

Economic Burden of Hepatitis B Virus Infection in Different Stages of Disease; a Report from Southern Iran

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ABSTRACT

BACKGROUND

To estimate the total annual cost due to chronic hepatitis B (CHB)-related diseases imposed on each patient and his/her family in Iran.

METHODS

Economic burden of CHB-related diseases (CHB, cirrhosis, and hepatocellular carcinoma) were examined. In this retrospective study, 100 Iranian patients were identified to obtain their socioeconomic status, utilization (direct and indirect costs) and costs of treatment, and work days lost due to illness with a structured questionnaire during 2012. Costs of hospital admissions were extracted from databases of Nemazee Hospital, Shiraz, Iran. The outpatient expenditure per patient was measured through the rate of outpatient visits and average cost per visit reported by the patients, while the inpatient costs were calculated through annual rate of hospital admissions and average expenditure. Self-medication and direct non-medical costs were also reported. The Human Capital Approach was used to measure the work loss cost.

RESULTS

The total annual cost per patient for CHB, cirrhosis, and hepatocellular carcinoma were US\$ 3094.5, US\$17483, and US\$ 32958 during 2012, respectively.

CONCLUSION

CHB-related diseases impose a substantial economic burden on patients, families, and the society. This study provides useful information on cost of treatment and work loss for different disease states, which can be further used in cost-effectiveness evaluations.

KEYWORDS

Chronic Hepatitis B infection; Cost of Illness; Health Care Economics

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INTRODUCTION

Viral hepatitis is the most prevalent liver disease worldwide. Among the human diseases that impose major health concerns, hepatitis B infection is a serious threat for human health. An estimated two billion people have been infected with hepatitis B virus (HBV) which is the 10th leading cause of death in the world. The annual death

rate for chronic HBV infection is 500000-700000 deaths, 75% of which are among Asians. 360 million people are infected with chronic HBV.^{1,2} The prevalence of HBV infection significantly differs in various geographical regions, ranging from 1% to 20% in different parts of the world.³ Generally 45% of the world's population live in areas with a high prevalence (positive HBsAg more than 8%) of infection.⁴ Chronic HBV infection can progress to cirrhosis and liver failure or hepatocellular carcinoma in a few decades. About half of all cases of cirrhosis and hepatocellular carcinoma in the world are caused by the long-term complications of chronic HBV infection.⁵

Iran is among the countries with mild to moderate infections; the exposure rate has been reported as high as 35% and the rate of chronic infection ranges from 1.7-5%. Half of the HBV infections in Iranians were found in newborns from mothers who were chronic carriers. The epidemiology of HBV infection in Iran has changed during the last two decades. In Iran, the mass vaccination program started in 1993 and reached coverage of 94% in 2005.⁶ The reported prevalence of HBV infection in Iran decreased from about 3.5% in the 1990s^{7,8} to 2.14% in the first decade of the 21st century.⁹ Studies show that about 51-56% of Iranian patients with cirrhosis had chronic HBV infection.¹⁰ This fact denotes the importance of the socio-economic burden of this infection,¹¹ the vast distribution of HBV infection, and the need for the development of safety and prevention.

Few studies have been published on the economic burden of HBV infection.¹² To the best of our knowledge, no study has been done on estimating the economic costs of HBV in Iran. We aimed to assess the direct and indirect expenses of chronic HBV infection and its related diseases. The economic burden of illness for patients referred to medical centers was estimated according to community perspectives in Iran during 2012.

MATERIALS AND METHODS

This research is a cross-sectional, descriptive-analytical and its population included all patients

with chronic hepatitis B infection, liver cirrhosis, and hepatocellular carcinoma who referred to the Hepatitis Outpatient Clinic, and Nemazee Hospital inpatient services in Shiraz, south of Iran, during 2012.

100 patients were randomly selected from about 1200 patient. The sample size was determined by statistical consultation based on pilot sampling. With respect to the risk of disease in Iran, 78 patients with chronic hepatitis B, 17 patients with cirrhosis, and 5 patients with HCC were included. Random sampling of the patients enrolled in the Research Center for Gastroenterology and Liver Diseases was done using the table of random digits.

The inclusion criteria were having chronic hepatitis B infection, liver cirrhosis, or hepatocellular carcinoma due to chronic hepatitis B infection. The system of billing and patient records were used as the data source and a standardized data collection form was prepared. The validity and reliability of the study was considered as one of the steps. The standard questionnaire included data on recalling information about the condition and use of inpatient and outpatient services as well as their socio-economic (such as age, sex, education, occupation, and insurance) and disease status (disease stage, elapsed time of diagnosis, follow-up results, and symptoms), expenses of the medical treatment (number of physician visits, levels of facility use, types of checkups, prescribed drugs, hospital stay, surgery, and other treatments such as liver transplantation and self-treatment). Moreover, days of absence from work (patient or his/her caregiver) and other services used outside of the health system were documented.

The economic burden of disease was estimated based on prevalence with an emphasis on direct medical costs. Patients with chronic HBV, cirrhosis, and hepatocellular carcinoma were followed up for 3 months and the costs were estimated using a bottom-up approach. Input costs are collected by per service with the bottom-up approach. In this case, the input data at the patient level was used for estimating the number and the type of services provided at each center.

Since major differences might exist between Iran and other countries with respect to the costs and the patients' social and economic status, specific cost information was evaluated for Iran. Total economic burden of chronic hepatitis B infection consisted of two parts, the direct economic burden (medical costs and non-medical costs) and the indirect costs during one year. With the use of economic resources of healthcare, direct medical costs could be measured including the average outpatient and inpatient costs, and the cost of drugs purchased from pharmacies outside the hospital, and other medical procedures. Annual outpatient or inpatient cost per patient was determined by the rate of visits and average cost of every visit. The formulas were:

- Direct medical cost=annual outpatient expenditure per patient+annual inpatient expenditure per patient+annual expenditure of self-medication per patient
- Annual outpatient expenditure per patient =average outpatient expense at a visit×the average rate of outpatient visits in three months×4
- Annual inpatient expenditure per patient =average inpatient expense at a time at the certain hospital level×proportion of inpatients at the certain hospital level)×annual rate of hospital admissions per patient

Cost of transportation and extra health products due to illness were summed up to obtain the direct non-medical cost. With the mean monthly consumption stated in the questionnaire, the average yearly amount could be measured.

With respect to the indirect costs, the Human Capital Approach was used. This technique measures health by improving productivity and income (especially through the reduction work absenteeism and increased life expectancy). It should be noted that the income of housewives and people who were unemployed before the disease was considered zero in this study. The indirect cost of each family depended on the daily income and days of sick leave of the patient, and the average daily income per caregiver, as well as the duration of their absence from work for the sake of nursing and caring. SPSS software, version 16 was used for data analysis.

RESULTS

Direct Medical Costs

Of the 100 patients, 87, 17, and 5 patients had chronic hepatitis, liver cirrhosis, and hepatocellular carcinoma, respectively, with a mean(\pm SD) age of 42(\pm 2.1) years (range:1-72 years). We found an increase in the total direct annual medical costs for patients with advanced disease. Most of the direct costs of medical services were related to diagnostic costs for chronic hepatitis B infection. However, for later stages of the disease (liver cirrhosis and hepatocellular carcinoma), hospital admission costs comprised a large portion of direct medical costs. The estimated annual cost of treatment per patient in different stages of the disease is shown in table 1. In 2012, the estimated annual direct medical costs per patient at different stages of chronic hepatitis B infection was 4098 U.S dollars (102450000 Rials, each dollar is equal to 25000 Rials).

Direct Non-Medical Costs and Indirect Costs

Direct non-medical costs and indirect costs per person in different stages of the disease are shown in table 2. The estimated annual direct non-medical and indirect costs for all stages of disease per patient with chronic hepatitis B infection were 1564.2 and 4079.8 U.S dollars, respectively.

Estimating the Economic Burden of Chronic Hepatitis B Infection

In table 3, the economic burden of chronic hepatitis B infection per patient has been shown in various stages of the disease during 2012. Total economic burden of chronic hepatitis B infection and its related diseases was estimated to be 657 million and 608 thousand dollars.

In the present study, with an increase in age, direct and indirect medical costs reduced. Therefore, there is an inverse relationship between age and direct medical costs. There was a direct correlation between sex and direct medical costs (direct costs were higher in women than men), but the association was not significant. Indirect costs were higher in men than in women, it is why that most women

Table 1: Estimated annual direct medical costs per patient at different stages of the disease in 2012

	Total direct non-medical costs (\$)	Total indirect costs (\$)
Chronic hepatitis B infection	334.19 (7.12%)	1436.2 (11.73%)
Cirrhosis	1480.8 (31.56%)	5159 (42.15%)
Hepatocellular carcinoma	2877.6 (61.32%)	5644.3 (46.12%)
Average	1564.2 (100%)	4079.8 (100%)

Table 2: Estimated annual direct non-medical costs and indirect costs per patient at different stages of the disease in 2012

	Visit costs(\$)	Diagnosis costs(\$)	Drugs costs(\$)	Other medical procedures(\$)	Total direct medical costs(\$)
Chronic hepatitis B infection	269.87 (20.39%)	618.45 (46.7%)	422.47 (31.9%)	61.41 (1.01%)	1324.19
Cirrhosis	7163.7 (66.06%)	1660.5 (15.31%)	1272.5 (11.73%)	746.3 (6.9%)	10843.13
Hepatocellular carcinoma	14504 (45.6%)	2220.8 (9.1%)	6871.6 (28.12%)	839.3 (3.44%)	24435.8
Total	2153.5	875.5	889.4	179.3	4098

Table 3: Estimated economic costs associated with chronic hepatitis B infections per patient in different stages of the disease in 2012

	Chronic hepatitis B infection	Cirrhosis	Hepatocellular carcinoma	Average(\$)
Direct medical costs(\$)	1324.19 (42.79%)	10843.1 (62.02%)	24435.8 (74.14%)	12201
Direct non-medical costs(\$)	334.19 (10.78%)	1480.8 (8.48%)	2877.6 (8.73%)	1564.2
Indirect costs(\$)	1436.21 (46.43%)	5159 (29.5%)	5644.37 (17.13%)	4079.8
Total economic costs(\$)	3094.59 (100%)	17483 (100%)	32957.8 (100%)	17845.13

in the study were housewives and therefore men lost more revenue due to illness. Comparison of costs together with Pearson's test revealed that the costs of this study have significant positive correlation with each other and the most relevance was between direct costs and indirect medical costs.

DISCUSSION

This study was the first study that attempted to estimate the direct costs at the national level and indirect costs in the terms of lost productivity or

absence from work due to chronic hepatitis B infection, cirrhosis, and hepatocellular carcinoma. We found that chronic infection with hepatitis B and related diseases imposes great financial burden on the health system and society in Iran.

In a study in Vietnam on 904 patients (226 with chronic hepatitis B infection, 358 with hepatocellular carcinoma, and 320 with cirrhosis), Hong's and colleagues estimated the total direct medical costs to be 4,038,537,132 U.S dollars. In this research, direct medical costs comprised 40% use of inpa-

tient services and outpatient visits and 21.7% for drug costs. The costs related to other procedures (such as physiotherapy and social services), similar to our results, had little impact on these costs.¹³

One of the most important factors affecting the cost of treatment is disease stage. Early stage of the disease is less expensive for treatment but later stages and their complications are associated with higher treatment costs. In patients with chronic hepatitis B infection, nearly 47% of direct costs are allocated to medical diagnostic services (such as laboratory tests, biopsy takings, ultrasonography, etc.), followed by the cost of drugs (32%). However, cost of outpatient visits and hospital admissions (46%) for patients in the later stages of the disease (cirrhosis and hepatocellular carcinoma) were among the highest direct costs. This can be attributed to the duration of admissions and stay in the intensive care units (ICUs). Shiraz is a center for liver transplantation in Iran. Many patients with chronic hepatitis B infection are referred from outside the city or nearby provinces. Also patients with liver cirrhosis and hepatocellular carcinoma are referred to our study centers for liver transplantation from all over the country so direct non-medical costs and indirect costs are considered as part of the cost of illness.

Our patients were 63% of men and 37% of women. Also, the financial burden on households due to chronic hepatitis B was affected by gender, age and severity of illness as well as length of stay ($p < 0.05$). Disease progression increased the requirement for hospital admissions. Therefore, direct and indirect costs rose with increased length of hospital stay. This is because costs of ICUs are higher than other wards.

In a study in Singapore, 71% of patients were men with a mean age of 46 years. Education, race, employment status, and household income had no significant impact on the economic burden of hepatitis B infection.¹⁴

In general, accurate data about the economic impact of hepatitis B infection is essential for health policy-makers with respect to prevention and treatment of this disease. The results of this study can

be considered in the governmental policy, and treatment expenses need to be considered with priority. Indeed, one of the priorities of Ministry of Health and Medical Education in recent years is supporting of cost of the cost of illness research.

This study had several limitations; firstly our sample may not be a good representative of our society. Many patients with chronic hepatitis B who lived in rural areas were farmers or had low-wage jobs; therefore, going to the clinic for outpatient visits on a regular basis was difficult for them. Moreover, our data were only collected from limited centers in Shiraz and we have generalized our results at the national level. However, these centers could be considered as referral ones. So treatment costs may be overestimated in Iran too. Even with the limitations listed here, this is the only study in Iran that has estimated the disease burden of chronic hepatitis B infection and can provide valuable information for health system managers and policy makers in the planning and allocation of resources.

For reducing the financial burden of diseases associated with chronic hepatitis B infection in Iran, the following recommendations can be provided: the use of screening programs and patients' access to timely detection of hepatitis B infection, improving the quality and quantity of health insurance for people with hepatitis B infections, providing subsidies by the government to reduce costs, management and resource allocation and proportional to the tariff, and improving comprehensive services and public health systems based on primary health care.

Considering the prevalence of hepatitis B infection in Iran and the massive financial burden it imposes, hepatitis B vaccination of infants at birth is recommended and to improve and restructure the drug policy, treatment and prevention measures seem necessary.

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CONFLICT OF INTEREST

The authors declare no conflict of interest related to this work.

REFERENCES

1. Lee WM. Hepatitis B virus infection. *N Engl J Med* 1997; **337**:1733-45.
2. Lai CL. Chronic hepatitis B in Hong Kong: immunization strategies for the control of hepatitis B virus infection. In : Zuckerman, ed. Hepatitis B in the Asia _pacific region vol. 1 screening, diagnosis and control London: *Royal College of Physician* 1997:79-87.
3. Lavanchy D. Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures. *J viral Hepat* 2004; **11**:97-107.
4. Kowdley KV. The cost of managing choronic hepatitis B infection: a global perspective. *J Clin Gastroenterol* 2004; **38**:S132-3.
5. Saffar MJ. Viral Infection and Protection: Iran. *J MazandaranUniv Med Sci* 2009; **67**:133-44.
6. Alavian SM, Fallahian F, Lankarani KB. The changing epidemiology of viral hepatitis B in Iran. *J Gastrointestin Liver Dis* 2007; **16**:403-6.
7. Farzadegan H, Shamszad M, Noori-Arya K. Epidemiology of viral hepatitis among Iranian population--a viral marker study. *Ann Acad Med Singapore* 1980; **9**:144-8.
8. Amini S, Mahmoodi MF, Andalibi S, Solati AA. Seroepidemiology of hepatitis B, delta and human immunodeficiency virus infections in Hamadan province, Iran: a population based study. *J Trop Med Hyg* 1993; **96**:277-87.
9. Alavian SM, Hajarizadeh B, Ahmadzad-Asl M, Lankarani KB. Hepatitis B Virus Infection in Iran: A Systematic Review. *Hepat Mon* 2008; **8**:281-94.
10. BagheriLankarani K, SaberiFiroozi M, Nabipoor I. Reassessment of the role of hepatitis B and C viruses in southern Iran. *Iran J Med Sci* 1999; **24**:117-21.
11. KargarF. The change of epidemiological pattern of Hepatitis B infection in Iran. Qazvin Blood Transfer, 2005.
12. Harbarth S, Szucs T, Berger K, Jilg W. The economic burden of Hepatitis B in Germany. *Eur J Epidemiol* 2000; **16**:173-7.
13. Hong AT, Woerdenbag HJ, Riewpaiboon A. Cost of Illness of Chronic Hepatitis B Infection in Vietnam. *Value in Health Regional Issues* 2012; **1**: 23-8.
14. 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**:53-63.