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Original Research Article

Retrospective Study of Etiology of Chronic Liver Disease in Northeastern India, Sikkim

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Abstract:

Introduction: Liver diseases can result from a spectrum of etiologies such as alcoholic liver disease (ALD), nonalcoholic fatty liver disease (NAFLD), viral infections like hepatitis B virus [HBV] or hepatitis C virus [HCV], autoimmune liver disease and drug-induced liver injury (DILI). Reports of etiologic assessment of CLD published in the past 25 years indicates that hepatitis B, hepatitis C and ALD are the leading causes of liver disease in India.

Aim and Objectives: To assess various etiology of chronic liver disease.

Material and Methods: This present study was carried out to find out the various etiology of chronic liver disease prevailing in the state of Sikkim, a Himalayan northeastern state of India. Patients data of chronic liver disease admitted in the department of gastroenterology, Sir Thutop Namgyal Memorial Hospital, Sochakgang, a tertiary care referral centre in the state of Sikkim from December 2022 till January 2023 was collected in the form of age, sex, alcohol intake duration more than 80gm per day for more than 10 years, liver function test, kidney function test, blood sugar, prothrombin time with international normalised ratio (INR), hepatitis B serology, hepatitis C serology.

Result: 94.1% study subjects were alcoholic, 1.1% study subjects were had autoimmune liver disease, 1.7% study subjects had wilsons disease, 0.8% study subjects had idiopathic liver disease, whereas 0.6% subject each had hepatitis B, IG G4, NASH induced cirrhosis, and primary biliary cirrhosis.

Conclusions: Alcoholic liver disease was the most common cause of chronic liver disease in Sikkim. This can be prevented by healthy lifestyle changes and changing the drinking alcohol habits.

Keywords: CLD, Cirrhosis, INR, Encephalopathy

Introduction

Chronic liver diseases (CLD) cause significant morbidity and mortality worldwide [1]. Liver cirrhosis is associated with both direct complications of the loss of liver function and portal hypertension, such as jaundice, encephalopathy, or variceal hemorrhage and indirect complications like hepatorenal syndrome, hepatocellular carcinoma, or infections [2]. These complications of cirrhosis lead to high morbidity and mortality, thus making this disease a major cause of global health burden. Liver disease continues to be a significant health problem in India. According to the recently available World Health Organization data, liver disease deaths in India has reached 259,749 i.e., 2.95% of total deaths [3,4]. The age-adjusted death rate is 22.93 per 100,000 of population, ranking India 63rd in the world.

Liver diseases can result from a spectrum of etiologies such as alcoholic liver disease (ALD), nonalcoholic fatty liver disease (NAFLD), viral infections like hepatitis B virus [HBV] or hepatitis C virus [HCV], autoimmune liver disease and drug-induced liver injury (DILI).

Reports of etiologic assessment of CLD published in the past 25 years indicates that hepatitis B, hepatitis C and ALD are the leading causes of liver disease in India [5,6,7] However, a surge in the incidence and prevalence of NAFLD in India has been recently noted, with the global epidemic of obesity, hypertension and type-2 diabetes mellitus (T2DM). NAFLD has also been recognized as one

of the most important causes of CLD in western countries as well [8,9].

This recent paradigm shift in etiologic spectrum of CLD in India could be attributed to the improved access to vaccination, tests and treatment, coupled with accelerated urbanization and adaptations such as sedentary lifestyle, fatty food, uncontrolled blood sugar, obesity, smoking and high alcohol intake.

Material and Methodology

This present study was carried out to find out the various etiology of chronic liver disease prevailing in the state of Sikkim, a Himalayan northeastern state of India. Patients data of chronic liver disease admitted in the department of gastroenterology, Sir Thutop Namgyal Memorial Hospital, Sochakgang, a tertiary care referral centre in the state of Sikkim from December 2022 till January 2023 was collected in the form of age, sex, alcohol intake duration more than 80gm per day for more than 10 years, liver function test, kidney function test, blood sugar, prothrombin time with international normalised ratio (INR), hepatitis B serology, hepatitis C serology, autoimmune liver profile test, 24hrs urinary copper, slit lamp examination for Keyser Fleischer ring, immunoglobulin IgG4 test, ultrasonography liver, firboscan of liver, computed tomography, liver biopsy percutaneous as well as (EUS) endoscopic ultrasonography guided, body weight, BMI(body mass index), triglycerides levels, upper gastrointestinal endoscopy reports, platelet counts. Patients above the age of 18yrs was included with physical examination findings, radiological, endoscopic, biochemical diagnosis of chronic liver disease. There was a total of 357 patients admitted during the period. The commonest etiology of chronic liver diseases was Alcoholic liver diseases followed by Hepatitis B, NASH-induced cirrhosis, wilsons disease, autoimmune hepatitis type 1, idiopathic. The clinical presentation of the patients was abdominal distension, Jaundice, ascites, hepatic coma, upper gastrointestinal bleeding, malena, haemotochezia, fatigue, anorexia, generalised weakness, abnormal talk, hepatic encephalopathy.

Result

In the present study 357 study subjects were included, The mean age of the study subjects was 51.54±13.60 yrs, with 60.8% study subjects were male and 39.2% subjects were female,

Table 1: Distribution of study subjects as per etiology of CLD

		Frequency	Percent
Valid	Alcohol	336	94.1
	Autoimmune Liver Disease	4	1.1
	Hepatitis B Cld	2	.6
	Idiopathic	3	.8
	Ig G4	2	.6
	Nash Induced Cirrhosis	2	.6
	Primary Biliary Cirrhosis	2	.6
	Wilsons	6	1.7
	Total	357	100.0

Table 1 shows Distribution of study subjects as per etiology of CLD, 94.1% study subjects were alcoholic, 1.1% study subjects were had autoimmune liver disease, 1.7% study subjects had wilsons disease, 0.8% study subjects had idiopathic liver disease, whereas 0.6% subject each had hepatitis B, IG G4, NASH induced cirrhosis, and primary biliary cirrhosis.

Table 2: Distribution of study subjects as per endoscopic findings

		Frequency	Percent
Valid	Early Varix	7	2.0
	Esophageal Varices Grade 2	61	17.1
	Esophageal Varices Grade 3	46	12.9
	Esophageal Varix Grade 1	55	15.4
	Mild Phg	1	.3
	Normal	183	51.3
	Phg	4	1.1
	Total	357	100.0

Table 2 shows Distribution of study subjects as per endoscopic findings, 51.3% study subjects had normal endoscopic findings, 17.1% esophagealvarices grade 2, 15.4% study subjects esophagealvarices grade 1, 12.9% study subjects in this study had esophageal grade 3,1.1% study subjects had PHG.

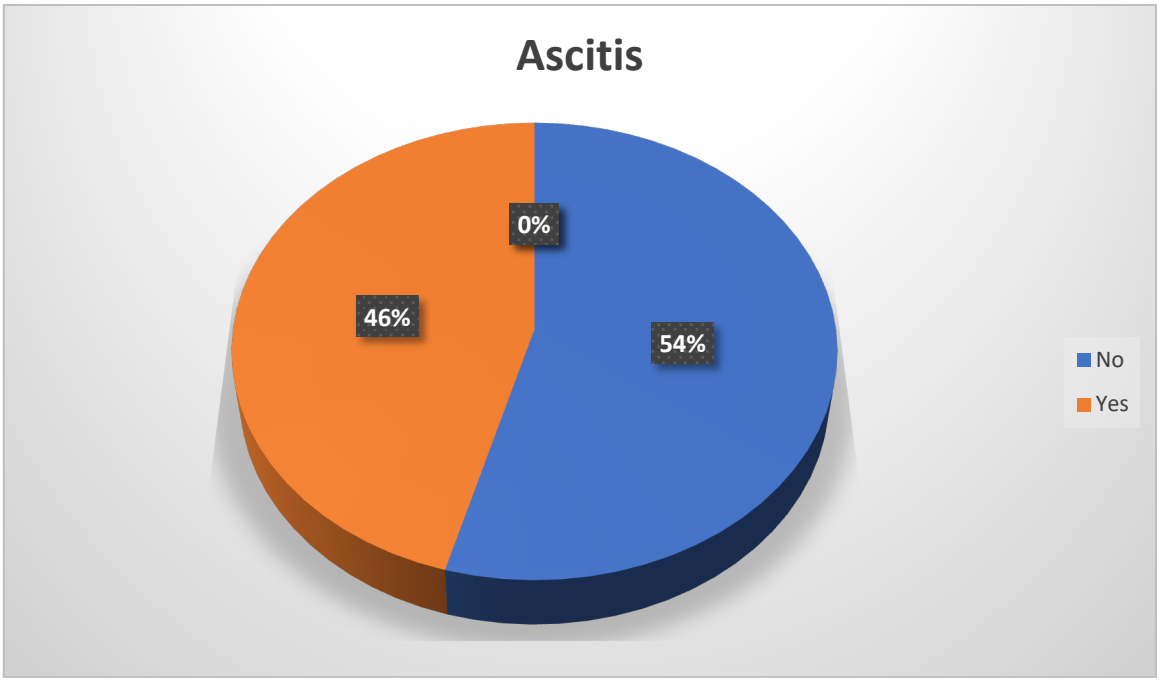

Figure 1: Distribution of study subjects as per presence of Ascitis

Fig 1 shows Distribution of study subjects as per presence of Ascitis, 45.7% study subjects had ascites in the present study.

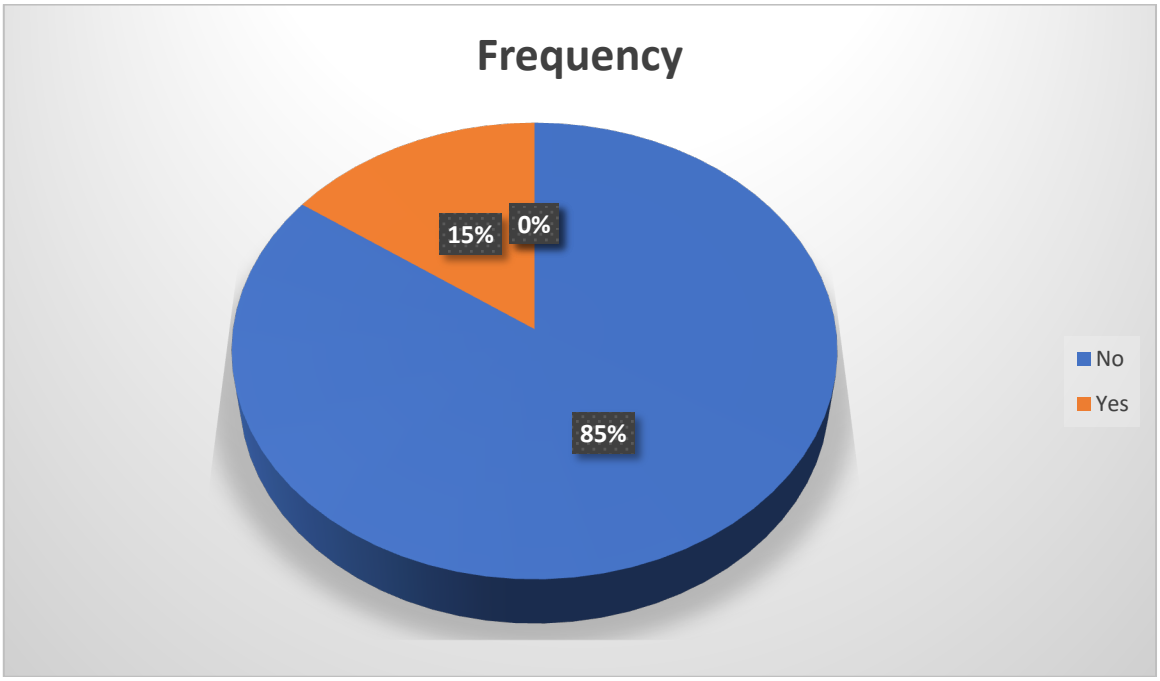

Figure 2: Distribution of study subjects as per encephalopathy

Fig 2 shows distribution of study subjects as per encephalopathy, 15.1% study subjects had encephalopathy.

Table 3: Distribution of study subjects as per Hepatorenal syndrome

		Frequency	Percent
Valid	N	314	88.0
	Y	43	12.0
	Total	357	100.0

Table 3 shows distribution of study subjects as per Hepatorenal syndrome. 12% study subjects had hepatorenal syndrome.

Table 4: Distribution of study subjects as per Death of study subjects

		Frequency	Percent
Valid	N	311	87.1
	Y	46	12.9
	Total	357	100.0

Table 4 shows Distribution of study subjects as per death of study subjects, 12.9% study subjects died

Table 5: Distribution of study subjects as per Jaundice of study subjects

		Frequency	Percent
	No	295	82.7
	Yes	62	17.4
	Total	357	100.0

Table 5 shows distribution of study subjects as per Jaundice of study subjects, 17.4% study subjects had jaundice in our present study.

Table 6: Distribution of study subjects as per hypertension of study subjects

		Frequency	Percent
	DM	15	4.2
	HTN	44	12.3
	Variceal Bleeding	55	15.4

Table 6 shows distribution of study subjects as per hypertension of study subjects, 12.3% study subjects had hypertension in the present study. 4.2% study subjects had DM, and 15.4% study subjects had variceal bleeding.

Discussion

Cirrhosis is progressive and chronic scarring of the liver caused by persistent injury. Various etiological factors of cirrhosis include alcohol, HBV, HCV, NAFLD, autoimmune liver disease, biliary cirrhosis, cardiac cirrhosis, celiac disease, inherited metabolic liver diseases, including hemochromatosis, Wilson's disease, α1 antitrypsin deficiency, etc. Liver cirrhosis is labelled as cryptogenic if no underlying cause can been identified. There has been a wide variation in the etiological factors of cirrhosis worldwide. Alcohol has been reported as the commonest etiological factor for cirrhosis in countries with high alcohol consumption, whereas in countries with low alcohol consumption, viral hepatitis is the most common cause of cirrhosis [10].

In the present study 357 study subjects were included, The mean age of the study subjects was 51.54±13.60 yrs, with 60.8% study subjects were male and 39.2% subjects were female.

In the present study, most CLD patients were males (96, 64%). Similar results were seen in a study by Sreenivas et al.[11] who included 50 patients, out of which 46 (92%) were males and four (8%) were females. Also, Cai et al.[12] study found that liver cirrhosis cases in males were 73.41%. Out of the 54 patients with cirrhosis enrolled in a study by Sungkar et al.[13] 37 were males (68.52%) and 17 were females (31.48%). Arul et al.[14] study included 100 patients of CLD, out of which 15% were females and 85% were males. Thus, the male preponderance of cases of CLD in our study matches those of other studies and this was probably due to higher alcohol-related CLD in males.

In the present study 94.1% study subjects were alcoholic, 1.1% study subjects were had autoimmune liver disease, 1.7% study subjects had wilsons disease, 0.8% study subjects had idiopathic liver disease, whereas 0.6% subject each had hepatitis B, IG G4, NASH induced cirrhosis, and primary biliary cirrhosis. Alcoholism is an emerging problem in the northeastern state of India, Sikkim. While it is difficult to put a figure on how many people are alcoholics, consumption is especially high among men over the age of 31.

The high percentage of study subjects with Alcoholic Liver Disease (ALD) is consistent with existing knowledge, as excessive alcohol consumption is a well-known risk factor for liver disease. ALD can lead to various liver conditions, including fatty liver, alcoholic hepatitis, and cirrhosis.

The presence of Autoimmune Liver Disease and Wilson's Disease in the study population suggests that some individuals might have liver damage due to their immune system attacking the liver or due to a genetic disorder causing copper accumulation in the liver, respectively.

Idiopathic Liver Disease refers to liver conditions of unknown origin, indicating that a significant proportion of the study subjects had liver diseases for which the cause remains unclear.

The low prevalence of hepatitis B is interesting, as it is a prevalent cause of chronic liver disease worldwide. This finding could be attributed to

several factors, such as the vaccination program's effectiveness, regional variations in hepatitis B prevalence, or other population characteristics.

Similarly, the presence of IgG4-Related Liver Disease, NASH-induced cirrhosis, and Primary Biliary Cirrhosis in the study subjects highlights the diverse etiologies that can lead to chronic liver disease.

In a study by Sreenivas et al[11] out of 50 CLD cases, 41 were attributed to alcohol as the causative factor, three to HCV infection, one to HBV infection, three to both alcohol and HBV, and one to both alcohol and HCV infection. In contrast, Sungkar et al[13]. reported that out of 54 patients with cirrhosis, HBV infection was the primary cause in 53.7% of cases, followed by an unknown causative agent (non-B and C) in 44.4% of patients. Acharya et al[8]. found that among 171 patients, end-stage liver disease resulted from alcohol in 51.46% of patients, alcohol and a virus in 6.43% of patients, and a pure viral etiology in 29.82% of patients. Specifically, hepatitis B was responsible for 21.05% of cases, hepatitis C for 6.43% of cases, hepatitis B + C for 1.75% of cases, and hepatitis B + A for 0.58% of cases. Additionally, end-stage liver disease was attributed to non-alcoholic steatohepatitis in 7.60% of patients, autoimmune hepatitis in 4.09% of patients, and Wilson's disease in 0.58% of patients.

UgoFedeli et al[15] in their study, the crude mortality rate of all CLD was close to 40 per 100,000 residents. In middle ages (35 to 74 years) CLD was mentioned in about 10% and 6% of all deaths in males and females, respectively. Etiology was unspecified in about half of CLD deaths. In females and males, respectively, HCV was mentioned in 44% and 21% and alcohol in 11% and 26% of overall CLD deaths. A bimodal distribution with age was observed for HCV-related proportional mortality among females, reflecting the available seroprevalencedata.

Sam J. Thomson et al [16] in their study, hospital admission rates for chronic liver disease was increased by 71% in males and 43% in females during their study period. This increase largely due to alcoholic liver disease, admission rates for which more than doubled between 1989/1990 and 2002/2003. While there was a smaller rise for chronic viral hepatitis B and C, admission rates declined for hepatitis A, autoimmune hepatitis, and primary biliary cirrhosis. Mortality rates for chronic liver disease more than doubled between 1979 and 2005. Two thirds of these deaths were attributable to alcohol-related liver disease in 2005. The highest rate of alcoholic liver disease mortality was in the 45–64 age group, and the largest percentage increase between 1979 and 2005 occurred in the 25–34 age group.

Waniet al [17] in their study in Kashmir, India, Over 2 year's period, 246 patients were enrolled. Mean age of patients was 57.09 ± 13.90 years. Hepatitis B virus is a major etiological contributor to the burden of CLD amounting to 28% in Kashmir with Non-Alcoholic Fatty Liver Disease (NAFLD) not so far behind at 23%. Whereas Alcohol related CLD disease is almost non-existent. Most patients were presenting at advanced stages signifying need of sensitizing people for emerging epidemic of CLD.

Conclusion

Alcoholic liver disease was the most common cause of chronic liver disease in Sikkim. This can be prevented by healthy lifestyle changes and changing the drinking alcohol habits.

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