

Etiology of chronic liver disease in patients admitted at the National Referral Hospital of Bhutan in 2020.

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Abstract

Background and Aim: Chronic liver disease (CLD) is a major cause of morbidity and mortality worldwide. Etiologically there are many factors including hepatitis B virus (HBV) and C virus (HCV) infections, alcohol, non-alcoholic fatty liver disease, autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis, Wilson's disease, hemochromatosis, etc. Though there is evidence in the literature regarding the etiologies of CLD, no study was done in Bhutan in this area. Therefore, this study was conducted to assess the etiology of CLD in patients admitted in the National Referral Hospital, Thimphu.

Methods: A descriptive study was conducted with 71 patients admitted to the National Referral Hospital. The study was done after seeking ethical clearance from the Research Ethics Board of Health (REBH) (Annexure 3) and was conducted from 1st January to 31st December 2020. The data were collected in pro forma and entered in Epi Data version 3.1 and analyzed using Epi Data Analysis version 2.2.2.183 and STATA version 15.1.

Results: Out of 71 patients who had CLD, majority 80.3 % were due to alcohol and the least 2 (2.8 %) was due to the combination of alcohol and HBV infection.

Conclusion: The study found that the commonest cause of CLD in patients admitted at the National Referral Hospital was alcohol. The findings from this study could help in strengthening the implementation of alcohol policy in the country.

Introduction

Chronic liver disease (CLD) is the term used to describe the disordered liver function lasting for six or more months [1]. CLD is defined as deranged transaminases for more than six months or the presence of hepatic parenchyma heterogeneity and/or surface irregularity on ultrasound OR the presence of clinical features suggestive of decompensated liver disease such as ascites, jaundice, and/or hepatic encephalopathy [2].

CLD is a major cause of morbidity and mortality and was responsible for an estimated 1.3 million deaths worldwide in 2015 [1]. It is the tenth leading cause of death in the United States resulting in more than 25,000 deaths annually [3]. There are an estimated four million known cases of hepatitis C in the United States and cause CLD [3]. An estimated two billion people consume alcohol worldwide and about 75 million are diagnosed with alcohol use disorders and are at risk of alcohol-associated liver disease [4]. Approximately two billion adults are obese or overweight and over four hundred million have

diabetes; both of which are risk factors for non-alcoholic fatty liver disease and hepatocellular carcinoma [4].

Non-alcoholic fatty liver disease (NAFLD) has become the most common cause of CLD in the United States [5]. National Health and Nutrition Examination Surveys conducted between 1988 and 2008 showed that the prevalence of NAFLD increased steadily whereas the other causes remained stable [5]. The data collected from the United Network for Organ Sharing and Organ Procurement and Transplant Network Registry between 2004 and 2013, showed that the number of new waitlisted liver transplant registrants with NAFLD increased by 170 %, compared with 45 % for ALD and 14 % for HCV. NAFLD was the second most common cause of cirrhosis leading to liver transplant after HCV [5].

In India, although there was significant regional variation in etiology across the country, HBV was the commonest cause of CLD. HCV was the commonest cause in the northern region, HBV in the south

and east, alcohol in the north-eastern region and NAFLD in the western and central regions of the country [1].

According to a study done, in Bhutan, CLD is a major cause of morbidity and mortality [6]. The prevalence of CLD in Bhutan is largely unknown but is assumed to be high. Alcohol is assumed to be the major cause of CLD in Bhutan. However, no proper study was done to find out the other causes of CLD. Alcohol liver disease was reported as the number one cause of death [6]. In Bhutan, although alcohol is the main cause of the chronic liver disease (CLD), causes of liver disease other than ALD are often not described. The layperson

Method and Data collection

This is a descriptive study carried out with the aim to explore the etiology of chronic liver disease in patients admitted in Medical Ward at Jigme Dorji Wangchuck National Referral Hospital (JDWNRH), Thimphu over the period of one year, from 1st January to 31st December 2020. The specific objective of the study was to determine:

1. The proportion of Chronic Liver Diseases caused due to alcohol.
2. The proportion of Chronic Liver Disease due to other causes mainly:
 - i) HBV
 - ii) HCV
 - iii) NAFLD
3. Description of presenting complaints, past history, CHILD score and the outcome

Data were collected from a total of 71 participants (Due to COVID 19 pandemic and prolonged lockdown in the country, the number of patients seeking health care services had decreased drastically which have also impacted the number of participants for this study), based on the following inclusion and exclusion criteria, participants were recruited:

Inclusion criteria:

- Age \geq 18years
- Bhutanese nationality

Results

A total of 71 patients were enrolled in this study. Of these patients, 46.5 % were male and 53.5 % were female with an average age of 50.46 years ($SD=11.75$, Range=28-76 years). A total of 65 (91.5 %) of patients were married, 45.1 % of the participants had no education followed by 18.3 % with non-formal education and the least with a

is often led to believe that alcohol abuse is the only etiological factor in CLD.

Although some of the causes of chronic liver diseases have no treatments, such as α 1- anti-trypsin deficiency, cryptogenic hepatitis, and primary sclerosing cholangitis, other causes, such as primary biliary cirrhosis, have treatments that delay progression even though not curable [7]. This study was thus conducted to estimate the proportion of CLD attributable to different etiologies as there is no study in the country on this subject.

Exclusion criteria:

- Patients presenting with severe acute hepatitis are defined as a liver injury of < 6 weeks duration, serum alanine aminotransferase (ALT) activity of > 100 U/L and the absence of coarsened echotexture and surface irregularity on ultrasonography.
- Patients with liver dysfunction secondary to comorbidities such as congestive cardiac failure, biliary obstruction, and septicemia.

Data was collected using a pre-validated pro forma (Annexure 1). Informed consent was obtained from the patients enrolled in the study. Information on the research was explained to all the patients and/ or patient attendants. For all the patients enrolled in the study, relevant demographic details, clinical history, examination, and investigation findings were collected. Clinical history was obtained not only from the patients but also from the patient attendants. After obtaining the history of alcohol consumption, the total quantity of alcohol consumed was calculated using the guide to standard drinks, NCD STEPS survey (Annexure 2).

All the data were double entered in EpiData Entry (version 3.1, EpiData Association, Odense, Denmark) and checked for data entry errors, and corrected where necessary. All the data were then analyzed in the EpiData analysis version 2.2.2.183 and STATA version 15.1 (StataCorp.2017.Stata Statistical Software: Release 15.College Station, TX: StataCorp LLC). The demographic characteristics of the participants and study variables were analyzed by descriptive statistics including frequency, percentage, mean and standard deviation.

college education of 1.4 %. Of the total patients, 32.4 % were doing private business followed by homemakers at 29.6 % and farmers at 21.1 %. 45 % of the total patients belonged to the eastern region as shown in table 1 below.

Table 1: Demographic characteristics of patients with CLD* admitted in Medical Ward, Jigme Dorji Wangchuck National Referral Hospital from 1st January - 31st December 2020.

Variable		Number (n=71)	Percentage (%)
Age (Years)	Mean=50.44, SD=11.8, Range= 28-76 years		
	<45	35	49.3
	≥45	36	50.7
Sex	Female	38	53.5
	Male	33	46.5
Marital status	Married	65	91.5
	Divorced	2	2.8
	Widowed	3	4.2
	Unmarried	1	1.4
Level of education	No education	32	45.1
	Non-formal	13	18.3
	Primary	4	5.6
	Middle	8	11.3
	Secondary	4	5.6
	Higher secondary	6	8.5
	College	1	1.4
	Monastic	2	2.8
	Post-graduate	1	1.4
Occupation	Farmer	15	21.1
	Home maker	21	29.6
	Civil servant	2	2.8
	Corporate worker	3	4.2
	Military	1	1.4
	Private business	23	32.4
	Retired civil servant	4	5.7
	Ex-military	2	2.8
Region	East	32	45
	West	22	31
	Central	11	15.5
	South	6	8.5

The descriptive statistics on alcohol consumption of CLD patients enrolled in this study are presented in **Table 2**. As shown in the table 73.2 % of the patients in this study consumed alcohol and 66.2 % of them consumed alcohol on a daily basis. Commercially brewed liquor

(CBL) was the commonest type of alcohol consumed. The mean duration of alcohol consumption was 13.65 years with SD 11.3 and a range of 0-45 years.

Table 2: Alcohol consumption by patients with CLD* admitted in Medical Ward, Jigme Dorji Wangchuck National Referral Hospital from 1st January - 31st December 2020.

Variable	Number (n=71)	Percentage (%)
Alcohol consumption		
Yes	52	73.2
No	9	12.7
Past consumer	10	14.1
Frequency of alcohol		
Daily	47	66.2
Weekly	6	8.5
Monthly	1	1.4
Occasional	8	11.3
No alcohol consumption	9	12.6
Quantity of alcohol (in grams)		
≤ 20	13	18.3
21-120	30	42.3
121-220	19	26.8
221-320	4	5.6
321-420	2	2.8
421-520	2	2.8
>521	1	1.4
The main type of alcohol consumed		
CBL**	47	66.2
Country (Ara)	15	21.1
Not known***	9	12.7
Duration of alcohol consumption in years Mean=13.65, SD=11.3 Range =0-45 years		
0-10	40	56.3
11-20	15	21.1
21-30	12	16.9
>31	4	5.7

*Chronic liver disease, **commercially brewed liquor, ***non-alcoholic

None of the participants had Anti-HCV detected but ten of them had HBsAg (14.1 %). And two of them had a metabolic syndrome (2.8 %) as shown in **table 3**.

Table 3: Laboratory parameters of patients with CLD* admitted in Medical Ward, Jigme Dorji Wangchuck National Referral Hospital from 1st January - 31st December 2020.

Laboratory Parameters	Number		Percentage	
	Yes	No	Yes	No
Anti-HCV**	0	71	0	100
HBsAg***	10	61	14.1	85.9
Anti-HIV	0	71	0	100
Metabolic syndrome	2	69	2.8	95.8

*Chronic liver disease, **Hepatitis C Virus antibodies, ***Hepatitis B surface antigen

Child-Pugh score

As shown in **Table 4**, of the 71 patients, 41 (57.7 %) of them had a CLD with the Child Score C and 28 (39.4 %) of them had Child Score

B. Only two of the patients had a good prognosis with the Child Score A.

Table 4: Child-Pugh score* of the patients with CLD** admitted in Medical Ward, Jigme Dorji Wangchuck National Referral Hospital from 1st January - 31st December 2020.

Score	Number	Percentage
A	2	2.8
B	28	39.4
C	41	57.7

*CHILD score A 5-6 points, B 7-9 points, C 10-15 points, **Chronic liver disease

Etiology

Table 5 shows the etiology CLD. In this study, it was found that alcohol (80.3 %) was the commonest cause of CLD, followed by

hepatitis B infection (11.3 %), while 2.8 % had both hepatitis B and alcohol, 2.8 % had NASH and 2.8 % had others.

Table 5: Etiology of CLD* in patients admitted in Medical Ward, Jigme Dorji Wangchuck National Referral Hospital from 1st January - 31st December 2020.

Etiology	Number	Percentage
Alcohol	57	80.3
Hepatitis B	8	11.3
Hep B+ Alcohol	2	2.8
NAFLD**	2	2.8
Unknown***	2	2.8

*Chronic liver disease, **Non-Alcoholic Fatty Liver Disease, ***Could not confirm the diagnosis

Discussion

The commonest cause of CLD among the study participants was alcohol consumption followed by Hepatitis B (80.3 %). The findings were contrary to that from a study done by Mukherjee P.S et al in India which reported HBV to be the commonest cause of CLD (33.3 %) among their study participants. These differences could be largely explained based on differences in the prevalence of HBV and HCV, and alcohol policy and cultural differences in alcohol consumption acceptability. In many states of India, the sale of alcohol is banned and culturally not accepted. One of the reasons for less HBV causing CLD in our country could be because of the initiation of immunization program and also early screening and preventive measures put in place by Ministry of Health. Similarly, we need to emphasize the existing programs for alcohol as it is one of the preventable causes of CLD. Other causes of CLD found in this study were NAFLD (2.8 %) and 2.8 % with unknown causes. As we do not have previous data on causes of CLD in our country it's difficult to comment whether there has been a change in the trend.

Important observations of this study include the finding of more than half of the CLD patients present at a remarkably advanced stage and with poor prognosis. It is also observed that most of the CLD patients were with no education (45.1 %) and with non-formal education (18.3 %). Care for liver disease is maximally effective if instituted early [1]. In view of this, creating awareness on liver diseases is recommended as it is considered as one of the important strategic interventions in liver disease a policy that needs to be prioritized in the Bhutanese context. The spectrum of ALD includes steatosis (fatty liver), alcoholic steatohepatitis, progressive fibrosis, cirrhosis, and the development of hepatocellular carcinoma. Although many individuals consuming more than 60 g of alcohol per day develop fatty liver, only a minority 29 of the patients with fatty liver progress to alcoholic steatohepatitis and 10-20 % develop cirrhosis [9]. This study also found that the majority of the patients consumed alcohol on daily basis and in excess amount (100 g per day).

There is an established relationship between the dose, amount, and the likelihood of developing ALD due to alcohol consumption. Fatty liver can be found in the 60 % of those who drink more than 60 g of alcohol per day and the risk of developing cirrhosis is highest in those who drink more than 120 g per day [9]. The alcohol consumption of more than 40 g per day increases the risk of progression to cirrhosis to 30% in patients with uncomplicated fatty liver and to 37 % in those with fibrosis [9].

Similarly in this present study, it was observed that those patients who had CLD with Child-Pugh score C had more amount and longer time of consumption of alcohol. As alcohol was the major cause of CLD we need to strengthen the existing programs for alcohol consumption reduction and develop comprehensive, evidence-based control on alcohol as it has major implications on public health, particularly considering exponential growth in non-communicable diseases in a

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References

1. Mukherjee PS, Vishnubhatla S, Amarapurkar DN, Das K, Sood A, et al. (2017) Etiology and mode of presentation of chronic liver diseases in India: A multi centric study. *PloS one*. 12(10): e0187033.
2. Orlien SM, Ismael NY, Ahmed TA, Berhe N, Lauritzen T, et al. (2018) Unexplained chronic liver disease in Ethiopia: a cross-sectional study. *BMC gastroenterology*. 18(1): 27.
3. Tsega E, Nordenfelt E, Hansson BG, Mengesha B, Lindberg J (1992) Chronic liver disease in Ethiopia: a clinical study with emphasis on identifying common causes. *Ethiopian medical journal*. 30(2 Suppl): 1-33.
4. Fuster D, Samet JH (2018) Alcohol use in patients with chronic liver disease. *New England Journal of Medicine*. 379(13): 1251-1261.
5. Setiawan VW, Stram DO, Porcel J, Lu SC, Le Marchand L, et al. (2016) Prevalence of chronic liver disease and cirrhosis by underlying cause in understudied ethnic groups: the multiethnic cohort. *Hepatology*. 64(6): 1969-1977.
6. Lham Dorji. Alcohol use and abuse in Bhutan. 2009.
7. Riley TR, Smith JP (1999) Preventive care in chronic liver disease. *Journal of general internal medicine*. 14(11): 699-704.
8. Pawlotsky JM, Negro F, Aghemo A, Berenguer M, Dalgard O, et al. (2020) European Association for the Study of the Liver. EASL recommendations on treatment of hepatitis C: Final update of the series. *Journal of Hepatology*. 73(5): 1170-218.
9. European Association for The Study of The Liver. EASL clinical practical guidelines: management of alcoholic liver disease. *Journal of hepatology*. 57(2): 399-420.

country. In a study done by Khokar N and Niazi SA, in Pakistan, it was found that CLD was the commonest cause of mortality and it was mainly because of HCV infection [8]. However, in this study none of the participants had HCV infection and the commonest cause of mortality was alcohol.

In the study done by Setiawan et al, NAFLD was the common cause of CLD [5]. Even in this present study, it was observed that two of the participants had CLD due to NAFLD.

The most common presenting complaints in my study was abdominal distention followed by edema (69 % and 66.2 % respectively). However, in the study done by Khokar N and Niazi SA, the most common presenting complaint was upper gastrointestinal bleeding. Although it was not found to be common in this study, it was the third most common presenting complaint.

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