



# Impact of Severity of Chronic Liver Disease on Health-Related Economics

Fakhar Ali Qazi Arisar <sup>1,\*</sup>, Muhammad Kamran <sup>1</sup>, Ramlah Nadeem <sup>1</sup> and Wasim Jafri <sup>1</sup>

<sup>1</sup>Section of Gastroenterology, Department of Medicine, The Aga Khan University, Karachi, Pakistan

\*Corresponding author: Section of Gastroenterology, Department of Medicine, The Aga Khan University, Stadium Rd., P. O. Box: 3500, Karachi, Pakistan. Tel: +92-3332724599, Email: fakhar.arisar@gmail.com

Received 2019 September 14; Revised 2020 May 09; Accepted 2020 May 09.

## Abstract

**Background:** Chronic liver disease (CLD) is one of the leading causes of morbidity and mortality worldwide. It is accountable for a multifaceted disease encumbrance upsetting the psychological, physical, and economic health of not only the patients but also their caregivers.

**Objectives:** The study purposes to cover the economic aspect of CLD to comprehend the financial burden imposed on the patients.

**Methods:** This cross-sectional study was conducted at a tertiary care hospital in Karachi, Pakistan. The CLD patients presenting in gastroenterology clinics were recruited, and their socio-demographic, financial, and disease-related information including Model for End-stage Liver Disease (MELD) score and Child Turcotte Pugh (CTP) scores were collected. Out of 190 CLD patients enrolled, 127 (67.2%) were males. The mean age was 50.09 years. Variables assessed include self-perceived social/economic status, self-perception of disease responsibility for worsening of social/economic situation, the impact of the disease on economic status due to medical expense, the impact of economic status on treatment compliance due to medical expenses, impact of severity of disease on socio-economic status and treatment compliance, and impact of gender on disease status and treatment compliance.

**Results:** Regardless of the disease duration, CLD significantly impacted a patient's life, as 81% and 69% of the patients blamed their disease responsible for the worsening of social and economic conditions, respectively. In our study, 85% of patients had consumed all savings during their course of illness, and 67% had to borrow money for medical expenses. Nearly half of the patients had to leave or cut short their medicines, skip the physician's appointment, or defer their children's education. One-third of patients had unpaid medical and utility bills or even skipped their meals. The severity of disease affected the socioeconomic status significantly (89% in CTP class C vs. 40% in CTP class A). Patients with worsening socioeconomic status had significantly higher MELD scores as compared to those with stable socioeconomic status.

**Conclusions:** Chronic liver disease imposes incredible socioeconomic encumbrance on patients and the family unit, and CLD associated expenditures influence the family unit's everyday working and therapeutic compliance, which is directly linked to the severity of disease expressed in terms of CTP and MELD scores.

**Keywords:** Health, Burden, Epidemiology, Healthcare, Cirrhosis, Economics, Chronic Liver Disease

## 1. Background

Chronic liver disease (CLD) is a global problem that is related to considerable economic encumbrance (1). It is ascribed to 1.16 million deaths each year, which is around 3.5% of all deaths worldwide, making it the 11th, 10th and 8th leading cause of mortality globally, in South Asia and the Middle East, respectively (2). It has the highest rate of inpatient mortality among all hospital admissions for gastrointestinal and liver disease patients (3).

Chronic illnesses are liable for long-term hassles and burdens, and in recent years, health-related quality of life (HRQoL) has now become a matter of prodigious concern.

Being a chronic disease, CLD substantially reduces HRQoL (4). Chronic liver disease comes in the top 20 causes of global morbidity (5). South-East Asia carries the maximum burden of CLD, with the highest calculated disease-related disability-adjusted life years (DALY) and years of life lost (YLL) (6).

An additional trait of chronic illnesses is not only the patient's quality of life but also the monetary burden imposed on the patient and the whole family unit altogether. Pakistan has been classified under the group of lower-middle-income economic countries by the World Bank with gross national income (GNI) per capita of 1580 United States Dollars (USD) (7, 8). Liver diseases are the cause of

significant burden and cost. Moreover, inpatient health care utilization has increased for patients with CLD during the last couple of decades (3). The overall cost of CLD takes into account the direct cost (including medications and hospital admissions) and unforeseen costs (owing to loss of work efficiency and drop in HRQoL)(1). In the United States, the approximate direct and indirect cost of CLD in 2004 was 2.5 billion USD and 10.6 billion USD, respectively (9). Analysis of data from the Medical Expenditure Panel Survey (MEPS; 2004 - 2013) showed that annual health expenditures were higher in CLD patients (USD 19,390 vs. USD 5,567 in non-CLD patients) (10). Though we don't have exact data for Pakistan, it is expected to be worse in our poor socioeconomic conditions.

In 2005, it was projected that without rigorous preventive and control action, chronic illnesses might cause 36 million deaths in the next 10 years. The majority of these preventable deaths will be in low to middle-income populations, with half of them having age under 70 years (11). Furthermore, the poorest individuals are most vulnerable to the development of chronic ailments, and this population is unable to handle the consequential financial impacts (12). Therefore because of the fairly higher prevalence of chronic disorders in the lower socioeconomic group, we looked into the economic stress faced by the patients and their families in the context of their disease and their employment status following the diagnosis and management of their CLD.

## 2. Objectives

The study was carried out with the objective of exploring the economic burden in CLD patients, with the principal hypothesis being that persons with longer-lasting and severe disease would have direr financial problems.

## 3. Methods

This was a cross-sectional, observational study wherein patients suffering from CLD were enrolled from the gastroenterology clinics at the Aga Khan University Hospital (AKUH), Karachi, Pakistan. The AKUH is one of the largest hospitals in the country with a large catchment area (both urban and rural areas) and catering diversity of patients who belong to every group of socioeconomic status. Around 6,000 to 8,000, new patients are seen in the AKUH gastroenterology clinics every year. Nearly half of them present for liver diseases, of which hepatitis B and hepatitis C makes three quarters (13).

All CLD patients between ages 18 to 80 years, presented to the clinic from January to December 2016 were ap-

proached, and those who consented were assessed using two validated questionnaires.

Exclusion criteria included patients suffering from acute viral hepatitis, chronic viral hepatitis without advanced fibrosis/cirrhosis, other chronic conditions that could have influenced the quality of life and could put a burden on finances, including Inflammatory rheumatic conditions (such as rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis), severe chronic obstructive pulmonary diseases, decompensated heart failure, obesity, vertebral fractures, solid organ transplant, chronic kidney disease requiring dialysis, irritable bowel syndrome, and a history of cancer (including hepatocellular carcinoma).

The patient's demographic and disease-related information was collected via a preset form for meticulous assessment of their CLD (including the cause of liver disease, duration of liver disease, decompensation of CLD such as encephalopathy, ascites, jaundice, variceal bleeding, spontaneous bacterial peritonitis, hepatorenal syndrome, as well as Child Turcotte Pugh (CTP) and Model for End-stage Liver Disease (MELD) scores, etc.). A CTP score of 3 to 6 was categorized as CTP class A, 7 to 9 as CTP B, and 10 to 15 as CTP C (14, 15).

The interview was conducted by a dedicated research officer and a medical student. The McArthur Social Status questionnaire was administered to all patients to inquire regarding their educational status, social class, and financial condition. The questionnaire is well validated in previous studies for the determination of subjective social status (16-18). An additional set of questions was used to enlist the economic and occupational problems confronted by the patients owing to their illness. From these two questionnaires, we tried to estimate the economic encumbrance that the CLD had put on them and their relatives and how it affected their employment status.

Variables analyzed included age, gender, etiology of liver disease, the severity of CLD (as defined by CTP and MELD scores), duration of CLD (years), number of family members, number of family members aged > 18 years, maximum number of the years of education, highest educational degree, and current monthly income in Pakistani rupee (1 USD = 135 PKR). Outcomes of interest were self-perceived social and economic status, self-perception of disease responsibility for worsening of the social and economic situation, the impact of the disease on economic status due to medical expense, the impact of economic status on treatment compliance due to medical expenses, impact of severity of disease on socioeconomic status and treatment compliance, and impact of gender on disease status and treatment compliance.

The study was conducted following approval from the ethical review committee of The Aga Khan Univer-

sity Hospital. Informed consent was provided by the patients/caregivers before the administration of research questionnaires after explaining the nature of the information required. The questionnaires were introverted, and the participants were excluded from the research in the event that any of the subjects showed uneasiness in providing private information, such as their monetary and emotional strains. Moreover, complete privacy and confidentiality were ensured. There was no funding associated with this work.

### 3.1. Patient and Public Involvement Statement

We did not involve patients or the public in our work.

### 3.2. Statistical Analysis

Data analysis was done in the Statistical Package for the Social Sciences (SPSS) for Windows (version 20). Continuous variables are presented as mean  $\pm$  SD, and categorical variables are presented as frequency and percentages. To determine the impact of gender on disease and treatment, continuous variables between groups were compared by using unpaired *t*-test, and categorical variables were compared by using the chi-square test. All P values were two-sided, and a P value of  $< 0.05$  was taken as significant.

## 4. Results

Out of 190 CLD patients enrolled, 127 (67.2%) were males. The mean age of our patients was  $50.09 \pm 12.05$  years. The predominant etiologies of CLD were hepatitis C (70.5%) followed by Hepatitis B (HBV) and Hepatitis D (HDV). Half of the patients were CTP class B. Diabetes and hypertension were the major comorbid conditions present in 44 (25.6%) & 35 (18.5%) of the patients, respectively. The majority of patients (94%) belonged to the lower or middle-class social status (Table 1). Only one-fourth of the patients were educated up to a bachelor's degree or above. More than half of the subjects were unable to sustain their present standard of living for even a month, while two-thirds of the patients did not have enough savings to retain their existing standard of living even for three months if their source of income vanishes out. Table 1 describes the basic demographic features of the patients.

Regardless of the disease duration, CLD significantly impacted a patient's life, as 81% and 69% of patients blamed their disease responsible for deteriorating their social and financial state, respectively. Of the patients, 85% had consumed all their savings during their course of illness, and 67% of patients required borrowing money for their medical expenditures. Nearly half of the patients had to defer their children's education. Around one-third of patients had unpaid medical and utility bills, or even skipped

their meals. Worst of all, 14% of patients had to leave their houses in a quest for cheaper residence, and one out of every 10 had reached the limit of mortgaging their houses (Table 2).

Due to the worsening economic status, treatment compliance in CLD patients was also considerably affected. Nearly half of the patients had to leave or cut short their medicines or skip physician's appointments due to expenditures and one-third were not able to afford a surgical procedure (Table 2). Less than 10% of patients were covered by any sort of medical insurance to cover their expenses.

The severity of disease affected the socioeconomic status significantly (89% in CTP C vs. 40% in CTP A). That also influenced the treatment compliance of the patients in terms of need to cut short medications (71.5% in CTP C disease vs. 33.8% in CTP A, P value: 0.012), delayed children education (60% in CTP C vs. 26% in CTP A), delay in loan payment (50% in CTP B vs. 28% in CTP A) and stopped saving (89% in CTP C vs. 50% in CTP A) (Table 2). Similarly, patients with worsening socioeconomic status had significantly higher MELD scores as compared to those with stable socioeconomic status (Table 2), which again signifies the impact of severity of disease on the financial burden faced by this group of patients.

In our analysis, we also found that although male patients were suffering from more severe disease, they gave more importance to work. This led to cutting short their medications and missing surgical procedures significantly more than the opposite gender (Table 3).

## 5. Discussion

Worldwide, around 2 million deaths occur every year due to liver diseases, half of them are attributed to complications of CLD (19). It not only causes high mortality but also highly impacts economics (5). Quality of life indices are found to be low in patients with CLD (10). According to WHO data, South-East Asia carries the highest morbidity of CLD, with 808 DALY per 100,000 population and 801 YLL per 100,000 population (6).

Chronic liver disease is the 8th leading cause of the healthy-life-year loss in Pakistan (20). Furthermore, it is one of the leading causes of hospital admissions and mortality in Pakistan (21-24). Due to a very high load of CLD, Pakistan was labeled as a cirrhotic state (25). Hepatitis C (40% - 90%), followed by Hepatitis B (10% - 46%), is by far the foremost cause of chronic liver disease in Pakistan (26-28). Pakistan carries a 7 million hepatitis C infected population, the second-highest after China (29).

Chronic liver disease puts a pronounced burden on the healthiness of the state (30). Even though the HRQoL in patients has been considered and has turned into a matter

**Table 1.** Demographics

Variables	Values <sup>a</sup>	Variables	Values <sup>a</sup>
<b>Age</b>	50.09 ± 12.05	<b>Current monthly income in Pakistani rupee (1 USD = 135 PKR)</b>	
<b>Gender</b>		< 5 K	10 (5.2)
Male	127 (67.2)	5 - 10 K	4 (2.1)
Female	63 (32.8)	10 - 15 K	12 (6.3)
<b>Etiology</b>		15 - 20 K	10 (5.2)
Hepatitis C	134 (70.5)	20 - 25 K	4 (2.1)
Hepatitis B	14 (7.3)	25 - 50 K	27 (14.2)
Hepatitis B + D	25 (13.1)	50 - 100 K	29 (15.2)
Hepatitis B + C	2 (1.1)	100 - 500 K	29 (15.2)
Alcohol	4 (2.3)	> 500 K	17 (8.9)
Non-B, Non-C	11 (5.7)	Unsure	48 (25.2)
<b>CTP Class</b>		<b>Self-perceived socioeconomic status</b>	
A	65 (34.2)	At the very top	9 (4.7)
B	97 (51.1)	Somewhere at the top	9 (4.7)
C	28 (14.7)	In the middle	97 (51.1)
<b>MELD score</b>	11.13 ± 3.9	Somewhere at the bottom	63 (33.2)
<b>Duration of CLD (years)</b>	7.81 ± 6.161	At the very bottom	12 (6.3)
<b>No of family members</b>	8.98 ± 7.562	<b>Maintenance of current standard of living with savings in hand, in the absence of any source of income</b>	
<b>No of family members age &gt; 18 years</b>	5.23 ± 3.714	< 1 month	106 (55.7)
<b>Max no. of the years of education</b>	8.88 ± 5.571	1 - 3 months	49 (25.7)
<b>Highest educational degree</b>		3 - 6 months	21 (11)
Illiterate	28 (14.7)	7 - 12 months	4 (2.1)
Primary	37 (19.4)	> 12 months	10 (5.2)
Middle	13 (6.8)		
Matric	28 (14.7)		
Intermediate	39 (20.5)		
Bachelor's	32 (16.8)		
Master's	11 (5.7)		
Ph.D.	2 (1)		

Abbreviations: CLD, chronic liver disease, CTP, child Turcotte Pugh; USD, United States dollar.

<sup>a</sup>Values are expressed as mean ± SD or No. (%).

of deep concern recently (4), the economic encumbrance of the illness on the whole family unit is yet an ambiguous area that entails additional exploration. This is fundamental as by means of this we would be able to guesstimate if the family can engross the cost of the treatment and whether or not there will be persistent compliance with therapeutics in the event of a liver transplant. Similar findings were observed in a study based on MEPS data

reporting lower employment rate (44.7% vs. 69.6%), higher disability-related loss of work (30.5% vs. 6.6%) and work-days (10.3 vs. 3.4), and substantial health care expenses each year (USD 19,390 vs. USD 5567) in patients with CLD vs. non-CLD (10). The study also reported worse self-reported health status, more daily activity limitations, and lower quality of life in CLD patients. Moreover, presence of CLD itself significantly predicted unemployment (odds ratio,

**Table 2.** Impact of Liver Disease and Its Severity on Socioeconomical Status and Treatment Compliance

		CTP A, N = 65 (34.3)	CTP B, N = 97 (51)	CTP C, N = 28 (14.7)	P Value	MELD Score	P Value
<b>Worsening social status due to liver disease</b>	Yes: 154 (81)	47 (72.3)	86 (88.7)	21 (75)	0.053	11.46 ± 4.06	0.077
	No: 36 (19)	18 (27.7)	9 (9.3)	7 (25)		10.09 ± 2.99	
<b>Worsening economic status due to liver disease</b>	Yes: 131 (69)	26 (40)	80 (82.5)	25 (89.3)	0.003 <sup>b</sup>	11.26 ± 4.24	0.572
	No: 59 (31)	39 (60)	17 (17.5)	3 (10.7)		10.95 ± 2.39	
<b>Stopped saving</b>	Yes: 132 (69.5)	33 (50.7)	74 (76.2)	25 (89.3)	0.001 <sup>b</sup>	11.64 ± 4.29	0.005 <sup>b</sup>
	No: 58 (30.5)	32 (49.3)	23 (23.8)	3 (10.7)		10.04 ± 2.61	
<b>Utilization of previous savings</b>	Yes: 162 (85.3)	57 (87.6)	79 (81.4)	26 (92.8)	0.347	11.52 ± 3.96	0.016 <sup>b</sup>
	No: 28 (14.7)	8 (12.4)	18 (18.6)	2 (7.2)		9.46 ± 3.03	
<b>Need to borrow money for expenses</b>	Yes: 127 (66.9)	37 (57)	70 (72.2)	20 (71.4)	0.119	11.60 ± 4.00	0.074
	No: 63 (33.1)	28 (43)	27 (27.8)	8 (28.6)		10.43 ± 3.58	
<b>House mortgage</b>	Yes: 20 (10.5)	5 (7.7)	14 (14.5)	1 (3.6)	0.304	13.25 ± 5.14	0.026 <sup>b</sup>
	No: 170 (89.5)	60 (92.3)	83 (85.5)	27 (96.4)		10.97 ± 3.69	
<b>Increasing loans</b>	Yes: 111 (58.4)	31 (47.6)	63 (65)	17 (60.7)	0.115	11.77 ± 4.13	0.03 <sup>b</sup>
	No: 79 (41.6)	34 (52.3)	34 (35)	11 (39.3)		10.40 ± 3.44	
<b>Delay in loan repayment</b>	Yes: 77 (40.5)	18 (27.7)	49 (50.5)	10 (35.7)	0.05 <sup>b</sup>	11.41 ± 4.15	0.5
	No: 113 (59.5)	47 (72.3)	48 (49.5)	18 (64.2)		10.98 ± 3.75	
<b>Delay in children's education</b>	Yes: 86 (45.3)	17 (26.1)	52 (53.6)	17 (60.7)	0.05 <sup>b</sup>	11.87 ± 4.82	0.103
	No: 104 (54.7)	48 (73.9)	45 (46.4)	11 (39.3)		10.72 ± 3.18	
<b>Electricity/gas supply cut off</b>	Yes: 59 (31)	14 (21.5)	41 (42.3)	4 (14.3)	0.006 <sup>b</sup>	11.94 ± 4.84	0.106
	No: 131 (69)	51 (78.5)	56 (57.7)	24 (85.7)		10.83 ± 3.42	
<b>Have to leave the current house</b>	Yes: 28 (14.7)	5 (7.7)	19 (19.5)	4 (14.3)	0.194	13.55 ± 5.90	0.042 <sup>b</sup>
	No: 162 (85.3)	60 (92.3)	78 (80.5)	24 (85.7)		10.77 ± 3.37	
<b>Have to leave food due to expenses</b>	Yes: 55 (29)	13 (20)	36 (37.2)	6 (21.5)	0.07	11.82 ± 4.96	0.192
	No: 135 (71)	52 (80)	61 (62.8)	22 (78.5)		10.90 ± 3.42	
<b>Unpaid medical dues</b>	Yes: 96 (50.5)	46 (70.7)	37 (38.2)	13 (46.5)	0.288	11.72 ± 4.26	0.199
	No: 94 (49.5)	19 (29.3)	60 (61.8)	15 (53.5)		10.89 ± 3.66	
<b>Skip medicines/treatment</b>	Yes: 96 (50.5)	22 (33.8)	54 (55.7)	20 (71.5)	0.012 <sup>b</sup>	11.63 ± 4.07	0.129
	No: 94 (49.5)	43 (44.2)	43 (44.3)	8 (28.5)		10.69 ± 3.69	
<b>Buy medicines in less than the required quantity</b>	Yes: 107 (56.3)	29 (44.6)	61 (62.9)	17 (60.7)	0.099	12.01 ± 4.29	0.002 <sup>b</sup>
	No: 83 (43.7)	36 (55.4)	36 (37.1)	11 (39.3)		10.11 ± 3.07	
<b>Missed surgeries due to expenses</b>	Yes: 64 (33.7)	19 (29.2)	29 (29.9)	16 (57.2)	0.004 <sup>b</sup>	12.81 ± 5.09	0.008 <sup>b</sup>
	No: 108 (56.8)	32 (49.3)	64 (66)	12 (42.8)		10.66 ± 3.03	
	NA: 18 (9.5)	14 (21.5)	4 (4.1)	0 (0)			
<b>Missed doctor's appointment due to expenses</b>	Yes: 110 (57.9)	42 (64.6)	51 (52.6)	17 (60.7)	0.052	12.29 ± 4.56	0.001 <sup>b</sup>
	No: 80 (42.1)	23 (35.4)	46 (47.4)	11 (39.3)		10.19 ± 2.91	

Abbreviations: CTP, child Turcotte Pugh, NA, not applicable.

<sup>a</sup>Values are expressed as mean ± SD or No. (%).<sup>b</sup>P value < 0.05.

0.60; 95% confidence interval, 0.50 - 0.70), yearly health care expenses ( $\beta$  = USD 9503 ± USD 2028), and effect on every facet of HRQoL (all  $P < 0.0001$ ). Although they had a comparison arm of non-CLD patients, however, their study was limited due to the retrospective nature and bias of coding in the database. Moreover, they did not compare the effect on the severity of liver disease on outcomes.

Taking into account the part of the world where this particular study was carried out, the majority of the patients with CLD belonged to the low socioeconomic status. We have shown that CLD poses a substantial monetary and socioeconomic burden on patients and their family, so much so that this population is incapable of functioning economically with these pressures and consequently ac-

**Table 3.** Impact of Gender on Disease Status and Treatment Compliance<sup>a</sup>

	Male	Female	P Value
The severity of disease using MELD score	11.65 ± 4.27	10.15 ± 2.87	0.009
Importance to work	94.5	50	< 0.0001
Dependency on others to bear expenses	46.4	75.8	< 0.0001
Need to cut short medicines	59.8	41.6	0.016
Miss surgical procedures	34.4	15	0.01

Abbreviation: MELD: Model for End-stage Liver Disease.

<sup>a</sup>Values are expressed as mean ± SD or percentage.

quire debts which sustain an additional economic burden. This vicious cycle thereby turns this chronic sickness into one which necessitates not merely medical management but also ample financial management. We have shown that numerous sacrifices are required to be made by the family in order to endure medical therapy. This is vital as economic problems backing up to medical compliance are not regularly explored (31).

The stage of the disease is an important factor influencing the cost of treatment. We demonstrated not only the effect of liver disease on daily living expenses and medical compliance but also the impact of severity of liver disease on their worsening economic status. Our findings were in accordance with Bajaj et al., who also showed that the severity of the liver disease is directly related to the financial and socioeconomic burden faced by the patients and their families. This impacted daily life activities significantly, including their capability to meet the expense of food and lodging. This, in turn, shakes the medication compliance and adherence to the treatment (32). However, in their study, all patients had effective health insurance. Hence the actual monetary load was not captured. While in our study, only 10% of patients were covered by health insurance which helped us determine the exact impact of a financial burden on daily life and medication adherence. Also, their potential geographical selection bias limited the generalizability to our country with the different health systems. In two similar studies from Iran, the total annual cost per patient based on purchasing power parity (PPP) increased with the severity of liver disease. It was 3094.5 USD, 17483 USD, & 32958 USD in the year 2012 for chronic hepatitis B, cirrhosis, and hepatocellular carcinoma (HCC), respectively (33). While it was 1625.5 USD, 6117.2 USD, and 11047.2 USD in the year 2015 for chronic hepatitis C, cirrhosis, and HCC, respectively (34). The cost of disease treatment has significantly impacted their household economy, and patients either had to sell their assets or get loans (34). However, they did not categorize the sever-

ity of cirrhosis on the basis of CTP or MELD score in both these studies. Miyazaki et al. demonstrated the high level of burden, stress, and depression in caregivers of liver disease patients, however, they did not look into the financial component (35).

We also tried to highlight the effect of gender on perception of liver disease and response in terms of health-seeking behavior, compliance with medication, and management of limited available finances. The Iranian study in chronic hepatitis B patients also confirmed that the gender, age, the severity of illness, and the length of stay has a profound impact on financial burden on households ( $P < 0.05$ ) (33).

Our report from a developing country highlighted the hidden problems faced by CLD patients as a family unit. Through this study, we are now well cognizant of the previously ignored economic facet of the problem of CLD, and as the public, in general, would be made attentive of this, improved support programs can be instigated and ample counseling of the patients and their caregivers can be done.

The cross-sectional design appears to be one of the limitations of our study. A prospective long-term study can gather evidence about indices of burden and stress at various stages of the disease in a single patient and can better inspect the relationship between burden and disease variables.

### 5.1. Conclusions

Chronic liver disease imposes incredible socioeconomic encumbrance on patients and the family unit. Chronic liver disease associated expenditures influence the family unit's everyday working and therapeutic compliance, which is directly linked to the severity of disease expressed in terms of CTP and MELD scores. There is an exigent requirement of development in social health structure with emphasis on improved preventive, diagnostic and therapeutic facilities at an affordable cost.

### Acknowledgments

We acknowledge the valuable contribution of Ms. Safia Awan, senior instructor research at the Department of Medicine, The Aga Khan University Hospital, Karachi, in reviewing and revising the statistical analysis component of the manuscript.

### Footnotes

**Authors' Contribution:** Study idea and design: Wasim Jafri; acquisition, analysis or interpretation of data: Fakhar

Ali Qazi Arisar, Muhammad Kamran, and Ramlah Nadeem; initial draft and revision: Fakhar Ali Qazi Arisar; critical revision for important intellectual content: Wasim Jafri. All authors approved the final version of the manuscript and are accountable for all aspects of the work.

**Conflict of Interests:** No competing interests for any authors.

**Ethical Approval:** Ethical Review Committee of The Aga Khan University Hospital, Karachi (3659-MED-ERC-15).

**Funding/Support:** This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

**Patient Consent:** All patients provided informed written consent.

## References

1. Neff GW, Duncan CW, Schiff ER. The current economic burden of cirrhosis. *Gastroenterology & hepatology*. 2011;7(10):661.
2. World Health Organization. *Global health estimates 2015: deaths by cause, age, sex, by country and by region, 2000-2015*. Geneva: WHO; 2016.
3. Peery AF, Crockett SD, Barritt AS, Dallon ES, Eluri S, Gangarosa LM, et al. Burden of gastrointestinal, liver, and pancreatic diseases in the United States. *Gastroenterology*. 2015;149(7):1731-1741. e3.
4. Younossi ZM, Boparai N, Price LL, Kiwi ML, McCormick M, Guyatt G. Health-related quality of life in chronic liver disease: the impact of type and severity of disease. *The American journal of gastroenterology*. 2001;96(7):2199-205.
5. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. *Journal of hepatology*. 2019;70(1):151-71.
6. World Health Organization. *Global health estimates 2015: disease burden by cause, age, sex, by country and by region, 2000-2015*. Geneva: WHO; 2016.
7. The World Bank. *World Bank Country and Lending Groups*. The World Bank; 2020.
8. The World Bank. *GNI per capita, Atlas method (current USD)*. 2020.
9. Ruhl CE, Sayer B, Byrd-Holt DD, Brown DM. *Costs of digestive diseases*. Washington, DC: US Government Printing Office, The burden of digestive diseases in the United States; 2008. 10 p.
10. Stepanova M, De Avila L, Afendy M, Younossi I, Pham H, Cable R, et al. Direct and indirect economic burden of chronic liver disease in the United States. *Clinical Gastroenterology and Hepatology*. 2017;15(5):759-766. e5.
11. Strong K, Mathers C, Leeder S, Beaglehole R. Preventing chronic diseases: how many lives can we save? *The Lancet*. 2005;366(9496):1578-82.
12. Suhrcke M, Nugent RA, Stuckler D, Rocco L. *Chronic Disease: An Economic Perspective*. London: Oxford Health Alliance; 2006.
13. Hashmi FL, Abid S, Hamid S, Jafri W, Ismail FW, Subhan A, et al. Spectrum of gastroenterology and liver disease: a changing trends. *J Clin Gastroenterol Hepatol*. 2018;2. doi: 10.21767/2575-7733-C2-006.
14. Child CG, Turcotte JG. Surgery and portal hypertension. *Major Probl Clin Surg*. 1964;1:1-85. eng. [PubMed: 4950264].
15. Pugh RN, Murray-Lyon IM, Dawson JL, Pietroni MC, Williams R. Transection of the oesophagus for bleeding oesophageal varices. *Br J Surg*. 1973;60(8):646-9. eng. doi: 10.1002/bjs.1800600817. [PubMed: 4541913].
16. Operario D, Adler NE, Williams DR. Subjective social status: Reliability and predictive utility for global health. *Psychology & health*. 2004;19(2):237-46.
17. Singh-Manoux A, Marmot MG, Adler NE. Does subjective social status predict health and change in health status better than objective status? *Psychosom Med*. 2005;67(6):855-61. eng. doi: 10.1097/01.psy.0000188434.52941.a0. [PubMed: 16314589].
18. Garza JR, Glenn BA, Mistry RS, Ponce NA, Zimmerman FJ. Subjective Social Status and Self-Reported Health Among US-born and Immigrant Latinos. *Journal of immigrant and minority health*. 2017;19(1):108-19. eng. doi: 10.1007/s10903-016-0346-x. [PubMed: 26895151].
19. Mokdad AA, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. *BMC medicine*. 2014;12(1):145.
20. Hyder AA, Morrow RH. Applying burden of disease methods in developing countries: a case study from Pakistan. *American journal of public health*. 2000;90(8):1235.
21. Niazi TK, Qureshi MO, Ahmed S, Sattar S, Khokhar N. Chronic Liver Disease Related Mortality Pattern in a Tertiary Care Hospital. *Pakistan Journal of Medical Research*. 2015;54(2):48.
22. Shah SMA, Mashia SA, Younus MF, Ghauri A, Ejaz R, Alshalabi H, et al. Hepatic cirrhosis-disease burden. *J. Rawalpindi Med. Coll. Stud. Suppl*. 2015;19:17-20.
23. Almani SA, Memon AS, Memon AI, Shah I, Rahpoto Q, Solangi R. Cirrhosis of liver: Etiological factors, complications and prognosis. *J Liaquat Uni Med Health Sci*. 2008;7(2):61-6.
24. Tariq M, Jafri W, Ansari T, Awan S, Ali F, Shah M, et al. Medical mortality in Pakistan: experience at a tertiary care hospital. *Postgraduate Medical Journal*. 2009;85(1007):470-4. doi: 10.1136/pgmj.2008.074898.
25. Ahmad K. Pakistan: a cirrhotic state? *The Lancet*. 2004;364(9448):1843-4. doi: 10.1016/S0140-6736(04)17458-8. [PubMed: 15565744].
26. Butt AS. Epidemiology of viral hepatitis and liver diseases in Pakistan. *Eurasian journal of hepat-gastroenterology*. 2015;5(1):43.
27. Qazi F, Khan SB, Umar A. Hepatic encephalopathy in chronic liver disease: predisposing factors in a developing country. *Asian Journal of Medical Sciences*. 2015;6(2):35.
28. Umar A, Qazi F, Sattar RA, Umar B. Non-invasive parameters for the detection of variceal bleed in patients of liver cirrhosis, an experience of a tertiary care hospital in Pakistan. *Asian Journal of Medical Sciences*. 2015;6(1):61.
29. Blach S, Zeuzem S, Manns M, Altraif I, Duberg A, Muljono DH, et al. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. *The Lancet Gastroenterology & Hepatology*. 2017;2(3):161-76.
30. Udompat P, Kim D, Kim WR. Current and future burden of chronic nonmalignant liver disease. *Clinical Gastroenterology and Hepatology*. 2015;13(12):2031-41.
31. Stilley CS, DiMartini AF, de Vera ME, Flynn WB, King J, Sereika S, et al. Individual and environmental correlates and predictors of early adherence and outcomes after liver transplantation. *Progress in Transplantation*. 2010;20(1):58-66.
32. Bajaj JS, Wade JB, Gibson DP, Heuman DM, Thacker LR, Sterling RK, et al. The multi-dimensional burden of cirrhosis and hepatic encephalopathy on patients and caregivers. *The American journal of gastroenterology*. 2011;106(9):1646-53.
33. Kavosi Z, Zare F, Jafari A, Fattah MR. Economic burden of hepatitis B virus infection in different stages of disease; a report from southern Iran. *Middle East journal of digestive diseases*. 2014;6(3):156.
34. Zare F, Fattah MR, Sepehrimanesh M, Safarpour AR. Economic burden of hepatitis C virus infection in different stages of disease: a report from southern Iran. *Hepatitis monthly*. 2016;16(4).
35. Miyazaki ET, Dos Santos RJ, Miyazaki MC, Domingos NM, Felicio HC, Rocha MF, et al. Patients on the waiting list for liver transplantation: caregiver burden and stress. *Liver Transpl*. 2010;16(10):1164-8. doi: 10.1002/lt.22130. [PubMed: 20879014].