, cirrhosis, or hepatocellular carcinoma in a few decades. Long-term complications of chronic HBV infection can cause about half of all cases of cirrhosis and hepatocellular carcinoma in the world. The prevalence range of HBV infection is from 1% to 20% in different parts of the world, and Iran is among the countries with mild to moderate infections. This autoimmune liver disease imposes a great socioeconomic burden on individuals and society. Although individual patients suffer greatly from chronic HBV infection, policymakers and budget holders must know if the benefit of prevention and treatment justifies the costs from social perspective. For this purpose, data on the burden of disease are regarded the basis of economic calculations. In 1993, Dean T. Jamison suggested the global burden of disease (GBD) for the first time (6). Consequently, this methodology was used by the world health organization (WHO) and the Harvard school of public health in order to assess the health of populations.

Several methods have been proposed to quantify population-level burden of disease. The disability adjusted life years (DALYs) is a way to measure population health and is being increasingly used to compare and analyze the burden due to diseases (7). It is a concept similar to healthy year that includes weights for time spent in less-than-perfect health. DALYs are composed of two components: (1) years of life lost (LLY) due to premature death and (2) years lived with disability (YLD) associated with nonfatal injuries and diseases (8, 9). To measure the economic burden of hepatitis, a considerable number of studies have been published in literature (10, 11). Economic burden of hepatitis B virus infection in different stages of disease was evaluated by Zahra Kavosi et al. in 2014. The results showed that the total annual costs per patient for chronic hepatitis B, cirrhosis, and hepatocellular carcinoma were US$ 3094.5, US$ 17483, and US$ 32958 during 2012, respectively (12). In another study, the average diagnostic and treatment costs of chronic HBV with respect to different therapeutic strategies in Iran were estimated. The results of this

study showed that the total cost of diagnostic services for HBV was US$ 1499.07 and the total costs of treatment varied significantly from US$ 73 to US$ 8256 (4). Kanwal et al. evaluated the cost-effectiveness of six strategies in HBV cirrhosis. Their results showed that both Entecavir and Adefovir strategies are cost-effective in patients with HBV cirrhosis. Choosing between Adefovir and Entecavir strategies is highly dependent on available budget. In patients with HBV cirrhosis with previous Lamivudine resistance, "Adefovir salvage" appears more effective and less expensive than "Entecavir salvage" (11).

None of these studies estimated the disability adjusted life years of hepatitis B in Iran. Therefore, it is essential to carry out studies on this subject. The main aim of this study was to estimate population-level burden of disease by calculating the disability adjusted life years.

2. Objectives

The aim of our study was to determine economic burden of hepatitis B virus (HBV) infection in Iran. To this end, direct and indirect costs, costs of DALYs, and social welfare were calculated.

3. Methods

This study is an applied, retrospective, descriptive, and analytical research aimed to evaluate the economic burden of HBV infection in Iran. To this end, 300 patients with HBV infection, who referred to hospitals in three cities of Iran during the year 2015, were randomly selected. Cochran's method was used to compute the sample size of our study. Data collection was based on the public library system and questionnaires. A questionnaire was prepared composed of questions in three aspects (demographic information and patient's history, quality of life and work productivity, and activity impairment). Content validity of the questionnaire was examined with reference to the gastroenterologists' comments and opinions. They were asked to evaluate relevance, completeness, scoring, and clarity of each question. The Cronbach's Alpha Coefficient for each question was determined to test the reliability of the questionnaire. Cronbach's Alpha Coefficients were obtained above 0.75. The correlation of each question with other questions was higher than the medium level and there was no negative correlation (i.e. an inverse relationship) between the questions. Following the preparation of the questionnaire, a review of the literature was undertaken to recognize the latest treatments available for patients with HBV in Iran. Subsequently, the process of HBV management, including diagnostic and laboratory tests, physician visits, and drug treatments as direct medical costs, and transportation, meals, and telephone conversations as direct non-medical costs was evaluated. We also calculated the accommodation costs as direct non-medical costs. However, we assumed that most of the patients were in their own cities and did not need accommodation. Therefore, we eliminated accommodation costs from total direct non-medical costs. The unit costs of the mentioned items (diagnostic and laboratory tests and physician visits) were calculated based on the price lists approved by the public and private health centers (irteb.com/tarefaghanoon/index.htm). The prices of medication were retrieved from the drug list of food and drug office of iranian ministry of health and medical education (fdo.behdasht.gov.ir). Costs of transportation and extra health products due to illness were documented to obtain the direct non-medical costs. Days of absence from work (patient or his/her caregiver) and other services used outside of the health system were calculated as indirect costs which implied loss of productivity and quality of life. They were calculated by the use of laspeyres index. To estimate the total burden of hepatitis, we also calculated DALYS (disability adjusted life years) using Murray methodology (13). The years of life lost (YLL) due to premature mortality and the years lived with disability (YLD) are the two components of DALYs. Mortality rate and standard life table are the specific inputs for YLL calculation. Life expectancy was considered 74 and 77 years for men and women, respectively, based on life expectancy in Iran. Incidence, duration, and disability weight are the data specifically required for calculating YLD.

According to the above mentioned scheme, DALYs are formed from years of life lost (LLY) because premature death and years lived with disability (YLD) consist of nonfatal injuries and diseases. In order to calculate the years of life lost (YLL) due to premature mortality, 150 patients who had passed away because of HBV were randomly selected and their age at death was determined. YLL was obtained as 0.87 years based on the differences between life expectancy and the average age at death in HBV patients.

Another dimension of the DALY is the time period in years that one lives in the states of poor health or disability due to a disease. The disability is measured in terms of length (in years) and severity. The disability severity weights have been pointed out by the WHO for each disabling condition on a scale from one to zero. The mentioned scale, patients' physical conditions, and experts' opinion were used to determine the weights. To this end, HBV patients' physical conditions and reasons for their disability were evaluated. The reasons for patients' disability were determined as depression, anxiety, insomnia, pain, physical weakness, nervousness, inability to flex knee, in-

ability to walk more than 2 km, inability to do intensive or moderate activity, inability to climb stairs, and inability to dress up.

To estimate components of economic burden based on calculated DALYs, we multiplied DALYs by GDP (gross domestic product) per capita. GDP per capita was considered 15572.83 purchasing power parity dollar (PPP$). PPP$ was used for all costs in our study in order to make inter-country comparisons. We also considered economic welfare index to calculate the total economic burden of hepatitis. Welfare index was calculated by social welfare cardinal function as below:

$$W = \frac{1}{n}\sum_{i=1}^{n} Y_i = \overline{Y} \quad (1)$$

Where W is social welfare, Y_i is the income of individual, and n is the number of individuals. Finally, total economic burden of hepatitis B is the algebraic sum of direct medical costs, direct non-medical costs, and indirect costs. Costs of DALYs and costs of economic welfare index were also calculated as intangible costs.

4. Results

4.1. Characterizations of Patients with HBV Infection

The study was conducted on 300 patients with HBV infection in Iran. The demographic characteristics of the patients are shown in Table 1. Mean age (± standard deviation) of the patients with HBV infection in our study was 35.5 ± 6.4 years. Regarding sex and marriage status, 214 patients (71.3%) were male and the majority of them (252 (86%)) were married.

In Table 2, the frequency of patients based on smoking, drinking, use of drugs and physical activities is shown. As can be seen, the majority of patients (247 (82.3%), 288 (96%), 260 (86.7), and 183 (61%)) had no history of smoking, drinking, use of drugs, and physical activities, respectively.

We have also evaluated HBV patients in terms of underlying diseases. Our data showed that liver disease and peripheral vascular disease were the most prevalent underlying diseases with frequencies of 158 (87.3 %) and 40 (22 %), respectively. Education and occupational status of HBV patients is displayed in Table 3. As shown, most of the patients were employed, but did not have any academic education.

4.2. Direct Medical and Non-Medical Costs

To estimate direct medical and non-medical costs of HBV infection, we calculated costs of laboratory and diagnostic tests, physician visits, and drug treatments as direct medical costs and transportation, meals, and telephone conversations as direct non-medical costs. Common laboratory and diagnostic tests and their costs are shown in

Table 1. Socio-Economic Characteristics of Patients with HBV Infection

Variables	Frequency	Relative Frequency, %
Gender		
Male	214	71.3
Female	86	28.7
Age group		
20 - 30	66	22
31 - 40	97	32.33
41 - 50	58	19.33
51 - 60	44	14.66
> 61	35	11.66
Marital status		
Single	48	16
Married	252	86

Table 2. Smoking, Drinking, Use of Drugs, and Physical Activity of HBV Patients

Variables	Frequency	Relative Frequency, %
Smoking		
Yes	53	17.7
No	247	82.3
Drinking		
Yes	12	4
No	288	96
Use of drugs		
Yes	40	13.3
No	260	86.7
Physical activities		
Yes	117	39
No	183	61

Table 3. Education and Occupational Status of HBV Patients

Variables	Frequency	Relative Frequency, %
Occupation		
Employed	171	57
Unemployed	129	43
Education		
Academic	119	39.7
Non academic	181	60.3

Table 4. As can be seen, total cost for tests was estimated about 624.9 $ equal to 2043.4 PPP$.

Table 4. Common Laboratory and Diagnostic Tests and Their Cost for Patients with HBV Infection

Laboratory and Diagnostic Test Name	Unit Price, $	Frequency of Test Per Year	Total Cost Per Year, $
Viral load	89	2	178
PCR	138	2	276
Anti HBV	10	1	10
Liver biopsy	86.2	1	86.2
Liver sonography	11.5	1	11.5
ALT	2.3	4	9.2
AST	2.3	4	9.2
ALP	2.3	4	9.2
UA-UC	3.7	4	14.8
Bilirubin	2.9	4	11.6
Creatinine	2.3	4	9.2
Total costs			624.9

In Table 5, common therapeutic protocol in HBV infection and its associated costs for treatment are presented. Accordingly, total drug treatment costs were 1049$ equal to 3566.6 PPP$.

Table 5. Common Therapeutic Protocol in HBV Infection and Its Associated Costs for Treatment

Drug Name	Unit Price, $	Number of Drug Per Year	Annual Cost, $
Tenofovir	0.4	365	152
PEG Interferon alfa 2b	74.7	12	897
Total			1049

Table 6 shows the annual direct costs. As can be seen, the total direct cost for HBV infection was 6436.93 PPP$ annually. Minimum direct cost for HBV infection included the cost of telephone conversations (93.8 PPP$) that formed 1.5% of total direct costs. The highest direct cost was for drug treatment (3566.6 PPP$).

4.3. Indirect Costs

Average indirect costs, ratio of direct to indirect costs, and total cost of HBV infection were estimated as 325.3$ (equal to 1064 PPP$), 6, and 2252.1 $ (equal to 7500.93 PPP$), respectively.

4.4. Dalys (Disability Adjusted Life Years)

Based on the mentioned scheme, mean of severity weight for patients with HBV was obtained as 0.25. Our results also showed that HBV patients lived 11 years in a health status lower than the ideal health (due to disability). YLD was calculated as follows:

YLD = mean of severity weight $\times$ years lived with disability

$= 0.25 \times 11 = 2.75$

According to the above mentioned results, YLL and YLD were obtained about 0.87 and 2.75 years, respectively. Finally, DALYs which are composed of two components were obtained as 3.625 years. Costs of DALYs were gained from GDP per capita through YLL and YLD estimation. In Table 7, mean costs of YLL, YLD and DALY for each patient have been shown.

4.5. Social Welfare Index

Cardinal social welfare is a function that takes numerical representations of individual utilities as input and returns a numerical representation of the collective welfare as output. Costs of social welfare were 15,312 $ equal to 50,072 PPP$.

Finally, total economic burden of HBV infection was gained by sum of direct costs and indirect costs. It was obtained as 2252.1$ which is equal to 7500.93 PPP$. Intangible costs of HBV were sum of costs of DALYs and costs of social welfare. It was 29596.4 $ which is equal to 96,782 PPP$.

5. Discussion

Our retrospective study was specifically designed to assess the economic burden of HBV infection in terms of direct and indirect costs and costs of DALYs and social welfare based on the available data. As previously mentioned, HBV infection is now considered a serious health problem all over the world especially in Iran. It has imposed countless costs on the health system as a result of medical and non-medical services, loss of productivity, and decreased quality of life (14). Therefore, it seems that calculation of economic burden of HBV infection in Iran could help our health care system with the management and control of this common disease. According to our results, total direct cost of HBV infection was estimated as 6436.93 PPP$ annually for each patient suffering from HBV. Regarding the HBV patients population in Iran in 2015 (15), total direct cost for all HBV population in Iran is obtained as 9,011,702,000 PPP$ annually from which the drug treatment costs had the largest share. Our results were similar to the results of previous studies in Iran and other countries (16-18).

Table 6. Average Annual Direct Medical and Non-Medical Costs Per Patient with HBV Infection

Type of Cost	$	PPP$	Percentage
Direct medical costs			
Laboratory and diagnostic test	624.9	2043.4	31.7
Physician visits	69	225.63	3.5
Drug treatments	1049	3566.6	55.4
Direct non-medical costs			
Transportation	120.7	394.7	6.1
Meals	34.5	112.8	1.8
Telephone conversation	28.7	93.8	1.5
Total	1926.8	6436.93	100

Table 7. Average Cost LLY and DLY of HBV Infection

Type of costs	$	PPP$
Cost of YLL	4167.04	13626
Cost of YLD	13008.87	42539
Total costs of YLL and YLD (DALYs)	14284.4	46710

Some portions of direct medical costs of HBV will decrease in case of insurance coverage. Based on the insurance coverage percentages in Iran, different behaviors of the insurance organizations, patient share of payment and those costs of services which are covered by the insurance, we estimate that up to 40% of direct medical costs will be compensated by insurance and the remaining will be deducted from the household consumption expenditure. Therefore, about 5,743,749,200 PPP$ will be imposed on HBV patients population in Iran. As the total health cost in Iran in 2015 was 90,799,249,123 PPP$ (data.worldbank.org), the total direct cost due to HBV infection covered 6.3% of total health costs. Kalantari et al. also estimated the average costs of diagnosis and treatment of HBC with respect to different therapeutic strategies in Iran. Their results confirmed that the total direct medical costs for HBV patients in Iran exceeded 5,500,000,000 $ in 2011 (19). Since the household consumption expenditure per capita in 2015 was about 9962 PPP$ (kushnirs.org), based on our obtained results, 41% of it would be deducted by total direct costs of HBV. It would force household members to reduce other costs, leading to decreased total quality of life of household members. Another point is about indirect costs of HBV. It will impose 1,057,041,440 PPP$ on community and health care systems due to loss of productivity. As it is clear, this cost is dramatic and can damage the economy of the society.

According to the above mentioned, it is evident that considerable economic costs will be saved if our government eradicates HBV in Iran. One of the most cost effective health interventions about HBV is investment on immunization which will be achieved by keeping children healthy via vaccination. The complete vaccination series consist of three doses of vaccine. The first two doses are usually given 1 month apart, followed by the third dose 1 - 12 months later. WHO-recommended schedule for HBV immunization of children consists of a dose within 24 hours of birth followed by a second and third dose of hepatitis B containing vaccines at intervals of at least 4 weeks. The cost of each dose of HBV vaccination is about 10.8 PPP$ (fdo.behdasht.gov.ir). Based on the data, since the average annual number of births during a year per 1,000 persons in 2015 was 18.23 (indexmundi.com), total cost of infant vaccination (three doses) per year is estimated about 45,935,875 PPP$. In comparison with total direct costs of HBV per population, our results showed that mass vaccination of infants will bring economic benefits for health care systems and can be considered as a cost-effective public health intervention. Chen DS has also mentioned that the most effective way to control the prevalence of HBV infection is to immunize all susceptible individuals (20).

One of the main measuring indices of disease frequency is the incidence. Since this index is just based on patient's number and basic population data, to make comparisons between different areas or different times, it must be standardized. On the other hand, DALYs consider both survival time and life quality; thus, it is more an objective and comprehensive index than the incidence (21). In addition, standardization inherently occurs in the calculation of DALYs. Therefore, it can be directly used to compare between areas or diseases (22, 23). Our results showed that the average DALYs was 3.625. According to the total HBV population in Iran, total DALYs for population were obtained

as 5,082,000 years lost from which, about 1,225,000 years were the lost years due to premature mortality. It means that 1,225,000 years will be deducted from life expectancy in the community.

Our study was carried out to estimate economic burden of HBV in Iran. Our results showed that, economic burden of HBV is dramatic in Iran which will decrease total quality of life of household members and can damage the economy of the society. Therefore, the benefit of prevention and control measures justifies the costs from social perspective.

References

1. Merican I, Guan R, Amarapuka D, Alexander MJ, Chutaputti A, Chien RN, et al. Chronic hepatitis B virus infection in Asian countries. *J Gastroenterol Hepatol.* 2000;**15**(12):1356–61. doi: 10.1046/j.1440-1746.2000.0150121356.x. [PubMed: 11197043].
2. Arnot R. The evolving efforts to control hepatitis B virus. *Pediatr Infect Dis J.* 1998;**17**(7 Suppl):S26–9. doi: 10.1002/hep.22881. [PubMed: 9688096].
3. Brechot C, Jaffredo F, Lagorce D, Gerken G, Meyer zum Buschenfelde K, Papakonstontinou A, et al. Impact of HBV, HCV and GBV-C/HGV on hepatocellular carcinomas in Europe: results of a European concerted action. *J Hepatol.* 1998;**29**(2):173–83. doi: 10.1016/S0168-8278(98)80001-9. [PubMed: 9722197].
4. Kalantari HA, Jalali M. A ten-year study of histological variations of liver and laboratory findings in 100 healthy hepatitis b carriers. *J Isfahan Med Sch.* 2003;**67**:32–4.
5. Lee WM. Hepatitis B virus infection. *N Engl J Med.* 1997;**337**(24):1733–45. doi: 10.1056/NEJM199712113372406. [PubMed: 9392700].
6. The World Bank.World Development Report 1993: Investing in Health. New York: Oxford University Press and the World Bank; 2010.
7. Murray CJL, Lopez. A. D. . The global burden of disease: a comprehensive assessment of mortality and disability from diseases, injuries and risk factors in 1990 and projected to 2020. Cambridge MA: Harvard University Press; 1996.
8. Murray CJ, Acharya AK. Understanding DALYs (disability-adjusted life years). *J Health Econ.* 1997;**16**(6):703–30. [PubMed: 10176780].
9. Murray CJL, Salomon JA, Mathers C. A critical examination of summary measures of population health. In: Summary measures of population health: concepts, ethics, measurement, and applications. Geneva: World Health Organization; 2002.
10. Kanwal F, Farid M, Martin P, Chen G, Gralnek IM, Dulai GS, et al. Treatment alternatives for hepatitis B cirrhosis: a cost-effectiveness analysis. *Am J Gastroenterol.* 2006;**101**(9):2076–89. doi: 10.1111/j.1572-0241.2006.00769.x. [PubMed: 16968510].
11. Kanwal F, Gralnek IM, Martin P, Dulai GS, Farid M, Spiegel BM. Treatment alternatives for chronic hepatitis B virus infection: a cost-effectiveness analysis. *Ann Intern Med.* 2005;**142**(10):821–31. doi: 10.7326/0003-4819-142-10-200505170-00007. [PubMed: 15897532].
12. Kavosi Z, Zare F, Jafari A, Fattahi MR. Economic burden of hepatitis B virus infection in different stages of disease; a report from southern iran. *Middle East J Dig Dis.* 2014;**6**(3):156–61. doi: 10.5812/hepatmon.32654. [PubMed: 25093064].
13. Murray CJ, Lopez AD. Quantifying disability: data, methods and results. *Bull World Health Organ.* 1994;**72**(3):481–94. [PubMed: 8062403].
14. Alavian SM, Fallahian F, Lankarani KB. The changing epidemiology of viral hepatitis B in Iran. *J Gastrointestin Liver Dis.* 2007;**16**(4):403–6. [PubMed: 18193122].
15. Salehi-Vaziri M, Sadeghi F, Almasi Hashiani A, Gholami Fesharaki M, Alavian SM. Hepatitis B Virus Infection in the General Population of Iran: An Updated Systematic Review and Meta-Analysis. *Hepat Mon.* 2016;**16**(4):ee35577. doi: 10.5812/hepatmon.35577. [PubMed: 27257428].
16. Ong SC, Lim SG, Li SC. How big is the financial burden of hepatitis B to society? A cost-of-illness study of hepatitis B infection in Singapore. *J Viral Hepat.* 2009;**16**(1):53–63. doi: 10.1111/j.1365-2893.2008.01042.x. [PubMed: 19192158].
17. Tu HAT, Woerdenbag HJ, Riewpaiboon A, Kane S, Le DM, Postma MJ, et al. Cost of illness of chronic hepatitis b infection in vietnam. *Value Health Reg Issues.* 2012;**1**(1):23–8. doi: 10.1016/j.vhri.2012.03.008.
18. Keshavarz K, Kebriaeezadeh A, Alavian SM, Akbari Sari A, Abedin Dorkoosh F, Keshvari M, et al. Economic burden of hepatitis B virus-related diseases: evidence from iran. *Hepat Mon.* 2015;**15**(4):ee25854. doi: 10.5812/hepatmon.15(4)2015.25854. [PubMed: 25977694].
19. Kalantari H, Davari M, Akbari M, Hejazi SM, Kalantari M, Zakerin S, et al. The estimation of direct medical costs of treating patients with chronic hepatitis B and C in iran. *Int J Prev Med.* 2012;**3**(3):191–6. [PubMed: 22448312].
20. Chen DS. Toward elimination and eradication of hepatitis B. *J Gastroenterol Hepatol.* 2010;**25**(1):19–25. doi: 10.1111/j.1440-1746.2009.06165.x. [PubMed: 20136972].
21. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet.* 2006;**367**(9524):1747–57. doi: 10.1016/S0140-6736(06)68770-9. [PubMed: 16731270].
22. Gaunt ER, Harvala H, McIntyre C, Templeton KE, Simmonds P. Disease burden of the most commonly detected respiratory viruses in hospitalized patients calculated using the disability adjusted life year (DALY) model. *J Clin Virol.* 2011;**52**(3):215–21. doi: 10.1016/j.jcv.2011.07.017.
23. Mathers CD, Vos ET, Stevenson CE, Begg SJ. The burden of disease and injury in Australia. *Bull World Health Organ.* 2001;**79**(11):1076–84. [PubMed: 11731817].