



The medical cost of liver cancer in a referral hospital in Indonesia during 2020

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ABSTRACT

Liver cancer inflicts a severe human and economic burden on patients, their families, and society. However, the cost-of-illness analysis of liver cancer and the patient-level data on healthcare resource use is still limited. This study aims to estimate the medical costs of liver cancer in Indonesia. A costing study using a provider perspective approach was employed. Direct medical cost data were retrieved retrospectively from medical records of 157 liver cancer patients divided into three disease categories [compensated cirrhosis (CC), decompensated cirrhosis (DC), and hepatocellular carcinoma (HCC)] from January to December 2020 from a large referral hospital in Yogyakarta, Indonesia. A bottom-up methodology based on the patient's perspective was used to calculate the cost. The estimated medical costs for the nation were obtained from the direct medical cost per patient per liver cancer stage multiplied by the number of the patients. The total direct medical cost attributable to liver cancer in 2020 was estimated to be approximately US\$3.8 million. The cost of surgery was the major contributor to liver cancer treatment in every stage. The annual direct medical cost per patient increased with the severity of the disease, with the estimated cost for CC, DC, and HCC as US\$20,339, \$24,784, and \$26,538, respectively. Liver cancer imposes a valuable burden not only on patients but also on the healthcare system. Effective interventions in the healthcare system are required to minimize the burden. However, the prevention of this disease such as healthy lifestyle changes, early screening, and vaccination would help the reduction in liver cancer incidence, reduction in mortality, and absolutely reduction in the cost of illness.

INTRODUCTION

Liver cancer is common in countries in Southeast Asia, including Indonesia. More than 800,000 people are diagnosed with this type of cancer each year throughout the world. Liver cancer is also a leading cause of cancer deaths worldwide, accounting for more than 700,000 deaths each year ([American Cancer Society, 2019](#)). In 2018, liver cancer contributed to 8.8% of 207,210 cancer deaths in Indonesia ([Cancer Country Profile, 2020](#)). The most common form of liver cancer in adults is hepatocellular carcinoma (HCC), which occurs more frequently in men, with the disease affecting men about three times more often than women. The incidence rate of the disease is also increasing exponentially

([American Cancer Society, 2019](#)). Hence, liver cancer is a vital public health problem, especially for developing countries like Indonesia, where the endemicity is often either intermediate or even high.

Hepatitis B virus (HBV) and hepatitis C virus infections are the primary cause of HCC. However, HBV infections are commonly found in Indonesia with a 4.7%–11.2% endemicity range ([Janevska et al., 2015](#); [Yano et al., 2015](#)). The high endemicity of HBV infection in Indonesia which leads to HCC complications would pose a heavy burden not only for the Indonesian healthcare system but also for Indonesian people due to the various healthcare payments applied in Indonesia. Indonesian people could use the out-of-pocket payment system and also the main government health insurance program, namely Jaminan Kesehatan Nasional, which is the national insurance scheme for all Indonesian citizens. For the health coverage provided by this national insurance, Indonesia has implemented Indonesian Case Base Groups tariff rates according to the diagnosis grouping based on clinical and homogeneity of

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resource utilization approaches (Satibi *et al.*, 2019). On the other hand, very little data exists about the financial burden caused by liver cancer in Indonesia. Given this, we carried out a cost-of-illness study of liver cancer by reviewing data from a large referral hospital in Indonesia. The results of this study should provide Indonesian health policymakers data to prioritize health interventions to allocate resources efficiently in devising health insurance schemes.

METHODS

Study design and study population

This study complies with the standards of the bottom-up approach in cost-of-illness analyses which demonstrate the quantification of the direct medical cost of liver cancer (Tan *et al.*, 2009). The study proposal was reviewed and approved by the Medicine and Health Ethics Committee of Universitas Gadjah Mada with approval number KE/FK/0908/EC/2020. This study included patients 18 years of age and older who were diagnosed and categorized into three mutually exclusive groups, compensated cirrhosis (CC), decompensated cirrhosis (DC), and other chronic liver diseases indicating the disease severity at the initial stage of HCC diagnosis, and having complete data documented. The investigators identified potentially eligible patients from consecutive visits monitored in the Integrated Cancer Installation Unit visit register.

Data sources

Data were collected from 157 liver cancer patients' medical and financial records in Sardjito Hospital, Yogyakarta, Indonesia, from January to December 2020. The records for both inpatients and outpatients treated at the Integrated Cancer Installation Unit were included. We identified and obtained information on liver cancer patients by using the codes established by the International Statistical Classification of Diseases, 10th Revision, such as K74 (CC and DC) and C22 (HCC). Patients coded with K74 were differentiated as either CC or DC through clinical diagnosis from patient case notes.

Calculation of direct medical costs

The direct medical cost consisted of the costs of hospitalization, outpatient visits, surgeries, costs of prescription drugs for liver diseases, costs of transarterial chemoembolization (TACE), and costs of interferons (IFNs) which were categorized per month for the length of each individual's follow-up (per patient per month). The financial burden to the Indonesian society during this study period is estimated by the total direct medical cost multiplied by the number of liver cancer patients in Referral Hospital Dr. Sardjito, a large referral hospital in Yogyakarta, Indonesia. The study examined resource utilization based on hospital charges in 2020, which is expressed in US\$ (US\$1 = Indonesian Rupiah 14,241).

Statistical analysis

Descriptive analysis was carried out in the form of mean with standard deviation for numerical data and frequency with percentage for categorical data. A normality test of the cost data was carried out using a histogram, a Q-Q plot, and the Shapiro-Wilk test. Data were analyzed using the Statistical Package for the Social Sciences version 21 and Microsoft Excel 2016. All results were demonstrated in the form of tables.

RESULTS

General characteristic of the study participants

Table 1 presents the characteristics of 157 patients, consisting of 34 patients with CC, 76 patients with DC, and 47 patients with HCC. The mean age was 54.12 (± 10.12) years with male predominance (74.5%) observed among the sample. Approximately 49.7% of the participants were primary school graduates, 35.7% were secondary school graduates, and 14.6% were university graduates. Around 35.7% of the participants had a monthly household income of not more than US\$100 and only 7.6% of the participants had a monthly family income of more than US\$500. More than half of the patients (63.1%) resided in the urban area and the majority of the patients were unemployed (49.7%). The majority of patients had a Charlson comorbidity index (CCI) score of more than 3 (37.6%) and only 13.4% of patients had a 0 score of CCI.

Types of direct cost for caring for liver cancer patients

The details of health service use and costs among liver cancer patients are demonstrated in Table 2. The total cost of hospitalization accounted for US\$5,096 with HCC treatment predominance (US\$2,032). The outpatient visits cost was found to be the highest for DC patients (US\$341) with the cumulative cost

Table 1. Characteristics of liver cancer patients in a tertiary hospital in Indonesia ($N = 157$).

Variables	Category	N	%
Gender	Male	117	74.5
	Female	40	25.5
Age (mean, SD)		54.12 (± 10.12)	
Educational level	Primary	78	49.7
	Secondary	56	35.7
	University	23	14.6
Family income (monthly)	<US\$100	56	35.7
	US\$100–300	55	35.0
	US\$300–500	34	21.7
	>US\$500	12	7.6
Living area	Rural	58	36.9
	Urban	99	63.1
Working status	Working	43	27.4
	Unemployed	78	49.7
	Housewife	12	7.6
	Retired	24	15.3
Disease category	CC	34	21.7
	DC	76	48.4
	HCC	47	29.9
CCI score ^a	0	21	13.4
	1	32	20.4
	2	45	28.7
	≥ 3	59	37.6

^aCCI = Charlson comorbidity index.

Table 2. Types of direct cost and average cost per patient among liver cancer patients.

Types of cost	CC (US\$)	DC (US\$)	HCC (US\$)	Average cost \pm SD (US\$)
Hospitalization	1,283	1,780	2,032	5,096 (2,218)
Outpatient visits	208	341	278	827 (327)
Prescription drugs	843	904	104	1,851 (628)
Surgery	15,354	18,890	21,453	55,697 (21,223)
TACE	670	978	837	2,485 (672)
IFNs	1,980	1,890	1,834	5,705 (2,091)
Total direct costs	20,339	24,784	26,538	71,661 (26,318)

accounting for US\$827. The cost of prescription drugs for liver cancer patients accounted for US\$1,851 for the cumulative three liver cancer stages. Surgery cost was the major cost driver in treating liver cancer patients with a cumulative US\$55,697 for all three stages. The total payment for TACE was around US\$2,485, and the total payment for IFNs accounted for US\$5,705. Overall, the results show that the direct cost of the treatment increased with disease progression, with the total direct medical costs for treating liver cancer patients during the study period being approximately US\$71,661.

The case-based estimation of annual direct medical cost among liver cancer patients

The estimation of annual direct medical cost based on disease category in treating liver cancer patients was roughly US\$3,822,375. The highest treatment cost was found in treating HCC patients with the total cost accounting for US\$26,538, followed by DC patients with a cumulative US\$24,784 and CC patients treated with an estimated total payment of around US\$20,339. However, as the consequence of the majority of DC patients involved in this study (48.4%), the estimated annual direct medical cost for DC patients' treatments was found to be the highest (US\$1,883,554). The particular case-based estimation of the annual direct medical cost of the liver cancer treatment is summarized in Table 3.

DISCUSSION

To our knowledge, this is the first study carried out in Indonesia to estimate the cost of illness of liver cancer in Indonesia. Our results demonstrated that liver cancer obtrudes a substantial financial burden on the Indonesian society and the healthcare system. Moreover, the burden of liver cancer described in this study would become a baseline study not only for the government to initiate the most effective regulation related but also for the Indonesian society to begin healthy lifestyle changes to prevent liver diseases. Therefore, the appropriate management of liver disease-related risk factors is very important to reduce the financial burden. Our key finding from this study was the cumulative annual direct medical cost of liver cancer patients that

accounted for US\$3,833,375. The increase of the direct medical costs with disease progression showed in our study was in line with the previously published study in Vietnam (Tu *et al.*, 2012).

The direct medical cost was high among patients with HCC (US\$26,538), resulting from a high cost of surgical interventions and a high hospitalization rate. These findings were similar to prior studies worldwide which demonstrated that the medical costs for treating HCC patients with advanced liver disease were higher than other etiologies of liver diseases (Nguang *et al.*, 2018; Thein *et al.*, 2013; Tu *et al.*, 2012). Expenses on surgery were the largest cost driver for the direct medical costs for all CC, DC, and HCC categories, contributing more than 70% to the total direct medical costs. This might be explained as the consequence of the high surgical intervention prices in Indonesia. However, expenses on outpatient visits, prescription drugs, and TACE intervention for DC patients are identified to be the highest among the other disease categories. These findings might be connected with prior studies which identified that the overall survival rate for DC patients was the lowest compared to patients with mild-to-moderate chronic liver disease (Miquel *et al.*, 2018; Nguang *et al.*, 2018).

Expanses on IFNs were higher in treating CC patients than other disease categories (US\$1,980). This result might be explained by the frequent use of IFNs in the management of CC in Indonesia based on the national consensus (Indonesian Association for the Study of the Liver, 2012). Cirrhotic patients with compensated stage disease were likely to be offered treatment with carefully persistent side effects monitoring. The majority of patients who participated in this study were DC patients. Therefore, this group was the major contributor to the estimated total direct medical cost (US\$1,883,554). Overall, despite the difference in the type of treatment expenses in each stage, this study highlighted that the total cost for treating liver cancer patients was estimated to be more than US\$20,000 per patient.

Liver cancer is highly fatal and is considered as the most common cancer that causes mortality in Indonesia. This study provides a comprehensive view of the cost burden of liver cancer care in Indonesia's healthcare setting. However, the majority of patients aged more than 50 years were in late stages or with comorbidities. Further research is warranted to investigate the detailed costs of screening and other therapies in practice. Several prevention strategies have been proposed to reduce the ever-increasing cost of liver cancer treatment. Early detection and chemoprevention of HCC occurrence or recurrence are examples of secondary or tertiary prevention strategies, accordingly, in patients who already received aetiological agents (Hoshida *et al.*, 2012). HCC screening was identified to be cost-effective and associated with improved early tumor detection, curative treatment rates, and

Table 3. Annual direct medical cost based on disease category among liver cancer patients.

Disease category	Number of patients	Direct medical costs per patient (US\$)	Total cost (US\$)
CC	34	20,339	691,540
DC	76	24,784	1,883,554
HCC	47	26,538	1,247,281
All types of disease	157	71,661	3,822,375

survival based on the results of a series of prior cohort studies and model-based simulation (Fujiwara *et al.*, 2018; Mittal *et al.*, 2016; Singal *et al.*, 2014).

The preventive strategies of liver diseases may help the reduction of the incidence which could decrease the cost. Unfortunately, in developing countries like Indonesia, people often begin seeking medical help only when the disease has already developed. Hence, this study would be helpful for the health policymakers in designing future practical interventions related to liver cancer and also providing adequate liver cancer screening as the most effective strategy to reduce the financial burden for both the government and patients. Additionally, this study would help the healthcare provider and the patient to not only identify and quantify the liver cancer attributable cost in Indonesia but also take the preventive actions appropriately.

As a prevalence-based cost-of-illness study from the patient's perspective, the strength of this study was the calculation of the cost which covered all the possible direct cost components based on real patient data. Even though the cost estimations accounted solely for one large referral hospital in Yogyakarta, Indonesia, the results of the analysis are still considered important since no relevant study analyzing the cost of liver cancer has been conducted before in Indonesia. Nevertheless, this study has several limitations that should be acknowledged. Firstly, there were a limited number of participants in this study. Secondly, direct nonmedical costs and indirect and intangible costs related to liver disease were not addressed in this study. Moreover, this was a descriptive cost-of-illness study that did not provide information on the efficiency of resource uses. Thus, the higher cost could not be interpreted as better services or value for money.

CONCLUSION

The current study highlights that the medical costs of liver cancer to the healthcare system are significant. This study's findings representing real-world cost estimates of liver cancer care provide insightful information for the future economic evaluation of early detection interventions, resource allocation, and health insurance reimbursement policies.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest in this study.

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