

## Clinical Spectrum and Demographic Profile of Alcoholic Liver Disease Among Females Attending Tertiary Care Center in Nepal

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### ABSTRACT

#### Introduction

Alcohol is the most common abused substance in Nepal. Women tend to present with more severe liver disease with a shorter period of excessive drinking and at a lower daily alcohol intake compared to men.

#### Methods

Adult female patients aged 16 years and above, with a diagnosis of ALD were included for a period of 1 year. Liver disease secondary to other causes were excluded. Demographic profiles, clinical features, laboratory, endoscopic findings, Child-Turcotte-Pugh (CTP), Model for End-stage Liver Disease (MELD) of the patients were recorded.

#### Results

A total of 144 female patients with ALD were included in the study. The mean age of the patients was 48.6 years (SD=12.7). Majority of the patients were from Hilly region (n=66, 45.8%), married (n=135, 93.8%), housewife (n=83; 57.6%), Hindu by religion (n=93; 64.6%), and Tamang (n=39; 27.1%) by caste. Most common clinical features of the patients were abdominal distension (n=117; 81.2%), bilateral lower limb swelling (n=89; 61.8%), jaundice (n=54; 37.5 %) and anorexia (n=53; 36.8%). The main reason for alcohol consumption was found to be family custom in 42.3%. Esophageal varix was present in 119 (82.6%) patients. Out of 124 patients with cirrhosis, 63 (50.8%) patients were in CTP stage C and 103 (83.1%) patients had MELD score  $\geq$  16.

#### Conclusion

ALD was predominantly seen among the younger female patients. The most common clinical presentations were abdominal distension, bilateral lower limb swelling, jaundice and anorexia. Among the cirrhotic patients, most of patients were in CTP class C and had MELD score  $\geq$  16.

#### Keywords

*Alcoholic liver disease, clinical profile, demographic profile, female*

## INTRODUCTION

Alcohol consumption is responsible for 3.8% of global mortality and 4.6% of disability adjusted life years (DALYs).<sup>1</sup> Alcoholic liver disease (ALD) is a spectrum of liver abnormalities caused by excessive and chronic alcohol consumption that includes steatosis, steatohepatitis and cirrhosis.<sup>2</sup> Alcoholic hepatitis is a clinically severe form of ALD that carries a high mortality depending on the severity.<sup>3,4</sup>

Females consuming alcohol at a significant amount are at a greater risk of ALD and acute on chronic liver failure than men.<sup>5</sup> Although men abuse alcohol more, women are more susceptible to the toxic effects of alcohol for any given dose of alcohol.<sup>6</sup>

Alcohol is the most common abused substance in Nepal.<sup>7</sup> The traditional liquors are jaad, rakshi, chyang, tongba and nigar are common in our country.<sup>8</sup> Drinks also have their traditional values according to one's culture and tradition. A drink is a must in some festivals, rituals, feasts, occasions, and funeral rites in some ethnicity. The females being the homemaker and brewing alcohol themselves are more likely to consume alcohol.<sup>9</sup>

Although, the prevalence and demographic profile of ALD has been performed in our country, but pertaining to female ALD patients no study has been performed. This study makes an effort to study the demographic, clinical profiles, spectrum of ALD, laboratory parameters, endoscopic findings and their severity of the presentation in female population.

## METHODS

This was a hospital-based, descriptive, observational, cross sectional study conducted at Tribhuvan University Teaching Hospital (TUTH), Institute of Medicine (IOM), Nepal. Patients attending Gastroenterology Ward and Out Patient Department (OPD) of TUTH were included in the study for a period of 1 year. Ethical clearance for the study was obtained from the Institutional Review Committee (IRC) of IOM. Sample size was calculated by applying following formula:  $N = Z^2 \times P(1 - P) / L^2$ . With prevalence of disease 32.2%, sample size was calculated 144.

A total of 144 female patients aged 16 years and above with a diagnosis of ALD meeting the inclusion criteria were enrolled in the study. Liver disease secondary to other causes like hepatitis B, hepatitis C, drug induced liver injury, autoimmune hepatitis and primary biliary cirrhosis; and those not giving informed consent were excluded from the study. The diagnosis of ALD was made by the treating physician based on American Association for the Study of Liver Disease (AASLD) guideline depending the history of alcohol consumption,

physical signs of liver disease and laboratory data. Liver biopsy was not performed.

Fatty liver was diagnosed on the basis of appropriate history of alcohol abuse with ultrasonological presence of fatty liver after exclusion of other causes of fatty liver.<sup>10</sup> Although, MRI is more accurate for quantifying fat than other radiologic techniques, with the added advantage that MRI can assess fat over the entire volume of the liver, it was not used due to its high cost. Clinical diagnosis of alcoholic hepatitis was considered if onset of jaundice within prior 8 weeks of alcohol consumption, ongoing consumption of >40 (female) or 60 (male) g alcohol/day for  $\geq 6$  months, with <60 days of abstinence before the onset of jaundice, AST >50, AST/ALT >1.5, and both values <400 IU/L, serum total bilirubin >3.0 mg/dL and ruling out other causes of hepatitis.<sup>11</sup> The case of clinical cirrhosis was defined as a patient having at least one clinical sign of hepatocellular failure and one portal hypertension.<sup>2</sup> For the presence of alcohol dependence CAGE questionnaire was evaluated.

A detailed history was obtained and physical examinations were conducted in all the patients. Demographic profiles, presenting features of ALD, stigmata of liver cirrhosis and laboratory and imaging results were noted in a pre-designed proforma. Upper gastrointestinal (UGI) endoscopy was performed and gastroesophageal varices were graded (I-III) according to AASLD classification. For the severity of the disease we used Child Turcotte Pugh (CTP) criteria and Model for End-stage Liver Disease (MELD) score. Informed consent was taken from all the participants. All patients received standard of care treatment.

IBM SPSS Statistics version 20 and Microsoft excel 2016 were used for data entry and statistical analysis. Descriptive statistics were used for analysis. In descriptive statistics, frequencies, mean and standard deviation were computed.

## RESULTS

A total of 144 female patients with a diagnosis of ALD meeting the inclusion criteria were enrolled in the study. The mean age of the patients included in the study was 48.6 years (SD=12.7). Majority of the patients were in the age group 31 to 60 (n=116; 80.6%). The age distribution of the patients is represented in Figure 1.

Majority of the patients were from hilly region (n=66, 45.8%). The three most common occupation of the patients were housewife (n=83;57.6%), farmer (n=33;22.9%), and retired or dependent population (n=21;14.6%). Unemployment contributed to the greater consumption of alcohol. There was significant number of patients (33 out of 144; 22.9%) who were farmer by occupation. Majority of

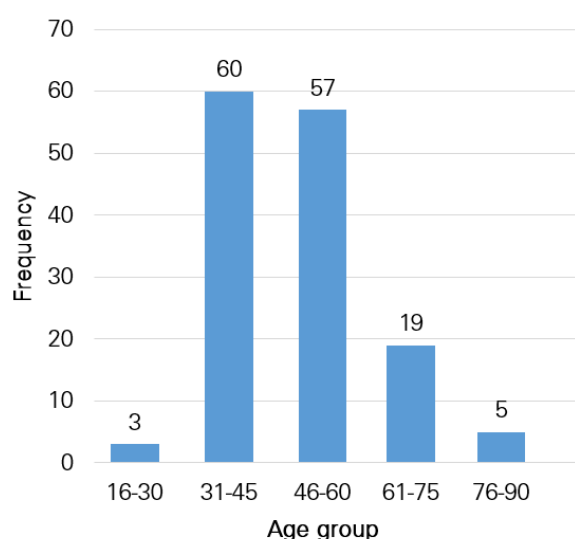


Fig 1. Age distribution of patients

the patients were Hindu by religion (n=93; 64.6%). Out of 144 patients, majority of the patients were married (n=135, 93.8%) (Table 1).

Out of 144 patients, the majority of the patients were Tamang (n =39; 27.1%) followed by Chhetri (n=23; 16%) and others (n=21; 14.6%). Only 2.8% of the patients were from Terai. This variation may be associated with their pattern of drinking which might be due to cultural differences and difference in the availability of alcohol products.

The main reason for alcohol consumption was found to be family tradition (which includes festival, rituals and feast) in 42.3% followed by multi-factorial in 41% of the patients, and under peers' influence in 12.5% of the cases. The mean age of starting of alcohol intake was at 18.6 years (SD=9.3). The

Table 1. Demographic profile of patients (n= 144)

Parameters	Frequency (%)
Location	
Hilly	66 (45.8)
Mountain	45 (31.2)
Terai	33 (23)
Occupation	
Housewife	83 (57.6)
Government employee	7 (4.9)
Retired or dependent	21 (14.6)
Farmer	33 (22.9)
Religion	
Hindu	93 (64.6)
Buddhist	51 (35.4)
Marital Status	
Unmarried	6 (4.2)
Married	135 (93.8)
Widow	3 (2.0)

Table 2. Grading of esophageal varices in patients (n= 119)

Grade	Frequency (%)
Grade 1	42 (35.3)
Grade 2	54 (45.4)
Grade 3	23 (19.3)

daily average amount of alcohol intake by patients was found to be 230 grams (SD=163.5). Similarly, the mean duration of alcohol intake was 28.6 years (SD=14.6).

The four most common clinical features of the patients were abdominal distension (n=117; 81.2%), bilateral lower limb swelling (n=89; 61.8%), jaundice (n=54; 37.5 %) and anorexia (n=53; 36.8%). Out of 144 patients, 124 (86%) patients presented with liver cirrhosis, and 10 (7%) patients presented with fatty liver and alcoholic hepatitis.

The mean±SD of hemoglobin and platelet were 8.9±2.2 gm/dl. Liver function test showed a mean±SD of total bilirubin, direct bilirubin and albumin of 95.9±116.9 µmol/L, 48.1±62.4 µmol/L and 26.6±6.5 gm/L respectively. Similarly, the mean±SD of AST, ALT and GGT were 113±118 U/L, 51±44 U/L and 206±189 U/L respectively.

Out of 144 ALD patients, 119 (82.6%) had esophageal varices and amongst patients who had esophageal varices (n=119), 54 (45.4%) had grade 2 varices (Table 2). Out of 124 patients of ALD, 63 (50.8%) patients were in CTP stage C and 103 (83.1%) patients had MELD score ≥ 16 (Table 3).

Table 3. CTP class of patients (n=124)

Stage/Score	Frequency (%)
CTP stage	
Stage A	3 (2.4)
Stage B	58 (46.8)
Stage C	63 (50.8)
MELD score	
< 16	21 (16.9)
≥ 16	103 (83.1)

## DISCUSSION

In this study, the mean age of the female patients was 48.6 years (SD=12.7). This highlights the young age in which the female population started consuming alcohol in our society and this correlates with other studies where ALD develops during the fifth decade as revealed by Becker et al.<sup>12</sup> The mean age of starting of alcohol intake was at 18.6 years (SD=9.3). Majority of the patients were from hilly region (n=66, 45.8%). This predilection could be due to the reason that females in Terai consume

less alcohol due religious and cultural barrier. Most patients were housewife (n=83;57.6%) followed by farmer (n=33;22.9%) and retired or dependent population (n=21;14.6%). Unemployment contributed to the greater consumption of alcohol. In a study done by Askgaard et al. with newly diagnosed ALD, 78% of whom had cirrhosis, 86% had a low or medium-low educational level and only 20% were employed.<sup>13</sup> The aforementioned study also revealed that ALD patients were less likely to be employed in the 10 years prior to diagnosis than controls.<sup>13</sup>

There was a significant percentage of patients (22.9%) who were farmer by occupation. This high number could be because of their economic difficulty that they cannot afford good food and thus rely on alcohol as a source of energy for doing strenuous work whole day in the field. This finding is in accordance with the study done in Western Nepal by Adhikari et al. who revealed that population involving in agriculture had higher odds of binge drinking as compared to other professions.<sup>14</sup> Majority of the patients were Hindu by religion (n=93; 64.6%) which was similar to the study done in tertiary care hospital in Central Nepal.<sup>15</sup>

A 12-year prospective study of alcohol use in over 13,000 participants in Denmark revealed that the risk of development of alcohol-related liver disease increased in women who consumed 7 to 13 beverages per week (84-156 g) compared with men who consumed 14 to 27 beverages per week (168-324 g).<sup>16</sup> A study in Japan showed the relative risk of developing ALD was 3.7 in men and 7.3 in women, indicating the increased risk of ALD for women.<sup>12</sup> In a study of 1,000 patients in an alcoholism clinic in Melbourne, Australia, women with cirrhosis had a mean daily alcohol intake of 140±55g compared with men who reported 210±80g of alcohol use per day.<sup>17</sup> This study also revealed that the duration of excessive drinking(>100g daily alcohol) resulting in cirrhosis was shorter in women (13.5 years) compared to men (20 years). One explanation for this predilection is that women are generally smaller in stature and have less body water than men resulting in more toxic injury to liver.<sup>18</sup> The other reason being women having a lower activity of a metabolizing enzyme in the stomach called alcohol dehydrogenase (ADH) thus, causing a larger amount of the alcohol to reach the blood and eventually in susceptible persons can lead to cirrhosis of the liver.<sup>19</sup> The daily average amount of alcohol intake in our population was found to be 230 grams (SD=163.5) and the mean duration of alcohol intake was 28.6 years (SD=14.6). This amount of alcohol was in concordance with the studies done in Denmark, Japan and Australia.<sup>11,15,16</sup>

Out of 144 patients, the majority of the patients were Tamang (n =39; 27.1%) followed by Chhetri

(n=23; 16%) which was similar to the study done by S. Bhattarai et al. in a tertiary care hospital in Central Nepal.<sup>15</sup> This variation may be associated with their pattern of drinking behavior which might be due to cultural differences and difference in the availability of alcohol products. The main reason for alcohol consumption was found to be family tradition (which includes festival, rituals and feast) in 42.3% followed by multi-factorial in 41% of the patients, and under peers' influence in 12.5% of the cases. Similar reasons were revealed by Abbey et al.<sup>20</sup>

Abdominal distension was the most common presentation followed by bilateral lower limb swelling, jaundice and anorexia. These are the most common presentations of a chronic liver disease patients as stated by AASLD.<sup>2</sup> Patients were more commonly found to have liver cirrhosis as compared to fatty liver and alcoholic hepatitis which could be due to late presentation of these patients. As these patients presented late in the course of the disease, they had more advanced cirrhosis thus having higher CTP and MELD scores. Concomitantly, they also had higher grade of esophageal varices.

Thus, this study highlights the early age of onset of drinking behavior in females in our society. Religious background, geographical location, ethnicity and occupation contributed significantly in the drinking behavior of this population. Overall, the presentation of the disease is similar to the general population. Nevertheless, the disease is more advanced in the female population at the time of diagnosis. This is small observational study which recommends a separate, large, multicenter, prospective study should be performed to evaluate the clinico-demographic profile of female patients with alcoholic liver disease.

## CONCLUSION

Our results suggest that ALD occurred in females at a relatively younger age. Most of the patients are married, Hindu by religion, from Hilly region, of Tamang caste and housewives. The most common clinical features are abdominal distension, bilateral lower limb swelling, jaundice and anorexia. The majority of the patients present with liver cirrhosis. Most of patients have grade 2 esophageal varices, are in CTP class C and have MELD score  $\geq$  16. This study concludes that females in our country are more predisposed to ALD, thus raising the concern of adequate health awareness among females in Nepal.

## CONFLICT OF INTEREST

None declared.

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