



ORIGINAL RESEARCH ARTICLE

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# Health care resources utilization and costs associated with different clinical stages of chronic hepatitis B in Egypt

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## Abstract

**Introduction:** Chronic hepatitis B (CHB) is associated with many serious clinical and social consequences. Despite Egypt being classified as a country of low endemicity, the infection is associated with a 15–25% risk of premature death from liver cancer or end-stage liver disease. The national committee of treatment and control of viral hepatitis has already offered a high-quality service for the diagnosis and treatment of CHB on a free basis. The current study aims to estimate the health care resources utilization and the annual direct medical cost associated with different clinical stages of CHB-related disease in Egypt.

**Methodology:** The data was retrieved through record review for three months in the General Administration of Hepatitis Viruses Control, Egypt. Then, the data was extrapolated to the population level by multiplying the prevalence in Egypt with a focus on the productive age groups (25–59 years).

**Results:** The cost and utilization of different health care resources increase with disease progression. The total annual direct medical costs due to CHB in Egypt is 21.3 L.E. Billion (4.7 Int\$ billion/year) for the management of estimated 1,420,700 CHB patients. The direct medical costs among the productive age group (25–59 years) constitute more than half of the total cost (57%). The highest disease burden is encountered among (25–29 years) age group; 2.695 L.E. billion (0.59 Int\$ billion/year). Despite liver transplantation phase being associated with the highest annual cost/patient, the number of patients in this stage is the lowest. Then, it only constitutes 0.04% of the disease direct medical cost in the country. The chronic hepatitis clinical stage constitutes 57.26% of the disease direct medical cost in Egypt's working age group.

**Conclusion:** Strengthening the preventive and control measures is mandatory to alleviate the disease's direct medical costs. Close monitoring of the chronic hepatitis stage is mandatory to prevent disease progression. Enhancement of vaccination efforts will lower the disease prevalence and its cost. The universal health insurance system which is gradually implemented in Egypt nowadays will be a cornerstone in relieving the economic stresses by allowing more access to high-quality health care services.

**Keywords:** Chronic hepatitis B, Egypt, Direct medical cost, Health care resources, Prevalence

## Introduction

Hepatitis B virus infection (HBV) is considered as an important public health problem due to its high morbidity and mortality. World Health Organization (WHO) defines CHB by the persistence of HBsAg more than 6 months [1]. CHB has many serious clinical consequences

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due to the progression into different clinical stages, cirrhosis, hepatic decompensation, and hepatocellular carcinoma (HCC), where liver cirrhosis and HCC are the main causes of death. Additionally, the course of treatment is life long and its main objective is to improve liver function and slow down the progression of the disease with no cure [2]. This clarifies the high economic burden of such infection which creates great financial stress on those infected as well as the health care systems [3, 4].

Health care resources utilization is reflected in the direct medical costs as well as indirect costs associated with the management of CHB-related diseases. The direct medical costs include cost of visits to doctors, investigations, treatment, and complications management. Indirect costs include costs of productivity loss, caregiver time, and transport to the health care facility [4]. In addition, CHB patients suffer from multiple intangible costs which include psychological stress and withdrawal from society [5].

Despite these serious outcomes, CHB is underestimated and undertreated. In 2016, WHO reported that approximately 240 million people have CHB worldwide. While, according to Global Health Sector Strategy (GHSS) service coverage indicators on Viral Hepatitis of the same year; only 9% of those infected with HBV are diagnosed and only 8% are on treatment [6].

Regarding Egypt, the prevalence of hepatitis B infection is 1% according to Egypt Health Issue Survey 2015, which is considered as low endemicity. However, in Egypt CHB is associated with a 15–25% risk of premature death from liver cancer or end-stage liver disease [7, 8].

Several efforts to control viral hepatitis have been carried out by the Egyptian Ministry of Health and Population (MoHP). A national treatment program was launched in Egypt, 2007, aiming at reducing the morbidity and mortality of both HCV and HBV. This program costed \$80 million annually which covered 40% of the total costs, while 60% of the cost was paid by other sources: insurance companies (50%) and patients (10%) as out-of-pocket expenditure. Then, a national committee to develop a National Control Strategy for Viral Hepatitis (2014–2018) was established. The implementation of this strategy led to a great reduction in the prevalence and better accessibility to treatment. The national committee of treatment and control of viral hepatitis has already offered a high-quality service for the diagnosis and treatment of CHB on a free basis [7]. Despite HBV is being a health threat with great economic losses, there is no published evidence about its burden in Egypt either in the form of direct or indirect cost [9].

The present study aims to estimate the health care resources utilization and annual direct medical costs associated with different clinical stages of chronic

hepatitis B-related disease in Egypt. Additionally, the age group, as well as the clinical stage of the greatest direct medical cost, will be identified. This in turn will help the decision-makers in targeting the proper prevention and control strategies to the most suffering cohort which will be subsequently reflected in the morbidity and mortality of the disease.

## Methodology

Health care resources utilization and their costs in Egypt were retrieved through record review from the General Administration of Hepatitis Viruses Control, Egypt, after getting approval using a well-structured study questionnaire. The questionnaire included items of health care resources utilized according to the different clinical stages of CHB. These items were identified from the healthcare perspective (Egypt MoHP) through an expert panel consultation from professors of the Hepatology Department, Alexandria Faculty of Medicine, and the National Liver Institute in Cairo. The review process focused on the frequency of utilization and the unit cost of each item, and it lasted for 3 months. The items included frequency of outpatient visits, frequency, and types of needed investigations, medication types, dosing, drug acquisition costs, and management of the associated side events. In addition to hospitalization length of stay and the per diem cost. Liver transplantation cost was included, when applicable. The cost of each item was considered from a health care perspective for both insured and non-insured patients.

To extrapolate the estimated costs to the population level, the data revealed from the above-mentioned questionnaire is multiplied by the overall prevalence of CHB in Egypt. The prevalence is estimated by reviewing the latest evidence published about Egypt. According to the most recent Egypt Health Issue Survey, 2015, the prevalence was 1% [8]. However, a systematic review in 2020 about the current HBV prevalence in Egypt reported it as 1.4% [10]. Additionally, to identify the age group which carries out a higher burden from the disease, the 5 year age group prevalence was considered as well. The total population, as well as the number of populations in each 5-year age group, is reviewed from Egypt Central Agency for Public Mobilization and Statistics (CAPMAS) 2020 [11]. This allowed estimating the total number of CHB patients in the whole population as well as in each age group to clarify the direct medical cost of the disease.

To compare the direct medical cost among the different clinical stages of the disease, the transition probabilities among disease stages is considered according to the European Association for the Study of the Liver (EASL) guidelines 2017 [12] and other references [13–17].

The references revealed that; CHB patients can progress into the following clinical stages according to the mentioned annual probabilities: chronic hepatitis (60%), compensated cirrhosis (14.25%), decompensated cirrhosis (4%), hepatocellular carcinoma (2.98%), liver transplantation (0.002%), and death (18.77%).

Regarding the currency, all costs were converted from the Egyptian pound to international dollars according to the world bank Purchasing Power Parity exchange rate in 2020 which was 4.5 [18].

## Results

The cost and utilization of health care resources per patient in different CHB clinical stages are displayed in Table 1. Regarding outpatient visits, the frequency of visits is increasing upon progression into the different clinical stages where the patient in the chronic hepatitis stage utilizes only 2 visits/year and the patient in the liver transplantation phase utilizes about 30 visits/year. The patient in the other stages which are compensated cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma utilizes 4, 12, and 18 outpatient visits/year, respectively. Each visit costs 20 L.E. according to the health care perspective from MoHP considerations. The average annual direct medical cost of outpatient visits per patient for all clinical stages is 264 L.E./year (58.7 Int\$/year).

Several laboratory investigations are ordered in the outpatient clinic, e.g., liver function tests, complete

blood picture, Alpha-fetoprotein, and polymerizing chain reaction test. The cost of each laboratory investigation test is displayed in Table 1. Also, there are some radiological investigations such as ultrasound, fibro scan, and liver biopsy are included upon the need to detect the level of liver fibrosis. The average annual direct medical cost of laboratory investigations per patient is 14,388 L.E./year (3197 Int\$/year).

Regarding the treatment modalities, oral antivirals (nucleos(t)ide analog (NAs)) are the main line of treatment of CHB in Egypt. The oral antivirals include Lamivudine, Entecavir, and Tenofovir. The treatment is assigned according to the clinical assessment of the patients. A combination of medications is recommended upon developing resistance or disease progression. Pegylated Interferon is limitedly used according to the virus load or the special medical comorbidities. The treatment is lifelong in nature. The treatment costs range from (2400–24,000 L.E./year) according to the modalities adopted. The median annual treatment cost per patient is 13,200 L.E./year (2933 Int\$/year).

As regards the treatment of side effects of medications; the side effects become more apparent with the progression of the disease. The highest cost is associated with the liver transplantation clinical stage which is 325,000 L.E./year. This is mainly due to the multiple side effects of immunosuppressive medications used after the transplantation operation to prevent rejection

**Table 1** Annual healthcare resources utilization and cost/patient, general administration of hepatitis viruses control Egypt

Item	Unit cost (L.E./Unit)	Annual cost of utilization/clinical stage (L.E./year)					Average/median of annual cost for all clinical stages
		Chronic Hepatitis	Compensated cirrhosis	Decompensated cirrhosis	Hepatocellular carcinoma	Liver Transplantation	
<b>I. Outpatient visit</b>	20	40	80	240	360	600	264 L.E.
<b>II. Investigations</b>							14,388 L.E.
II.1. Liver function	150	300	600	1800	2700	4500	
II.2. CBC	40	80	160	480	720	1200	
II.3. AFP	100	200	400	1200	1800	3000	
II.4. PCR	800	1600	3200	9600	14,400	24,000	
<b>III. Treatment</b>	Median annual cost: 13,200						
<b>IV. Treatment of side effects</b>		NA	NA	3250	13,000	325,000	Median annual cost: 13,000 L.E.
<b>V. Hospitalization</b>		NA	NA	25,200	25,200	8400	19,600 L.E.
<b>VI. Liver Transplantation operation</b>							
VI.1. Preoperative diagnosis and laboratory investigations						20,000–40,000	Median annual cost: 186,500 L.E.
VI.2. Operation cost						150,000	
VI.3. Postoperative care						3000–10,000	

CBC Complete blood count, AFP Alpha feto protein, PCR Polymerase chain reaction

incidents. The median annual cost for treatment of side effects per patient is 13,000 L.E./year (2889 Int\$/year).

Hospitalization costs according to MoHP differ according to the clinical stage. In the decompensated cirrhosis and hepatocellular carcinoma clinical stage, the annual hospitalization cost is 25,200 L.E. The cost of hospitalization is calculated according to the following:

- The average hospitalization incidents/year in decompensated cirrhosis and hepatocellular carcinoma clinical stage is 6 incidents/year.
- The average hospitalization stay is 14 days.
- The cost of hospitalization day is 300 L.E.

However, in the liver transplantation clinical stage, after the success of transplantation operation, the patient's clinical condition becomes more stable, and the hospitalization incidents become only 2/year. Then, the cost of hospitalization is 8400 L.E./year. The average annual direct medical cost of hospitalization for all clinical stages is 19,600 L.E./year (4356 Int\$/year).

Finally, as regard liver transplantation operation cost, the operation costs include preoperative diagnosis and laboratory services, operation cost (surgery, anesthesia, instruments, consumables) as well as post-operative care. The median annual direct medical cost of liver transplantation operation is 186,500 L.E./year (41,444 Int\$/year).

Table 2 displays the total annual direct costs incurred per patient according to the different stages of CHB related disease. The annual cost increases according to disease progression where the liver transplantation stage constitutes the highest cost per patient with 3,231,900 L.E./year. (718,200 Int\$/year).

To extrapolate the estimated costs to the population level, the number of CHB patients is estimated by multiplying the population number by the disease prevalence. The total population, as well as the population/age group, is reviewed from the CAPMAS Egypt, March 2020 [11]. The overall prevalence of the population is considered as 1.4% [10]. The prevalence of CHB in each 5 year age group is reviewed from Egypt Health Issue Survey 2015

[8]. The estimated number of CHB patients in the general population in Egypt is 1,420,700 patients.

Table 3 demonstrates the estimated number of CHB patients/age group in Egypt. Calculations among 5-year age groups are focused on those aged (25–59 years). This age group is considered as the working group in which the burden of the disease will lead to more suffering on both personal and societal levels. Additionally, the hepatitis B vaccine was implemented in the expanded program on immunization in Egypt since 1992 which makes the prevalence among those below 25 years in Egypt nowadays very low (0.5%) [8, 19].

Table 4 displays the direct medical costs of CHB patients in each 5-year age group between 25 and 59 years in Egypt. In addition to the total direct medical costs of CHB patients among the whole population (0–75+). The total annual direct medical costs due to CHB in Egypt is 21.3 L.E. Billion (4.7 Int\$ Billion/year) for the management of 1,420,700 patients.

The direct medical costs of CHB patients among the productive age group of (25–59) years constitute more than half of the total cost (57%). The highest disease burden is encountered among 25–29 years age group (22%) followed by 35–39 years age group (20.8%) and 45–49 years age group (14.6%).

Additionally, the transition probabilities among different clinical stages are applied to each age group (25–59

**Table 3** Estimated number of CHB patients/age group, Egypt Health Issue Survey, 2015 and CAPMAS 2020

Age group	Population	Prevalence	Estimated number of CHB patients
25–29	8,986,594	2%	179,732
30–34	7,712,133	1.4%	107,970
35–39	7,068,566	2.4%	169,646
40–44	5,955,295	1.9%	113,151
45–49	4,758,085	2.5%	118,952
50–54	4,193,427	1.5%	62,901
55–59	3,705,615	1.7%	62,995
<b>Total</b>	<b>42,379,715</b>		<b>756,553</b>

**Table 2** Annual direct costs/per patient, the General Administration of Hepatitis Viruses Control, Egypt

Total cost	Chronic hepatitis clinical stages				
	Chronic hepatitis	Compensated cirrhosis	Decompensated cirrhosis	Hepatocellular carcinoma	Liver transplantation
Total cost/clinical stage (L.E./year)	81,420	83,640	263,220	328,380	3,231,900
Total cost/clinical stage (international dollar/year)	18,093	18,587	58,493	72,973	718,200

**Table 4** Total annual direct medical costs due to CHB per 5 years age group, Egypt

Age group	Total cost L.E Billion	International dollars (Billion)	% Contribution
25–29	2.695	0.598,888	2.0
30–34	1.619	0.359,778	13.2
35–39	2.544	0.565,333	20.8
40–44	1.697	0.377,111	13.9
45–49	1.784	0.396,444	14.6
50–54	0.943	0.210	7.7
55–59	0.945	0.210	7.7
Total (25–59)	12.225	2.717	100
Total population (0–75+)	21.301	4.733	

years) to properly calculate the total cost of health care resources utilization per clinical stage and subsequently identify the direct medical cost of the disease. Table 5 displays the number of CHB patients in 25–59 years age groups distributed among the different clinical stages of the disease as well as the contribution of each stage in the direct medical cost of the disease. Despite, liver transplantation phase is associated with the highest annual health care utilization cost per patient, the number of patients in this stage is the lowest. Then, it only constitutes 0.04% of the total CHB direct medical cost. On the other hand, the number of patients in the chronic hepatitis clinical stage is the highest and it constitutes 57.26% of the CHB direct medical cost in Egypt's working age group.

## Discussion

In Egypt, there is a scarcity of published evidence about the economic burden of CHB. The current study depends on the data collected from the General Administration of Hepatitis Viruses Control, Egypt to formulate an overview about the health care utilization and annual direct

medical costs incurred by the health sector for management of CHB.

Our findings show that the total annual direct medical costs due to CHB in Egypt is 4.7 Int\$ billion/year for the management of estimated 1,420,700 patients in the whole population. These findings are different from the results of a study carried out in Singapore, 2009 [20], where the total annual direct costs incurred due to CHB were 161 \$ Million for estimated 209,305 patients. Moreover, in a study about CHB economic burden in Vietnam, 2012 [21], the annual direct medical costs reached 4.0 \$ Billion for estimated 8,651,497 patients.

The wide difference in patients' number between countries and subsequently the annual costs is attributed to introducing hepatitis B vaccination in the national childhood immunization program in Singapore in 1985 which led to a great reduction in the disease prevalence while Egypt introduced it in 1992 [19, 22]. Additionally, Vietnam is considered as a high endemic country for HBV with a prevalence rate 15% [23].

In the current study, the maximum utilization of outpatient visits is incurred in the liver transplantation clinical stage while in a study carried out in the USA, 2019 [24], the highest frequency is incurred among HCC patients.

Our findings demonstrate that the patient in decompensated cirrhosis and hepatocellular carcinoma clinical stage has around 6 incidents of hospital admission/year with an average hospital stay of 14 days in each incident. These findings are consistent with the study in Vietnam in 2012 [21] where HCC patients experienced (2–6) hospitalization incidents/year with an average of (10–14 days) of hospital stay. However, in the study in the USA, 2019 [24], the hospitalization incidents ranged from 3–4 incidents/year in the same clinical stages with an average hospital stay of 6–10 days/incident. Additionally, in a study about Chinese CHB patients during 2015 [25], the average duration of hospital stay was 33 days.

The current study clarifies that the annual cost/patient increases according to disease progression from chronic hepatitis to liver transplantation stage (18.093–718.200

**Table 5** Number of CHB patients and cost% contribution of different CHB clinical stages

Clinical stage	Estimated number of patients	Total cost L.E Billion	International dollars (Billion)	% Contribution
Chronic hepatitis	453,932	7.001	1.556	57.26
Compensated cirrhosis	113,483	2.050	0.456	16.77
Decompensated cirrhosis	30,262	1.703	0.378	13.93
Hepatocellular carcinoma	21,940	1.467	0.326	12.00
Liver Transplantation	23	0.005	0.001	0.04
Deaths	136,913			
Total (25–59)	756,553	12.225	2.717	



Int\$/year respectively). In the study of Singapore [20], there was a doubling in the direct medical costs with disease progression from chronic hepatitis to liver transplantation clinical stage. Additionally, in a study carried out in Japan, 2021 about the economic burden of CHB [26] the average annual cost incurred/patient was  $1,332,417 \pm 2,049,712$  Japanese Yen irrespective of the clinical stage.

In the current study the average annual direct medical cost/patient regarding outpatient visits, laboratory investigations, treatment, and hospitalization is 59- 3.197- 2.993- 5.600 Int\$/year respectively. The health care costs in Egypt are lower than the costs reported in the study of Japan [26] where it was 711.523- 168.466- 633.063- 621.894 Japanese Yen for the same categories respectively. The Japanese study calculated the cost for 11,125 CHB patients.

Regarding the total annual direct costs/patient according to different stages of CHB related disease, the current study reported 18.093- 18.587- 58.493- 72.973- 718.200 Int\$ for chronic hepatitis, compensated cirrhosis, decompensated cirrhosis, HCC, and liver transplantation respectively. The costs reported in the study of Vietnam [21] were higher for the same clinical stages (450.35- 690.43- 1114.50- 1883.05 respectively) without considering the liver transplantation clinical stage.

In our study, the annual direct medical costs incurred in chronic hepatitis, decompensated cirrhosis, HCC, and liver transplantation clinical stage in the working-age group are 1.5, 0.37, 0.32, and 0.001 Int\$ Billion respectively for estimated 756,553 patients. However, the annual direct medical costs reported for the same clinical stages in the USA [24], China [2], and Southern Iran [27] were lower than our study findings.

In the study about the economic burden among US CHB patients in 2019 [24], the costs for the same clinical stages were \$142,870, \$124,123, and \$171,851 respectively for a sample of 33,904 CHB patients. In the study of China [2] the lower cost is attributed to the availability of affordable oral antivirals for Hepatitis B treatment as a part of a nation-wide strategy in China towards zero new hepatitis B infections [28]. In the study of Southern Iran [27], the costs reported for CHB, cirrhosis, and HCC were US\$ 30.945, US\$17.483, and US\$ 32.958, respectively, for 100 CHB patients. All these studies weren't focusing on the productive age group economic burden.

The wide range of differences regarding the frequency of health care resources utilization and their costs among different countries can be explained by the variation of the methodology of cost assessments, the differences in treatment protocols adopted, and the prices of healthcare goods in each country in addition to a variety of fiscal years among studies. Moreover, the

currency of the direct medical costs was not standardized in all studies which makes the comparison more difficult [29].

The direct medical costs of CHB patients among the productive age group (25–59 years) constitute 57% of the total cost in the current study. The highest disease burden is reported among 25–29 years age group which is 0.5 Int\$ billion/year. These results are consistent with a study carried out in Togo, West Africa [30] where the highest burden of HBV is reported among 20–29 years, age group. However, in the USA, the disease causes a higher burden among the elderly [31].

The main limitation of the current study is the inability to estimate the indirect cost of CHB in Egypt due to a lack of data on productivity loss secondary to CHB. Additionally, extrapolation of the findings to the population level was done without adjustment to the contextual factors (e.g., occupation and residency).

Finally, the inability to compare the current study results with previous Egyptian studies due to lack of published data about the CHB economic burden in Egypt.

## Conclusion

The current study clarifies the great burden of CHB related disease in Egypt. Strengthening the preventive and control measures is mandatory to alleviate such a burden. The health care resources utilization increases with the disease progression. This makes close monitoring of the CHB patients among 25–29 years regarding the liver condition as well as adherence to treatment is crucial to postpone the disease progression. This age group is the highest productive, highest fertile, and unfortunately contains the highest number of CHB patients in Egypt.

Enhancement of the vaccination efforts especially among those above 25 years is highly important. Hepatitis B vaccine is considered as a cost-effective measure for prevention of the disease with high efficacy as well.

The universal health insurance system which is gradually implemented in Egypt nowadays will be a cornerstone in relieving the economic stresses due to CHB by allowing more access to high-quality health care services.

Finally, further studies are needed to allow formulating a comprehensive view about the disease burden in Egypt and subsequently guiding the health policies in Egypt towards better allocation of resources.

## Abbreviations

CHB: Chronic hepatitis B; HBV: Hepatitis B virus infection; WHO: World Health Organization; HCC: Hepatocellular carcinoma; GHSS: Global Health Sector Strategy; MoHP: Ministry of Health and Population; CAPMAS: Central Agency for Public Mobilization and Statistics; EASL guidelines: European Association for the Study of the Liver guidelines.

**Acknowledgements**

Not applicable.

**Authors' contributions**

JA collected and analyzed the data. GG and GE revised the methodology, research objective, research tools, and data validity. AM and EA supervised the validity and relevance of the research results. All authors read and approved the final manuscript

**Funding**

Not applicable.

**Availability of data and materials**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Declarations****Ethics approval and consent to participate**

The study was approved by the Alexandria Faculty of Medicine Research Ethics Committee.

**Consent for publication**

Not applicable.

**Competing interests**

The authors declare that they have no competing interests.

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Received: 27 August 2021 Accepted: 4 December 2021

Published online: 20 December 2021

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