



The Economic Burden of Liver Cirrhosis in Iran: a Cost of Illness Study

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Abstract

Background: According to importance of cirrhosis of the liver and the lack of information about the economic burden of the disease, we performed this study to estimate the economic burden of liver Cirrhosis in Iran in 2011.

Methods: The cost-of-illness method, based on the human capital theory, has been used. Both direct and indirect costs have been estimated using a prevalence approach and bottom-up method. The inpatient and outpatient records were investigated for obtaining the medical costs. Also, a questionnaire was used for collection the other data such as transportation costs, out of pocket payment and times of inpatients, etc. Costs consisted of expenditures which happened during March 2011 to February 2012 and the perspective of the study was Iranian society.

Results: The total cost of the disease was 2014.5 billion Rials (USD164.32 million). Direct and indirect costs were 1384.16 and 630.4 billion Rials (86.7% and 11.3% of the total cost), respectively. Cost due to premature death was USD 38.66 million, included 23.52% of the total cost and 75% of indirect cost.

Conclusion: Liver Cirrhosis impose enormous economic burden on Iranian society. Policymakers should therefore take this into consideration and according to available health resources provide services and facilities for the prevention and treatment of the disease.

Keywords: Liver cirrhosis, Economic burden, Cost of illness, Out of pocket payments, Iran

Introduction

Today chronic liver disease is developing and liver cirrhosis mortality is increasing. Cirrhosis is a chronic liver damage. In this disease, normal liver tissue and its normal function are impaired. As the disease progresses the symptoms of decreased mental and physical function and biochemical failures appear. The result of this process leads to complete liver failure and death (1).

Etiology of cirrhosis is different in variety parts of the world such as America and countries with

high alcohol consuming, the most common cause of cirrhosis is associated with alcohol-related cirrhosis, and other main causes of the disease are hepatitis B and C (2). Cirrhosis is most common in men ages 20 to 59 year, at the age of productivity (2, 3).

Liver cirrhosis leads to 800,000 yearly deaths, 1.3% of total deaths, in the world. According to WHO classification is one of the eighteen significant causes of death. The five year survival of pa-

tients with alcoholic cirrhosis and nonalcoholic cirrhosis are 36% and 14%, respectively (4).

In recent years the use of health care services in the patients has been increased, for example, in Britain between 1989 and 2002, the hospital reception and the mortality of chronic liver disease, such as cirrhosis, have been increased. Moreover, cirrhosis in Europe led to the loss of 3.1 million Disability Adjusted Life Years (DALYs) (2% of total DALYs) which is the ninth cause of disease burden. The years lost due to disability (YLD) associated with cirrhosis have been estimated more than 3.79 million in 2000 (4).

In the recent years, many studies have been performed to estimate the economic burden of hepatitis and cirrhosis of the liver, because cirrhosis is one of the most important health problems and has a significant rate of mortality, morbidity, social psychological and economic burden (5-8). For example a study analyzed the scale and trends of the social and economic costs of liver disease in Korea for 5 years, and social and economic costs of illness were predicted 5858 KRW billion in 2004, the cost of production lost in premature deaths caused by liver cirrhosis was estimated 5572 KRW billion in 2005, 8104 KRW billion in 2006, 6095 KRW billion in 2007, and 5689 KRW billion in 2008 (9). In South Korea total resulting costs (direct plus indirect) from HBV related disease was 936.1 KRW billion (833.1 million USD) which 45.3% of that was attributable to cirrhosis (10). Besides, a study in China examined the total annual cost per patient for CHB, compensated cirrhosis, decompensated cirrhosis, and liver carcinomas (7). Liver cirrhosis has imposed enormous direct and indirect costs on society in Germany and Mexico, as well (11, 12). The study performed in Mexico to estimate the annual cost of treating patients with cirrhosis at the Mexican Institute of Social Security. They determine the cost of cirrhosis according the three stages of disease (Child-Pugh A, Child-Pugh B and Child-Pugh C) using micro-costing techniques and medical experts. The annual cost of treatment, in USA dollars, by Child-Pugh stage was: a) micro-costing results: \$1110.17 stage A, \$549.55 stage B and \$348.16 stage C; b) opinion of medical experts: \$1 633.64,

\$6564.04 and \$19660.35, respectively; and c) IMSS costs: \$4269.00, \$16949.63 and \$30249.25, respectively (13).

According to increasing the prevalence of liver cirrhosis and its heavy costs that have been imposed to the human societies and according to lack of information about the costs of the disease in Iran, this study has been performed. It is notable that there is no comprehensive study about economic aspects of liver cirrhosis in Iran so far. Also, having the correct information about the cost of diseases, it could be useful in making appropriate decisions about prevention and treatment of diseases. The aim of this study was to estimate the direct and indirect costs of liver cirrhosis and out of pocket payment as well.

Materials and Methods

Cost analysis

This is a descriptive and a retrospective study performed by cost-of-illness method based on the human capital approach. In this method, three domains should be determined, first the approach is incidence-based or prevalence-based, second the approach is bottom-up or top-down, and third how the direct and indirect costs will be determined (12). In the current study, prevalence-based and bottom-up approaches have been used and the method used to determine the cost shall come following. Outcome measures of the study were direct cost, indirect cost, out of pocket payments and total cost of the disease. Costs were consisting of expenditures, which happened during March 2011 to February 2012, and the perspective of the study was Iranian society.

Types of costs

The total economic burden of disease consists of two parts, first the direct cost, which consists of direct non-medical costs and direct medical costs, second indirect costs (7). In our study, all costs have been considered:

a) Direct costs: it contains medical and nonmedical direct costs that they describe following:

1. *Direct medical costs:* These costs measure the used economic resources for medical care and involve

the outpatient costs, inpatient costs, and costs of medications (12). Inpatient and outpatient costs or annual costs per patient have been calculated according to the average number of annual visits, diagnostic tests and medications and their price and these items were determined from patient's medical records in Shariyati hospital and outpa-

tient centers in Tehran for outpatient and inpatient care, respectively.

In order to calculate these costs inpatient and outpatient patients' medical records were investigated. Diagnosis tests, medication and visit fees were retrieved from the Ministry of Health tariff in 2011(14). The formulas that have been used here are:

$$\begin{array}{l} \text{The average cost for} \\ \text{outpatient diagnostic} \\ \text{tests for a patient in} \\ \text{2011=} \end{array} \quad \begin{array}{l} \text{The average number of tests per patient in 2011} \times \text{average cost of diagnostic} \\ \text{tests} \end{array} \quad [1]$$

$$\begin{array}{l} \text{Total cost of} \\ \text{hospitalization =} \end{array} \quad \begin{array}{l} \text{Average cost of} \\ \text{hospitalization} \end{array} \quad \times \quad \begin{array}{l} \text{The total number of patients admitted in a year} \\ [2] \end{array}$$

$$\begin{array}{l} \text{Total outpatient costs for patients=} \text{the cost of drugs purchasing without prescription} + \text{Cost of prescribed} \\ \text{drugs} + \text{cost of outpatient diagnostic tests} + \text{visit costs} \end{array} \quad [3]$$

$$\begin{array}{l} \text{Total cost of outpatient care} = \text{total cost of outpatient care for a patient} \times \\ \text{The total number of patients} \end{array} \quad [4]$$

2. *Direct nonmedical costs:* These costs include transportation costs, for patients and their families, the cost of purchasing additional health products due to the disease, costs of stay, and cost of home care. These were obtained from a questionnaire which designed according to the objectives of the study. The characteristics of the questionnaire shall come in the data source in fallow.

b) Indirect Costs: Indirect costs are divided into two major parts, indirect costs due to disability and indirect costs due to death. Indirect costs due to disability depend on the number of absent days from work, income and average revenue for caregiver (12). The daily wage was retrieved from Ministry of Labor and Social Affair (15) and used to calculate income loss for household women and anyone who does not have defined income. To calculate potential productivity lost due to premature death, Gross Domestic Product approach has been used. The per capita GDP was obtained from World Bank data (16).

We divided disability in two parts, disability caused by hospitalization and ambulatory care. There are three kinds of potential production lost for liver cirrhosis in this study:

1. *Potential production lost by death*

According to available data and related studies (17, 18) the Years of Life Lost due to Fatality (YLLF) associated with liver cirrhosis in 2011, and the prevalence of disease and probability of annual death in patients (0.0053) were obtained. The amount of production lost for one death has been calculated by the following formula (19):

$$\begin{array}{l} \text{Production lost for premature death for one} \\ \text{death=} \sum_{i=1}^N \frac{W(1+g)^i}{(1+r)^i} \end{array} \quad [5]$$

Where here: W = GDP per capita G = economic growth rate I = average years lost due to premature death

According to World Bank Report (20) GDP Per capita in the year 2011, was USD 4,526, which was considered. 0.05 and 0.03 use for discounting the cost. For developing countries 0.05 usually use because the future costs have a little value in now. Then we used 0.05 for discounting the costs and for GDP growth, according to its average in 30 past years, 3.7%was considered (16). Then the total cost of productivity lost caused by death obtained with multiply this by the number of deaths.

The number of deaths and average years lost due to premature death was obtained from related studies (18, 21).

2. Production lost cause by inpatient care

The mean of bed-days has been obtained by studying hospital records and this amount, multiply by inpatient cases and daily average wage in Iran 2011.

Finally, potential production lost was calculated by following formula: production lost in inpatient care in 2011 = $S \times J \times W_r$ (PL inP) [6]

where Here: S = the average days of inpatient care for cirrhotic patients in 2011 J = The total number of patients admitted in 2011, W_r = the average daily wage in 2011.

3. Production lost due to outpatient care

For calculating the potential production lost from outpatient care, the average of visits for each patient has been gained by outpatient records. The days with a disability because of the disease, and the days those losses for patient partners and caregivers have been obtained from the questionnaire. This amount multiplied by the average daily wage and total outpatients cases as following formula:

Potential production lost due to outpatient care = $(U \times F \times W_r)$ PL outP [7]

Where here: U =the average days of outpatient care for cirrhotic patients in 2011 F = total number of cirrhotic patients in 2011 W_r = daily wage in 2011.

Finally the total production lost was obtained by following formulas:

Total production lost = (PL f) + (PL inP) + (PL outP) [8]

Where here: PL f = production lost due to premature deaths in 2011, PL inP = production lost for inpatient care in 2011, PL outP = production lost due to outpatient care in 2011. Finally the total cost has obtained by the sum of the direct and indirect costs.

Data Source

For obtaining required data to calculate the costs, all inpatient records in Shariati Hospital of Tehran University of Medical Sciences (N=103) and 58

outpatient records in Tehran Hepatitis Center - Baghiatallah Research Center of Gastroenterology and Liver disease (THC-BRCGL), and Shariati Gastroenterology Research Center of Tehran University of Medical Sciences, were selected randomly and continuously. It is notable that we need to have an average of inpatient care and with use of this records obtained it. Also, 50 ambulatory patients have been participated in the Tehran Hepatitis Center - Baghiatallah Research Center of Gastroenterology and Liver disease (THC-BRCGL) and the Shariati Gastroenterology Research Center, randomly and continuously. The criteria for including the patient were: 1) patients with definitive diagnosis of liver cirrhosis, 2) patients who pass at least one year with the disease. They were interviewed via the questionnaire which developed based on the National Health Accounts Questionnaire and the objectives of the study. This questionnaire has been approved by expert opinion. It has two parts, the first part comprises demographic information (age, sex, marital status, education status, job, number of family members, etc.), income, length of illness, and insurance information and the second one contains information about indirect costs (absenteeism, sick leave, disability, etc.) and out of pocket payments. The costing analysis has been done with Excel 2010 software.

Sensitivity analysis

Considering that some of the used variables for estimating the burden of the disease were uncertain and to evaluate the impact of changes in these variables sensitivity analysis was performed. For sensitivity analysis the uncertain variables were determined, and then the different possible values of them used for calculating the costs. The uncertain variable including were the disease prevalence, the annual risk of death and life expectancy lost due to a premature death. For estimation the total cost of the disease 0.0013, 0.0053 and 18 were considered for the uncertain variables, respectively.

Results

Table 1 shows the data, their values and the data sources that have been used to estimate the eco-

conomic burden of the disease in Iran. According to data in Table 1 and cost of illness method we estimated the total cost and other cost related to the liver cirrhosis. Table 2 shows the total cost and other sub-costs in US dollar that in here each dol-

lar equals 12260 Iranian Rials, total cost was USD164.32 million, direct and indirect costs were USD 112.9 million and USD 51.42 million, respectively. The result for the subgroup of costs comes following.

Table 1: The used items for estimation of the economic burden of disease (monetary items are in Iran Rials)

Variables	Amount	Source
Population in 2011	75149669	Census of year 2011(26)
Number of patients with liver cirrhosis	99269	(21)
Prevalence of the disease	0.0013	(21)
Probability of hospitalization in a year	0.0571	Medical records and interview
The average cost of transportation and stay	1419020	Interviews with patient
The average cost of stay and transportation between cities	1122400	Interviews with patient
The average cost of transportation within the city	296620	Interviews with patient
The annual cost of visit in the private sector	780000	Tariff of 2011(14) and interviews
The average annual cost of visit in public sector	325000	Tariff of 2011(14) and interviews
The minimum monthly wage	3303000	(15)
Daily minimum wages	125000	(15)
Out of pocket payments for medication (for each patient at each visit)	418000	Interviews with patient
Out of pocket payments for purchasing the drugs per patient in 2011	2717000	Interviews with patient
Annual out-of-pocket payments for outpatient care (per patient)	6856583	Interviews with patients, outpatient records
Out of pocket payments for the Inpatient care	549600	Interviews with patients, inpatient records
The total out of pocket payments in 2011 (per patient)	7406183	Interviews with patients, outpatient and inpatient records

Table 2: Costs of cirrhosis of the liver disease in Iran, in 2011 (in USD millions)

Direct costs				Indirect costs				Cost of the illness					
Medical		non-medical		total		Production lost due to disability		Production lost due to premature death		total		total	
Amount	*%	amount	%	amount	%	amount	%	amount	%	amount	%	amount	%
101.42	61.72	11.48	6.98	112.9	68.7	12.79	7.76	38.66	23.52	51.42	31.3z	164.32	100

*percent of total cost

Total cost

According to our estimation total cost of cirrhosis in Iran in one year is approximately USD164.32 million (in 2011) which USD 112.9 million is related to total direct cost (Table2). Also, total indirect cost which the disease imposed to Iranian society was USD 51.42 million in 2011.

Direct costs

Direct costs were the most proportion (68.7%) of the total cost of the disease. The most proportion of the costs is related to direct medical costs. 62%

of the total cost is related to medical costs. Direct nonmedical costs, the cost of transportation and stay, include only 7% of the total cost. Costs due to premature mortality were accounted for 23% of the total costs.

The largest portion of the medical costs of the disease was related to purchasing outpatient drugs (Table 3). Hospitalization costs had a minimum portion of the costs. Totally, 97.15% of the direct medical costs were related to the outpatient care. Besides, the greatest portion of medical cost was for outpatient drug (64.12%).

Table 3: Medical costs of liver cirrhosis in 2011 (In USD millions)

Medical costs											
Outpatient costs								Inpatient cost		Total	
Drug		Diagnostic costs		Outpatient visit		total		Total			
Amount	%	Amount	%	Amount	%	Amount	%	Amount	%	Amount	%
65	64.12	27.18	26.8	6.31	6.2	98.5	97.15	2.88	2.84	101.41	100

Out of Pocket Payment (OOP)

Out of pocket payment is presented in Table 4. According to the table total out of pocket was USD 55.71 million and 99.59% of out of pocket payment was related to outpatient care and 39.45% of OOP costs were for buying outpatient drugs. The lowest portion of out-of-pocket pay-

ment (0.4%) was associated with inpatient care. Totally 49.3% of the direct medical costs were paid in the form of out of pocket payment. It should be noted out-of-pocket payment consists of the costs that were paid directly from the patient (including co-payments, costs of drugs, clinical tests and hospitalization).

Table 4: Out of pocket payments in cirrhosis of the liver in 2011 (in USD million)

Total		Out of pocket payments					
Amount	percent	For inpatient care		For outpatient care		For outpatient drugs	
		amount	percent	amount	percent	amount	percent
55.71	100	0.24	0.41	55.48	99.59	21.98	39.45

Indirect costs

Total production lost due to liver cirrhosis was USD 51.42 million in 2011 (Table5). Production lost due to disability was USD 12.76 million which USD 10.87 million of it is related to production lost due to outpatient care for patients and their

families. The cost of production lost per a death has been estimated 72,525 dollars, and total cost of production lost due to premature death was USD 38.66 million. Also, 75.17% and 14.83% of the indirect costs was related to premature deaths and disability, respectively.

Table 5: The cost of production lost according to different prevalence (number of deaths) and in USD millions

Years of life lost	Cost per a death	Production lost according to different prevalence (number of deaths)				
		0.0011 (452)	0.0012 (492)	0.0013 (533)	0.0014 (573)	0.0015 (614)
18	0.07	32.78	35.68	38.66	41.56	44.53
19	0.08	34.40	37.44	40.56	43.60	46.72
20	0.08	35.99	39.18	42.44	45.63	48.89

Sensitivity analysis

Considering that the used variables for estimating the burden of the disease are uncertain, the sensitivity analysis has been performed. According to different values of uncertain variables, related costs have been calculated. In Table 6, total cost of cirrhotic patients (in USD millions) was obtained by considering the probability of hospitalization equals to 0.0517. The total cost of illness, according to prevalence from 0.0011 to 0.0015, was 139.41, 151.83, 164.32, 176.74 and USD 189.23 million, respectively. Total direct cost varied from USD 95.79 million to USD 130.01 million and total indirect cost was approximately from USD 43.61 million to USD 59.23 million

according to different prevalence of liver cirrhosis in Iran.

The cost of production lost due to premature death according different number of deaths and average life expectancy lost per premature death have been shown in Table 5. Minimum and maximum cost of premature death, for 18 year life expectancy lost in a death, were USD 32.7 million and USD 44.53 million, respectively. In calculating total cost, according to the risk of death from cirrhosis of the liver (0.0053) and the prevalence of the disease (21), we consider 18 and 533, for the years of life expectancy lost and the number of deaths from diseases, respectively. Therefore, the cost of premature death has been estimated USD 38.66 million.

Table 6: Cost of liver cirrhosis in terms of the likelihood of hospitalization 0.0517 (in USD million)

	Prevalence	0.0011	0.0012	0.0013	0.0014	0.0015
Direct cost for outpatient care		83.6	91.07	98.53	106	113.46
Cost of outpatient drug		55.18	60.11	65.04	69.96	74.89
Cost of outpatient diagnostic test		23.06	25.12	27.18	29.24	31.3
Cost of outpatient visit		5.35	5.83	6.31	6.79	7.27
Total cost of visit		2.45	2.67	2.89	3.11	3.33
Production lost due to disability		10.83	11.8	12.76	13.73	14.7
Production lost due to outpatient care for patients and their family		9.23	10.05	10.87	11.7	12.52
Production lost due to outpatient care for patients		5.79	6.31	6.83	7.34	7.86
Production lost due to outpatient care for patients' family		3.43	3.74	4.05	4.35	4.66
Production lost due to premature death		32.78	35.68	38.66	41.56	44.53
Production lost due to inpatient care		1.6	1.75	1.89	2.03	2.18
The total cost of transportation		9.74	10.61	11.48	12.35	13.22
The total cost of transportation between cities and stay		7.71	8.39	9.08	9.77	10.46
The total cost of transportation within the city		2.04	2.22	2.4	2.58	2.76
Out of pocket payments for purchasing drugs		18.65	20.32	21.98	23.65	25.31
Out of pocket payments for outpatient care		47.07	51.27	55.48	59.68	63.88
Out of pocket payments for inpatient care		0.2	0.21	0.23	0.25	0.26
Total out of pocket		47.27	51.49	55.71	59.93	64.15
Total indirect cost		43.61	47.48	51.42	55.29	59.23
Total direct cost		95.79	104.35	112.9	121.46	130.01
Total cost		139.41	151.83	164.32	176.74	189.23

Discussion

The main objective of this study was the evaluation the economic burden of the liver cirrhosis in Iran, 2011. Direct and indirect costs of illness and out of pocket payments have been calculated.

The total cost of illness was 2,014.57 billion Rials (USD 164.32 million). The total direct and indirect costs were 1384.16 and 630.41 billion Rials (USD 112.9 million and USD 51.42 million) and direct cost is consist of direct medical costs, and direct nonmedical costs that were 1243.4 and 140.76 billion Rials (USD 101.42 million and USD11.48 million) ,respectively. Indirect costs include the productivity lost due to disability (for patient and family) and production lost due to premature death that was estimated at 156.4 and 473.9 billion Rials (12.79 and USD 38.66 millions).

Also, 68.7% of the total costs were related to direct costs, and indirect costs were 31.3% percent of the total cost. In the case of direct costs, 61.72% of the cost was related to medical expenses and 64.08% of medical expenses were related to outpatient drugs. 75.17% of indirect costs and 23.52% of the total cost were due to premature death. 97.15% of total costs were related to outpatient care. The annual treatment cost per patient was USD 1,023.

49.3% of direct medical costs paid in the form of out of pocket payments that it's close to the total OOP in Iran. It should be noted that the out of pocket payment in 2002, 2005 and 2008, was 52.4, 52 and 52.7 percent of total health care expenditure, respectively (22). We shall pay for the results of other studies in this field and mention weakness and strength of the study.

In South Korea the economic costs of liver disease were KRW 5,858 billion in 2004, KRW 5,572 billion in 2005, KRW 8,104 billion in 2006, KRW 6,095 billion in 2007, and KRW 5,689 billion in 2008 (9). The future production lost resulting from premature death was the greatest, from 73.9% to 86.1%, followed by the direct medical costs, from 9.0% to 18.1%. The productivity loss resulting from absent from work accounts for 3.3-5.5%, followed by the direct nonmedical costs

such as transportation and caregiver costs, at 1.5-2.5%. In liver diseases, liver carcinoma had the greatest portion of indirect cost. As it appears in direct costs in lee's study is higher than our study (31% vs.73.9%) because in that study all of liver disease had been considered and as we know liver carcinoma has a higher mortality in liver diseases. Besides, in our study direct nonmedical cost consist a little portion of costs that it correspond with that study (9).

The socioeconomic cost of the HBV infection in 1997 was 1078.3 billion won (USD 959.7 million), which 142.3 billion won or 13.2% being attributable to the costs of prevention and 225.4 billion won or 20.9% was attributable to HBV-related disease (23). The total societal costs (direct plus indirect) associated with HBV-related disease was 936.1 billion won (\$US 833.1 million) of which the 45.3% (377.4 million) was attributable to cirrhosis costs. In terms of disease-related direct costs alone (710.5 billion Won or \$US 696.2 million), the annual cost per patient was estimated 1.37 million KRW (\$US 1,219 dollars). In our study, the total direct and indirect costs were equal to USD 112.9 and USD 51.42 million dollars and total cost was estimated USD 164.32 million. Medical and non-medical direct costs were 101.42, and USD 11.48 million, respectively. In our study indirect cost is higher than that study (20.9% vs. 31% of total costs), which probability is due to this point that they considered all diseases related to hepatitis which the majority of them have lower disability and deaths in compare of liver cirrhosis (23). Also, both studies showed that the direct costs consist of a large part of the burden of disease. In South Korea, liver cirrhosis had 45.3 of total cost of HBV-related disease and other diseases were responsible for 54.7% of costs. It has showed that cirrhosis impose a high portion of costs of HBV infection otherwise that it has a low prevalence (23).

Lisa Inez study (24) examined premature death and the life years lost due to cirrhosis. Cirrhosis mortality consisted 48.7% and 24.1% of death caused by gastroenterology disease in men and women, respectively. On average about 15.5 po-

tential productive years was lost in a death, for both sexes. Another study that examined the burden of cirrhosis in Canada (25) showed that the cost of treatment of liver cirrhosis in the first year of illness for each patient is 983 dollars that is very close to 1023 dollars that we found. The differences between these two may be the result of different price of medical cares and inflation in drug cost because that study conducted in 2005.

As it appears from the studies, direct costs usually consist of the higher portion of costs and indirect costs increase with increase life expectancy lost and deaths due to the disease. According to the fact and high mortality in liver cirrhosis, policy makers should be careful about and take policies for prevention and decrease of incidence and mortality of the disease.

Like similar studies we have some limitations and assumptions that these may cause the actual costs of the illness in society be a little different from what we estimated. We shall pay to these limitations, assumptions and weakness and strength of the study.

This study was the first attempt to examining the economic burden of liver cirrhosis in Iran. According to lack of some data, such as prevalence of the disease, we used an estimation of them. Also the annual probability of annual hospitalization didn't exist, thus we survey medical records of the patient and interview with a sample of patient about their hospitalization, as well. We assume that all patients take the medical care that they need, but there may be some patients not receive the necessary care. Therefore, we may overestimate the cost of the disease. On the other hand, this study had some strength points such as estimating different component of costs like transportation cost and production lost, the cost of disability for patients, families and in terms of inpatient and outpatient care, separately, that usually in other studies didn't pay to. Estimating the cost of outpatient treatment in terms of its components, costs of outpatient visits, diagnostic tests and drugs, can be mentioned as other strength of the study. Also, we estimated out of pocket payments in inpatient and outpatient care, separately. It is recommended that future studies examine the

costs of disease based on incidence approach and stages of liver cirrhosis.

Conclusions

Totally, the result of our study shows that liver cirrhosis imposes enormous economic burden on Iranian society. Therefore, policymakers should provide facilities and services for the prevention and treatment of the disease and according to high out of pocket in treatment process it seems we should promote the insurance programs for decreasing it, and complete the treatment of the disease especially in outpatient care that has a greater cost.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors. Patients were interviewed after gaining their consent.

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References

1. Lefton HB, Rosa A, Cohen M(2009). Diagnosis and epidemiology of cirrhosis. *Med Clin N AM*,93(4):787-99.
2. Schuppan D, Afdhal N (2008). Liver cirrhosis. *The Lancet*, 371 (9615): 838-851.

3. Tarricone R (2006). Cost-of-illness analysis: What room in health economics? *Health Policy*, 77(1):51-63.
4. Fleming CM. The epidemiology of cirrhosis and abnormal liver function in the general population of the UK [ph.D thesis], University of Nottingham, United Kingdom, 2010.
5. Zhiqiang G, Zhaohui D, Qinhuai W, Dexian C, Yunyun F, Hongtao L, et al (2004). Cost of Chronic Hepatitis B Infection in China. *J Clin Gastroenterol*, 38(10):S175-S8.
6. Metcalf J, Bhopal R, Gray J, Howel D, James O (1997). Incidence and prevalence of primary biliary cirrhosis in the city of Newcastle upon Tyne, England. *Int J Epidemiol*, 26(4):830-6.
7. Hu M, Chen W(2009). Assessment of total economic burden of chronic hepatitis B (CHB)-related diseases in Beijing and Guangzhou, China. *Value in Health*, 12:S89-S92.
8. Neff GW, Duncan CW, Schiff ER(2011). The current economic burden of cirrhosis. *Gastroenterol Hepatol*, 7(10):661.
9. Lee S, Chung W, Hyun KR (2011). Socioeconomic costs of liver disease in Korea. *Korean J Hepatol*, 17(4):274-91.
10. Kao JH, Chen DS(2002). Global control of hepatitis B virus infection. *Lancet Infect Dis*, 2(7):395-403.
11. Harbarth S, Szucs T, Berger K, Jilg W(2000). The economic burden of hepatitis B in Germany. *Eur J Epidemiol*, 16(2):173-7.
12. Henriksson F, Jönsson B(1998). Diabetes: the cost of illness in Sweden. *J Intern Med*, 244(6):461-8.
13. Quiroz ME, Flores YN, Aracena B, Granados-García V, Salmerón J, Pérez R, et al. (2010). Estimating the cost of treating patients with liver cirrhosis at the Mexican Social Security Institute. *Salud Publica Mex*, 52(6):493-501.
14. Treatment Association of Ministry of Health (2012).: <http://medcare.behdasht.gov.ir/index.aspx?siteid=312&siteid=312&siteid=312&pageid=30144>.
15. Ministry of Labour and Social Affair (2013). Available from: <http://www.mcls.gov.ir/fa/lawlist/kar>.
16. World Bank Group (2013). Available from: <http://search.worldbank.org/data?qterm=economic+growth+rate&language=&format=>.
17. Aalabaf-Sabaghi M (2010). Iran Mortality and Measures of Risk: Rankings for Public policy. *Iran J Public Health*, 39(1):42.
18. Forouzanfar M, Mohammad K, Majdzadeh Sr Mr, Abolhasani F, Naghavi Ravandi M (2005) A model for hepatitis b mortality and the effects of HBV-related outcomes on life expectancy in Iran. *Payesh*, 4(3): 163-173(persian).
19. Anh TT, Dao N, Anh T (2005). The cost of road traffic accident in Vietnam. *EASTS*, 5:1923-33.
20. World Bank Group (2013). Available from: <http://search.worldbank.org/data>.
21. Statistics by Country for Cirrhosis of the liver (2012). Available from: file:///H:/Data91-10-22/Statistics%20by%20Country%20for%20Cirrhosis%20of%20the%20liver%20-%20RightDiagnosis_com.htm.
22. Abolhallaje M, Hasani S, Bastani P, Ramezani M, Kazemian M (2013). Determinants of Catastrophic Health Expenditure in Iran. *Iran J Public Health*, 42(1):155-60.
23. Yang BM, Paik SW, Hahn OS, Yi DH, Choi MS, Payne S (2001). Economic evaluation of the societal costs of hepatitis B in South Korea. *J Gastroenterol Hepatol*, 16(3):301-8.
24. Lessa I (1997). Cirrhosis of the liver in Brazil: mortality and productive years of life lost prematurely. *Rev Panam Salud Publica*, 1(2):125-32.
25. El Saadany S, Coyle D, Giulivi A, Afzal M (2005). Economic burden of hepatitis C in Canada and the potential impact of prevention. *Eur J Health Econ*, 6(2):159-65.
26. Iran statistics center(2012). Available from: <http://www.amar.org.ir/Default.aspx?tabid=1485>.