A STUDY OF CLINICAL PROFILE AND PROGNOSTIC INDICATORS OF ALCOHOLIC LIVER DISEASE IN A TERTIARY CARE CENTRE OF NORTH EAST INDIA

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ABSTRACT

BACKGROUND

Alcoholic Liver Disease (ALD) is a major cause of mortality and morbidity worldwide. ALD has varied clinical and biochemical presentation ranging from the subtle features of fatty liver to obvious findings of decompensated cirrhosis.

OBJECTIVE

To study the clinical profile and their prognostic implications among patients of alcoholic liver disease.

MATERIALS AND METHODS

The study population included total 138 patients proven to have ALD on the basis of clinical, biochemical and ultrasonographic parameters admitted in Jorhat Medical College and Hospital, Jorhat (Assam), over a period of 1 year (July 2015 to June 2016).

RESULTS

Out of 138 patients (113 males and 25 females), majority of the patients were in the age group of 41-50 years (34.78%). The mean age of presentation was 45.91±10.34 years, with a male to female ratio of 4.5:1. The common clinical presentations were abdominal distension and swelling of feet (51.45%), jaundice (49.29%), Melaena/Haematemesis (29.72%) and altered sensorium (19.57%). The common clinical findings were pallor (62.32%), ascites (59%), pedal oedema (55.8%), icterus (54.35%), hepatomegaly (44.20%) and splenomegaly (36.96%). Features of hepatic encephalopathy were seen in 16% patients. The mean liver function test values were total bilirubin (6.59±6.61 mg/dL), albumin (2.46±0.7 g/dL), AST (155.61±85.24 U/L), ALT (81.65±37.59 U/L), ALP (150.59±66 U/L), GGTP (217.30±203.01 U/L) and PT (17.30±4.65 secs.). The mean platelet count was 125,421.7±65,910 /cu.mm and mean prolongation of PT was 5.37±5.02 secs. The average duration of alcohol intake in fatty liver, hepatitis and cirrhosis were 12.77±3.70, 14.56±6.83 and 20.53±6.08 years, respectively. A total of 21 (15.22%) patients expired during the hospital stay. Hepatic encephalopathy (42.86%) and hepatorenal syndromes (28.56%) were the major causes of death.

CONCLUSION

ALD patients had a longer duration of hospitalisation. Longer duration rather than the patterns of alcohol intake was associated with development of liver disease. Jaundice, ascites at presentation, hepatic encephalopathy, lower serum albumin, lower platelet count, AST/ALT ratio >2 and discriminant function >32 were found to be significantly associated with mortality.

KEYWORDS

Alcoholic Liver Disease, Clinical Profile, Prognostic Indicators.

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INTRODUCTION: Alcohol related health disorders are global public health problems that threaten the economies of all nations, particularly the developing countries. Alcohol consumption causes 3.8% of total deaths and Alcoholic liver disease (ALD) represents 9.5% of alcohol-related disability-adjusted life years worldwide.[1,2]

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The National Family Health Survey (NFHS) 2007 reported that 30% of adult Indians have been consuming alcohol and of which 4% to 13% are daily users. There are reports of high prevalence of ALD in India and about 50% of cases of cirrhosis may be due to alcohol.[3] Alcoholic Liver disease encompasses a spectrum of injury, ranging from simple steatosis to frank cirrhosis.[4,5] Although liver biopsy is the gold standard in the diagnosis of ALD.[6], it is rarely performed in clinical practice. This is because a combination of clinical and laboratory data can make an accurate diagnosis of ALD with the prebiopsy diagnosis of ALD being 98% specific and 79% sensitive.[7,8] However, every person consuming alcohol does not develop the disease and a number of factors determine the overall risk of developing the disease in a given patient.

These may include amount, duration and type of alcohol consumed, nutritional status, comorbid conditions, race, sex and genetic factors, etc. Various studies have shown different results about the role of drinking pattern including amount, duration and type of alcohol in the pathogenesis of disease. A few of them showed a dose dependent effect on the risk of developing ALD, while others showing a threshold effect, above which the risk of development of cirrhosis was not further influenced by the amount of alcohol.[9-11] South Asian race and female sex are more prone to develop liver disease with lesser alcohol consumption and in shorter duration of time than their counterparts.[11-15] Illicitly brewed liquor has been found to be more toxic than licit drinks despite low level of alcohol in a study.[16] The extent of protein calorie malnutrition may also play an important role in determining the outcome of patients with ALD.[17,18] The prevalence of usage of alcohol among Indian women is reported to be much lower than their male counterparts but it reaches up to 10% in the North Eastern states.[19-21] Alcoholic liver disease (ALD) is very common in this part of the country while very few studies have been done on this subject. Hence, we planned this study to get a detailed demographic profile, laboratory parameters, complications and their prognostic implications among patients of ALD.

MATERIALS AND METHODS: The study was carried out on 138 patients admitted in medicine ward of Jorhat Medical College and Hospital, Jorhat (Assam). The study was carried out for a period of one year from July 2015 to June 2016.

Inclusion and Exclusion Criteria: Adult patients of both the sexes diagnosed with ALD were included in the study. Liver disease from other causes like NASH, Viral hepatitis, Drug-induced hepatitis, Haemochromatosis, ALD with diabetes mellitus, ALD with known heart disease and ALD with previous history of kidney disease and immunocompromised patients were excluded from the study. The diagnosis of ALD is based on a combination of features including.[22,23] (a) History of significant alcohol intake evaluated with the help of CAGE questionnaire; (b) Clinical evidence of liver disease based on symptoms and signs; and (c) Supporting laboratory and radiological abnormalities. After having selected cases for the study, a detailed clinical history, physical examination and investigations were done in particular relation to ALD.

RESULTS: A total of 138 patients were analysed, of which 113 (81.88%) were males and 25 (18.12%) were females with a male to female ratio of 4.5:1. Majority of cases (48 cases, 34.78%) were in the age group of (41-50) years. This was followed by the age group of (31-40) years with 39 cases (28.26%). The mean age of the patients was 45.91±10.34 years and the range was 26-72 years. 98 patients (71.01%) belonged to the lower socio-economic status group, 34 patients (24.64%) belonged to the middle and 6 patients (4.35%) belonged to upper socio-economic status group.

Among the study group, 120 patients (86.95%) were taking alcohol for more than 10 years and 18 cases (13.04%) for ten years or less than ten years. 40 cases (28.99%) were in the 11-15 years duration group and 44 cases (31.88%) in 16-20 years duration group. 36 cases (26.09%) were taking alcohol for > 20 years. The average duration of alcohol intake was 18.39±6.24 years for males and 16.76±6.59 years for females with "p value"= 0.244 between the two mean durations. The overall average duration of alcohol intake was 18.09±6.29 years [Table 1].

Duration (In years)	Male		Female		Total	
	n	%	n	%	N	%
<5	1	0.72	0	0.00	1	0.72
5-10	11	7.97	6	4.35	17	12.32
11-15	32	23.19	8	5.80	40	28.99
16-20	40	28.99	4	2.90	44	31.89
>20	29	21.01	7	5.07	36	26.08

Table 1: Showing Duration of Alcohol Intake

Majority of the patients (104 cases, 75.36%) took both foreign and country-made liquors while 18(13.04%) patients took foreign liquor only and 16(11.59%) patients took only country-made liquor. Eighty six patients (62.32%) were taking alcohol throughout the weekdays and fifty two (37.68%) were taking alcohol confined to 1-2 days a week. The most common clinical presentation was abdominal distension and swelling of feet (71 cases, 51.45%) followed by jaundice (68 cases, 49.28%) and anorexia (56 cases, 40.58%). Forty six patients (33.33%) complained of weight loss and fever was present in 35(25.36%) cases. Twenty seven (19.57%) cases presented with altered sensorium and 41 cases (29.71%) presented with symptoms of upper GI bleeding followed by palpitation (16 cases, 11.59%) [Table-2].

Clinical Symptoms	Number	Percentage
Abdominal Distension and Swelling of Feet	71	51.45
Jaundice	68	49.28
Anorexia	56	40.58
Weight Loss	46	33.33
Melaena/Haematemesis	41	29.71
Fever	35	25.36
Pain Abdomen	37	26.81
Altered Sensorium	27	19.57
Palpitation	16	11.59
Convulsions	15	10.87
Tingling and Numbness Of Extremities	11	7.97

Table 2: Showing Clinical Symptoms of Patients with ALD

The most common clinical finding was pallor (86 cases, 62.32%) which was followed by ascites (82 cases, 59%), pedal oedema (77 cases, 55.8%) and icterus (75 cases, 54.35%).

Hepatomegaly was found in 61(44.20%) cases and splenomegaly was found in 51(36.96%) cases. Parotid swelling was seen in 29(21.01%) cases and gynaecomastia in 20 (14.49%) cases. Hepatic flaps were seen in 13(9.42%) cases and 9(6.52%) cases presented with hepatic coma [Table-3].

Clinical Signs	Number	Percentage
Pedal Oedema	77	55.80
Ascites	82	59.00
Pallor	86	62.32
Icterus	75	54.35
Hepatomegaly	61	44.20
Spider Naevi	19	13.77
Palmar Erythema	26	18.84
Dilated Veins over Abdomen	59	42.75
Splenomegaly	51	36.96
Bruit over Liver	1	0.72
Parotid Swelling	29	21.01
Gynaecomastia	20	14.49
Dupuytren's Contracture	8	5.80
Hepatic Flaps	13	9.42
Hepatic coma	9	6.52

Table 3: Showing Clinical Signs in Patients with ALD

Basic biochemical investigations showed that haemoglobin level was less than 10 g% in 83(60.15%) cases and the mean haemoglobin level was 8.6±2.02 g%. The mean WBC count was 9,183.33±3,955.86/cu.mm. MCV was > 98 fl in 65.94% cases and the mean value was 98.3±6.43 fl. Ninety six (69.57%) patients were having platelet count <150,000/cu.mm and mean platelet count was 125,421.7±65,910/cu.mm. Liver function tests revealed that mean serum bilirubin level was 6.59±6.61 mg/dL, mean albumin was 2.46±0.7 g/dL, mean AST was 155.61±85.24 U/L, mean ALT was 81.65±37.59 U/L, mean ALP was 150.59±66 U/L, mean GGTP was 217.30±203.01 U/L, mean PT was 17.30±4.65 secs. The mean prolongation of PT was 5.37±5.02 secs [Table-4].

Mean LFT VALUES	Mean	Range
Bilirubin	6.59±6.61 mg/dL	0.38-36.5 mg/dL
Albumin	2.46±0.7 g/dL	1-4.8 g/dL
AST	155.61±85.24 U/L	25-564 U/L
ALT	81.65±37.59 U/L	21-264 U/L
ALP	150.59±66 U/L	17-373 U/L
GGTP	217.30±203.01 U/L	29-1310 U/L
PT	17.30±4.65 secs.	12.1-48 secs.

Table 4: Showing Mean Liver Function Test Values in ALD Patients

The AST/ALT ratio was <2 in 86 (62.32%) cases and ≥ 2 in 52(37.68%) cases. The mean AST: ALT ratio was 1.95±0.67. Ultrasonography of Abdomen revealed cirrhosis of liver in 60.14% cases, fatty liver in 20.29% cases and hepatomegaly with hepatitis in 19.57% cases.

Ascites was found in 64.75% and splenomegaly in 44.93% cases. Pancreatitis was seen in 5.07% cases. UGI endoscopy was done in 105 cases and the most common finding was oesophageal varices (56.19% cases) [Grade I-13.32%, Grade II-26.67%, Grade III-16.1%], followed by erosions (21.9% cases) and ulcers in 7.6% cases. Endoscopy could not be done in 33 patients due to poor condition of the patients. It is observed that the average duration of alcohol intake in fatty liver, hepatitis and cirrhosis were 12.77±3.70, 14.56±6.83 and 20.53± 6.08 years, respectively. Of the 138 patients, 117(84.78%) patients were discharged, while 21(15.22%) patients expired during the hospital stay. The average duration of hospital stay among those that were discharged was 10.35±2.71 days and among those that expired was 13.23±3.52 days. The overall average duration of hospital stay was 10.76±2.9 days. Hepatic encephalopathy (42.86%) and hepatorenal syndromes (28.56%) were the major causes of death. 19.04% of the expired patients died of massive variceal bleed and 9.52% patients died of sepsis. It is observed that jaundice, ascites at presentation and hepatic encephalopathy were significantly associated with mortality [Table-5].

Clinical Parameter		Number of Patients	Patients Expired	"p" Value
Jaundice	No	70	2	0.0006
	Yes	68	19	
Ascites	No	49	00	0.0003
	Yes	89	21	
Hepatic Encephalopathy	No	116	12	0.0092
	Yes	22	9	

Table 5: Showing Mortality and Different Clinical Parameters

There was significant difference between the mean serum albumin, mean platelet count, mean AST/ALT ratio and mean discriminant function of those discharged and those expired during the hospital stay [Table 6].

Laboratory Parameters	Discharged	Expired	"p" Value
Mean serum albumin (mg/dL)	2.5±0.7	2.24±0.62	0.04
Mean Platelet Count (per cu. mm)	131,484.6± 68,204.99	91,642.86± 36,920.23	0.005
Mean AST/ALT ratio	2.01±0.68	1.61±0.46	0.005
Mean discriminant function	27.39±23.83	58.72±38.75	<0.0001

Table 6: Showing Mortality and Different Laboratory Parameters

DISCUSSION: In our study, males accounted for 81.88% and females accounted for 18.12% of the cases in a ratio of 4.5:1.

The female proportion in this study was higher than previously reported from this region.[19] In Singh et al study in central India, the male to female ratio was 37:1.[24] However, Pathak OK et al reported a male to female ratio of 4:1 in their study in Nepal.[25] The increase in female patients in this study may be because of difference in cultural and traditional values in Northeast India from the Indian mainland, where females more commonly indulge in alcoholism. The mean age of the patients was 45.91±10.34 years. This was comparable to Chacko and Chacko et al study (48±11 years) and Sarin et al study (43±8.7 years).[26,27] Majority of the patients (63.04%) were in age group 31-50 years, which are the most productive years in a person's life. In this study, 71.01% patients were from lower, 24.64% from middle and 4.35% from the upper socioeconomic status class of Kuppuswamy's scale 2012. However, Sarin et al and Suthar H et al reported much lower number of patients in the lower socioeconomic status group, 20% and 24% respectively.[27,21] More number of patients in lower socioeconomic status group in this study may be to be due to admission bias in a public sector healthcare institute and the high prevalence of ethnic tribes and tea garden labourers in the area, who are mostly poor and illiterate.

Most patients (86.95%) in this study were taking alcohol for >10 years with an average duration of 18.09±6.31 years, which is consistent with the earlier population based studies, which documented a duration of 10-12 years of significant alcohol intake for developing the risk of liver disease.[28] Males were taking alcohol for a longer duration (18.39±6.24 years) when compared to females (16.76±6.59 years). However, the difference between the mean durations of alcohol intake was not found to be significant (p value=0.244). The average duration of alcohol intake in fatty liver, hepatitis and cirrhosis in this study was 12.16±3.41, 14.71±6.87 and 20.46±6.10 years, respectively. The role of pattern of alcohol intake in the development of ALD is not conclusive. [29] In this study group, majority of patients (62.32%) were taking alcohol regularly throughout the weekdays and 37.68% were taking alcohol confined to 1-2 days a week regularly. The role of country-made liquors in the development of ALD had been controversial.[16,20] Most patients (75.36%) in this study were not beverage specific. Since they were taking both foreign as well as country-made liquors, the effect of individual drinks could not assessed in this study. It may be possible that a nonspecific beverage drinking habit may increase the risk of liver injury.

Due to the prevalence of consuming country-made liquors of various alcohol concentrations in this part of the country, it was not possible to quantify the exact amount of alcohol consumed. The most common clinical presentation in this study was abdominal distension and swelling of feet (51.45%). Jaundice was seen in 49.28% cases which is slightly less than Suthar H et al study (60%) and Pathak OK et al study (57.5%).[21,25] Symptoms of upper GI bleed were present in 29.71% patients in this study which is comparable with Pathak OK et al study (26%).[25]

Hepatic encephalopathy was seen in 16% cases which is slightly more than but comparable to Pathak OK et al study (12.2%).[25] Ascites was observed in 59% patients in this study which was comparable but slightly more than Mandenhall et al (50.9%) but less than Bell H et al study (67%).[30,31] Palpable hepatomegaly was present in 44.20% cases in this study which was slightly less but comparable with the finding of Suthar H et al (50%).[21] Palpable splenomegaly was present in 36.96% cases in this study which was slightly more than Pathak OK et al(29.8%) study.[25] The more number of ascites and lesser number of jaundice and palpable hepatomegaly in this study may be because the study group consisted only of hospitalised patients, majority of which were in stage of cirrhosis of liver. Features like parotid swelling (21.01%), gynaecomastia (14.49%), spider naevi (13.77%), Dupuytren's contractures (5.8%) were not very commonly seen though these are said to be more common in alcoholic cirrhosis.[32] The mean haemoglobin level in our study was 8.6±2.02 g% which is slightly less but comparable to Suthar H et al (10.1 g%).[21] The mean WBC count was 9183.33/cu.mm, which is comparable to Suthar H et al (9521/cu.mm). [21] The MCV was > 98 fl in 65.94% cases in our study. The mean value of MCV was 98.3±6.43 fl which is comparable to Mandenhall et al (99.8-102.8 fl).[30]

The mean platelet count in our study was 1,25,421.7±65,910/cu. mm and 69.57% patients were having platelet count <1,50,000/cu.mm. A higher mean platelet count (1,62,490±89,230/cu.mm, and a lower percentage of platelet count <1,50,000/cu.mm (33.6%) was reported by Pathak OK et al.[25] The mean AST level in our study was 155.61±85.24 U/L which is comparable with Pathak OK et al (142.95±159.85 U/L).[25] The mean ALT level in our study was 81.65±37.59 U/L which is slightly higher than Mandenhall et al (47-50 U/L).[30] In our study, the AST/ALT ratio was > 2 in 37.68% cases which is comparable with Biswas et al (32%) study.[33] The mean AST: ALT ratio was 1.95±0.67. Similar results were reported by Pathak OK et al (2.27± 1.33).[25] The lesser number of patients with AST/ALT ratio >2 in our study may be because of the greater proportion of cirrhotic patients in our study group. The mean serum ALP in our study was 150.59±66 U/L which was similar to Antonio Chedid et al (163-219 U/L) study.[34] Mean serum bilirubin in our study was 6.59 mg/dL, which is comparable with Chacko and Chacko et al (3.3 - 4.5 mg/dL) study.[26] Average serum albumin in our study was 2.46±0.7 g/dL. Similar results were reported by Chacko and Chacko et al study (2.5 g/dL). [26] Average prolongation in PT in our study was 5.37±5.20 sec. Suthar H et al also reported a similar reading (5.6 sec.).[21]

Among the 105 cases in which UGI endoscopy were done and the most common finding was oesophageal varices (56.19%) followed by erosions (21.9% cases). Ulcers were seen in (7.6%) cases. This finding was less than that of Aswad Ai Obeidy et al study [Oesophageal varices in (77%), erosions (33.3%) and ulcers (15%)].[35] Ultrasonography of

whole abdomen showed fatty liver (20.29%), hepatomegaly with hepatitis (19.57%) and cirrhosis of liver (60.14%).

Suthar H et al had reported fatty liver in 40% cases, hepatitis in 24% and cirrhosis in 36% cases. Increased number of cirrhotic patients in our study was because more number of cirrhotic patients are admitted in the hospital and patients with fatty liver are usually admitted only with comorbid conditions. Ultrasonography showed splenomegaly in 74.70% cases whereas clinically splenomegaly was palpable in 61.4% of those cases. Gibson et al reported 52% palpable splenomegaly and 56% splenomegaly on ultrasound in patients with ALD and portal hypertension.[36] During the hospital stay, 15.2% patients expired. Hepatic encephalopathy (42.86%) and hepatorenal syndrome (28.56%) were the major causes of death. This finding was almost comparable to Suthar H et al study, where the mortality rate was 20% and the most common cause of death was hepatic encephalopathy (40%).[21] The average duration of hospital stay of those expired during the hospital stay (13.23±3.52 days) was more than that of those discharged (10.35±2.71 days). The overall average duration of hospital stay was 10.76±2.9 days. Pathak OK et al had reported a mean duration of 13.41 days in their study.[25] Jaundice (p =0.0006), ascites at presentation (p=0.0003) and hepatic encephalopathy (p=0.0092) were found to be significantly associated with mortality. A lower serum albumin, lower mean platelet count, mean AST/ALT ratio >2 and discriminant function >32 were also found to be associated with mortality which is consistent with previous studies.[25,37,38].

CONCLUSION: Alcoholic Liver Disease (ALD) was more common in males of lower socioeconomic status in their productive years of life. The prevalence of ALD in females was found to be higher in this region as compared to other parts of the country. Longer duration rather than the patterns of alcohol intake was associated with development of liver disease. Distension of abdomen, swelling of feet and jaundice were found to be the most common clinical presentations, while pallor, ascites and pedal oedema were the most common clinical findings. ALD patients had a longer duration of hospitalisation. Jaundice, ascites at presentation, hepatic encephalopathy, lower serum albumin, lower platelet count, AST/ALT ratio >2 and discriminant function >32 were found to be significantly associated with mortality.

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