Original Research Article

CLINICAL SPECTRUM OF ALCOHOLIC LIVER DISEASE IN SUBJECTS ATTENDING OUTPATIENT DEPARTMENT AT A TERTIARY CARE HOSPITAL

ABSTRACT:

Background: Alcoholic liver disease is one of the primary medical complication of chronic ethanol abuse. It encloses a wide spectrum of diseases comprising of fatty liver, alcoholic hepatitis, alcoholic cirrhosis and hepatocellular carcinoma.

Methodology: A prospective ,observational study was done at AIG hospitals in the department of hepatology for a period of 6 months . A total of 200 patient's diagnosed clinically and biochemically with various spectrum of ALD were recruited for the study.Non-invasive prognostic scores were calculated at the time of admission and correlated with severity of disease.

Results: Among 200 study participants, 34.8% belongs to age group of 36-45 years. All were male patients with age group ranged from 25 to 73 years. We observed the high levels of alkaline phosphatese, aspartate aminotransferase/alanine aminotransferase ratio, mean corpuscular volume, total bilirubin and international normalized ratio in Severe Alcoholic hepatitis patients. Non-invasive prognostic markers like child-turcotte-pugh score,model for end stage liver disease-sodium and maddrey's discriminant factor were assessed for all patients.Prevalence of different stages of ethanol mediated liver disease were-12% of alcoholic fatty liver,17.5% of alcoholic hepatitis,6% of acute on chronic liver failure,32.5% of chronic liver disease,24% of decompensated chronic liver disease,6% of past decompensated chronic liver disease with current living donor liver transplant and 2% cases of hepatocellular carcinoma.

Conclusion: Hazardous ethanol abuse is more typical in adult males especially among productive age group. The subjects were cautioned on their personal basis regarding fallout of alcoholic liver disease, and guided for latency of alcohol not immediately but definitely.

Keywords: Spectrum, alcoholic liver disease, child-turcotte-pugh score,model for end stage liver disease-sodium, maddrey's discriminant factor.

1. INTRODUCTION

Over decades, Ethanol or ethyl alcohol (CH3 CH2 OH), the primary psychoactive substance and CNS Depressant used in all alcoholic beverages [1]. Alcoholic liver disease is a general term indicating the spectrum of ethanol mediated liver damage and symbolize primordial form of hepatic illness known to human race [2]. Ethanol is a hepatoxin related with a spectrum of liver diseases such as fatty liver/steatosis [3], alcoholic hepatitis, cirrhosis and hepatocellular carcinoma. Alcoholic hepato-steatosis is not a lethal status, but alcoholic hepatitis and cirrhosis are lethal and can be fatal [4]. Ethanol mediated noxious is the third most typical agent of morbidity. The WHO Proclaimed that, about 150 million people globally are living with alcoholism [5].The threshold for advancing severe form of alcohol related liver disease is consuming >60-80gm/day of ethanol for 10 years for men, while for women, with ethanol intake of 20-40gm/day. Only 15% of alcoholics

progress to ethanol induced liver disorders [6]. Globally, ethanol accounts for about one-third of incident realities of primary liver cancer with notable variations between countries and regions [7].ALD and its complications are the dominant cause of morbidity and mortality worldwide. The direction of this study was to estimate percentage of different stages of alcoholic liver disease which helps to know prevalence of disease in diverse population. The objectives of this current study was to determine the current status, clinical profile and burden of alcoholic liver disease.

2. MATERIALS AND METHODS

2.1. Study Design And Setting: A Hospital based Prospective, Observational and Non-Interventional study was conducted at Asian institute of gastroenterology hospitals, Hyderabad, for a period of six months . A total of 200 patients of age >18 diagnosed with alcoholic liver disease attending the department of Hepatology, who met the inclusion and exclusion criteria of the study were analysed and enrolled for study. Non-Invasive prognostic markers like MELD, mDF, MELD-NA were calculated at admission and correlated with severity of disease.

2.2. Study Criteria:

2.2(a). Inclusion Criteria:

- ✓ People who are positive for Alcohol Use Disorder.
- ✓ Patients diagnosed with any form of alcoholic liver diseases.
- ✓ Individuals of greater than 18 years.

2.2(b). Exclusion Criteria

- ✓ Intravenous drug users
- ✓ Individuals with liver illness other than alcoholism such as auto immune hepatitis, , viral hepatitis-B infection, viral hepatitis – C infection Wilson's disease, Hemochromatosis, post necrotic cirrhosis and any other forms of CLD were excluded.
- ✓ Individuals who unable to cooperate due to mental retardations.

2.3 Study Procedure: Approval from Institutional Ethics Committee was taken prior commencement of the study and written informed consent for the study purpose was obtained from all the enrolled participants. All the participants was asked about the details enlisted in pre-tested pro-forma involving demographic data such as age, gender, weight, height, BMI, smoking, socioeconomic status, drug allergies, co-morbidities and detailed history of alcohol intake ,smoking, any substance abuse ,dietary history, abdominal ultra-sonographic findings, Laboratory investigations like CBP, LFT, RFT, Coagulation reports were recorded. Biochemical parameters of Albumin, International normalized ratio, prothrombin time, total bilirubin, ALT, AST, ALP ,Serum creatinine ,Serum sodium ,potassium levels were documented via interviewing patients with help of Patient profile form and questionnaires Like CAGE (to identify current alcoholic's) and AUDIT-C (used to determine hazardous alcohol consumption). Each patient's liver function status /Severity of disease was assessed by prognostic score markers like Child-Turcotte Pugh(to assess the severity of liver disease among cirrhotic patient's), MELD-Na (To estimate need for liver transplantation and to estimate 3-month mortality rate in end stage liver disease), Maddrey's Discriminant Function (to evaluate severity and need for corticosteroid therapy in alcoholic hepatitis patient's). ALD were recognised with

the aid of clinical and biochemical findings.The captured clinical data and the test outcomes were reassessed and entered in data collection forms and further results were tabulated and graphs were plotted .

2.4 . Stastistical Analysis: The captured data was entered in to MS EXCEL2010 version. Descriptive analysis was determined in terms of mean value ± standard deviation for continuous variables and percentage for categorical variables. Pie diagrams, tables were constructed using Microsoft Excel 2016 version to illustrate percentages.

3. RESULTS

3.1. *Age and Gender Distribution of Patient's with ALD:-*

Observed patients with age extending from 25-73years, out of which the maximal number of the subjects were assorted in the age group of 36-45 years (35%). Next common age group was among 25-35 years accounting for 19% cases. The mean age of the patients was 40 ±22.3years. In the present study, it was found that all were males with median age of 38 years.

3.2. *Distribution Of Cases Based On Quantity Of Alcohol Consumption:-*

Ethanol ingestion more than two drinks (22-30 g) per day in women and three drinks (33-45 g) in men was studied as significant. In the Current study, on the base of ethanol abuse,35.5% of subject's had current history of taking >60 grams of ethanol /day, 54% had current history of intake between 50-60grams of ethanol/day and only 10.5 % consumed <50grams of ethanol /day.

3.3. *Distribution Of Cases Based On Duration Of Alcohol Consumption:*

Median duration of alcohol intake among study participants was 17 years, which was not quite different among individual liquor groups with a minimum of 4 years and a maximum of 30 years. This sign the impact of duration of alcoholic consumption in alcoholic liver disease.In the current study, on basis of duration of alcohol intake, most of subject's (42.5%) had a history of alcohol intake ranging between 11-15years of duration and while, only (4%) have history of shorter duration i.e., less than or equal to five years of consumption and 6.5% of cases are on Chronic duration of ethanol ingestion i.e, greater than or equal to 20years.

3.4. Distribution Of Cases Based On Type Of Alcoholic Beverages and Frequency of alcohol consumption:

Among 200 cases, Majority of them have been consuming branded spirits (91.5%) like Beer, whisky, Rum, Vodka and other country-made spirits (8.5%).It is observed that out of 200 total study participants, only 5.5 % of cases had alcohol occasionally, 61.5% of patients had alcohol regularly and while,30.8 % had thrice in week.

3.5. Distribution Of Cases Based On Questionnaire:

According to CAGE questionnaire out of 200 subjects, 94.5% of cases were treated clinically significant followed by 5.4% patients were non-significant for alcohol abuse/alcohol related consequences.

In adults, a score of 4 for men and 3 for women on the AUDIT-C is considered optimal for recognizing hazardous drinking or active for AUD. All 200 participants were positive for alcohol use disorders.

3.6. Distribution Of Cases Based On Clinical Features:

In the Current study, the most typical clinical manifestations documented among patients of acute form of liver disease was nausea and vomiting found in 82.5% of patients, which was followed by jaundice documented among 80.5% of cases. The third most common symptom was abdominal pain was observed in 59% of patients, followed by anorexia, abdominal distension and fever was present in 48% ,50.7% and 33% of patients respectively.The most typical Clinical Sings such as Splenomegaly (20.3%) Anaemia (37.3%), Jaundice (80.5%), pedal edema (34.8%), Hepatomegaly (19%) and Haematuria (5.9%) was summarized in Table1:

Clinical Symptoms:	Percentage
Nausea, vomiting	82.5%
Weight loss	13%
Jaundice	80.5%
Abdominal pain	59.4%
Abdominal distension	48.2%
Anorexia	50.7%
Melena	17.4%
Fever	33.8%
Generalised weakness	31.8%
Constipation	25.8%
Haematemesis	7.9%
Clinical signs	
Splenomegaly	20.3%
Anaemia	37.3%
Pedal edema	34.8%
Hepatomegaly	19%
Haematuria	5.9%
Palmar erythema	6.5%
Bilateral parotid gland enlargement	2.5%

Table 1: Clinical Features

SECONDARY DEVELOPMENTS TO ALD:

The most of secondary complications of ALD seen in patients were portal hypertension (56.5%), Ascites (52.7%), and anaemia (37.3%) and others were mentioned in Table 2: Abstinence reforms the survival and prognosis of patients with ALD and restricts advancement to liver cirrhosis through histologic improvement and decline in portal pressure.

Secondary Developments to ALD	Percentage
Portal Hypertension	56.5%
Ascites	52.7%
Diabetes (Co morbid)	55%
Anaemia	37.3%
Psychotic syndrome	5.5%
Jaundice	80.5%
Alcohol withdrawal symptoms	63.5%
Oesophageal varices	60.5%
Hepatorenal syndrome	2.5%
Hepatic Encephalopathy	3.9%

Table 2: Secondary complications of ALD.

3.7. Distribution Of Cases Based On Bio-Chemical Parameters:

In the prevailing study, Hypoalbuminemia was observed in 42.2%, Hyperbilirubinemia was found in 73.6% cases. The enzyme GGT was raised in 49.2% cases and ranged from 75 to 200 IU/L. Raised GGT is typical and specific for alcoholic liver disease. The enzymes such as AST, ALT each were also increased around 79 % cases. ALP enzyme was also increased in 32.3% and AST/ALT ratio was more than 2 in 59 % of cases. Basic biochemical investigations revealed anaemia in 37.3% of patients and leucocytosis in 42%.

Table 3: Haematological, Biochemical and Coagulation characteristics in patients with Various forms of ALD.

Variables	*AFL*	*AH*	*ALC*		*ACLF*	*P-value*
			CLD	*DCLD*		
Haemoglobin	*12.5±1.71*	*10.9±1.6*	*9.5±1.7*	*8.7±1.98*	*8.2±2.07*	*<0.001*
MCH	*28.5±2.5*	*26.6±1.9*	*26.5±2.5*	*25.6±1.9*	*25.9±2.01*	*<0.001*
MCHC	*32.6±2.5*	*31.5±1.61*	*31.6±2.5*	*30.9±1.87*	*30.6±1.71*	*<0.001*
RBC	*4.5±0.5*	*4.3±0.51*	*4.2± 0.55*	*4.08± 0.51*	*3.7± 0.56*	*<0.001*
MCV	*86.3±8.5*	*82.6± 6.4*	*86.35±8.5*	*79.43±10.18*	*81±6.54*	*<0.001*
PCV	*41.1±4.8*	*37.8±4.7*	*41.01±4.9*	*36.8±4.71*	*36±4.36*	*<0.001*
TLC	*8688.7±1612.3*	*7726.4±2132.7*	*7653.06±2321.1*	*7633.9±20003.1*	*7019.1±1711.8*	*<0.001*
ALT	*37.6±13.4*	*38.3±10.9*	*105.6±512.4*	*38.9±14.5*	*39.9±13.1*	*<0.001*
AST	*34.6±15.2*	*35.3±15.2*	*120.8±668.7*	*37.1±15.3*	*38.7±14.1*	*<0.001*
ALP	*124.5±74.2*	*152.06±116.7*	*174.4±156.7*	*183.4±79.8*	*189.3±84.5*	*<0.001*
Blood Urea	*31.9±13.9*	*35.5±14.4*	*35.8±14.4*	*36.1±13.6*	*40±27.7*	*<0.001*
Serum Creatinine	*0.8±1.14*	*1.43±1.23*	*1.66±0.96*	*1.68±1.22*	*1.721.±02*	*<0.001*
PT	*13.7±1.98*	*13.8±2.19*	*14.2±1.8*	*14.9±79*	*15.8±2.99*	*<0.001*
INR	*1.77±0.87*	*1.79±0.95*	*1.95±0.885*	*1.97±1.49*	*1.78±0.73*	*<0.001*
Albumin	*3.86±1.20*	*2.56±0.68*	*2.47±0.700*	*2.42±2.79*	*1.96±0.81*	*<0.001*

**Correlation is significant at the 0.01 level(2-tailed).

3.8. Distribution Of Cases Based On Severity Of Cirrhosis Using Child-Turcotte-Pugh Score:

The patient's attending out-patient department, while admissions liver function status and severity of liver disease is predicted using Child-Turcotte-Pugh score.Among 200 participants 18% were accounted as Mild (Class A) form of disease,42.5% categorized as Moderate (Class B) severity of disease and while 39.5% were determined as Severe (Class-C) form of liver disease.

3.9. Distribution Of Cases Based On Meld-Na Score:

MELD-Na score measures mortality in a period of 3 months among end-stage chronic liver disease.Among 200 cases,37%,13% and 2 % of study participants having risk of 19.6%,52.6% and 71.3% respectively were at estimated 3 month mortality rate and need for liver transplantation.

3.10. Distribution Of Cases Based On mDF Score:

Maddrey's score measures disease severity and prognosis particular to alcoholic hepatitis.Out of 200 cases, 39.5% of patients were determined with good prognosis(mDF<32) while,60.5% were associated with poor prognosis(mDF>32).

3.11 Distribution Of Cases Based On Diagnosis:

Among 200 study participant's 12% of AFL,17.5% of AH,6% of ACLF,32.5% of CLD,24% of DCLD,6% of Past DCLD with current living donor liver transplant and 2% of HCC patients were observed.

4. DISCUSSION

All the patient's attending Hepatology department were screened for alcohol use disorder and to detect physical signs of dependency using AUDIT-C and CAGE questionnaires. The AUDIT-C screening device has been proven to be 73% sensitivity and 91% specific for an AUD and 85% sensitive ,89% specific for alcohol dependence. The Finest score for identifying chronic ethanol abuse is 5 for men (sensitivity 77%, specificity 76%) and 3 for women (sensitivity 86%, specificity 76%) [8].The recommended cut off for CAGE is greater than /equal to 2 to detect for alcohol dependence. In a meta-analysis of 10 studies, for a cut off greater than /equal to 2, the sensitivities were 0.87 in hospital inpatients, 0.71 in primary care patients, and 0.60 in ambulatory medical patients [9].

In our study, the prevalence of ALD is highest i.e.,35% among 36-45 age group is found similar to the study by Chavan et al [10]. In Present Study, age distribution on basis of different stages of ALD, found that end stage liver disease i.e., cirrhosis cases were higher in the age group of 56-65 years, found that the study participants became older with diagnosis from AFL to those with ALC. These age group subjects are more reasonable to be affected due to hazardous alcohol ingestion, as ALD needs years together to display its advancement and lethal effects. But this is contradictory to the study organized by Vinayak S. Jamdade [11].In the Current study, all were male study participants, analogous to the study organized by Nand et al [12] documented male dominance by constituting, a total of 201 male patients with alcoholic liver disease with the mean age of 46 ±9.9 years with the mean weight of 59±6.2 kg. Comparably, Suthar HN et al [13], Bode et al [14], studies also reported all male alcoholic patients. The percentage of male patients diagnosed with ALD was found to be 100% as all admitted patients were male, which is contradictory to the study organised by Vinayak S. Jamdade [11].In India, because of traditional and cultural value, females are not involved in alcoholism. They are less likely to take part in social events and have little chance of alcohol abuse while in Sarin et al [15] study and Chacko et al [16] study found median age of patients were 48 ± 11 years and 43 ± 8.7 years respectively. Comparingly lower age in our study is suggestive of raising burden of alcoholic liver disease. Michael J. Thun et al [17] & Susumu Itoh et al [18] study have shown 21:1 and 17:8 male to female ratio respectively, while in our study all patients were male.

In the Current study, the most typical clinical findings documented among patients were nausea and vomiting, anorexia, abdominal pain, Abdominal distension, Hepatomegaly and ascites. This study authenticates with the clinical detections of Medenhall et al [19] excluding hepatic encephalopathy was observed in 27% of the patients in that study whereas we found only 3.9% of patients with hepatic encephalopathy. Jaundice and Hepatomegaly were observed to be the most typical clinical assessments. Hepatomegaly was present in 2.3%, 9.2% and 8.4% in fatty liver, hepatitis and cirrhosis respectively and ascites was found in 52.7% of cases and all of them were cirrhotic patients in our study. Analogous to present study, other studies organized by Mitra et al [20] and Mendenhall et al[19] also documented ascites was the most typical findings present in 53.7% and 55.6% patients respectively.

Hyperbilirubinemia was noticed in 73%of ALD patients in our study. Medenhall et al [19] study observed raised levels of bilirubin in 65% of hepatitis and 90% of cirrhosis patients. In Leiber et al [21] study observed elevated level of ALT were noted in 50%, 95% and 50% cases of fatty liver, hepatitis and cirrhosis respectively which differs from the findings in our study. ALP was raised in 19% patients in our study. In the study of Medenhall et al [19] ALP was raised in 67% of alcoholic hepatitis patient.

In this study hypalbuminaemia and hyperglobulinaemia were noticed in 42.2% and 24.3% cases of ALD respectively. In the study of Leiber et al [21] hypoalbuminaemia and hyperglobulinaemia were detected in 50% and 62% of ALD patients. PT was increased (3 seconds more than control) in half of the subjects in our study and most of them were compensated and decompensated cirrhotic patients. We observed the high levels of ALP, the AST/ALT ratio, MCV, TBIL and INR in Severe AH patients. By contradictory, serum levels of ALB, HGB, were reduced in Severe AH group. The SAH study population has the poor prognosis.

Both MELD-Na and CTP scores were identified as good predictors of long-term survival in patients with decompensated liver cirrhosis. In a validation study, the c-statistic correlated with the CTP score in the prediction of 3-month survival was 0.84 (95% CI 0.78-0.90), in comparison to 0.87 for MELD. Thus, the MELD scale is thought to be at least as good as the CTP score in predicting short-term mortality [22].Initially aim of MELD score was to anticipate 3-month survival rate in patients who go through a transjugular intrahepatic porto systemic anastomosis. Later the MELD score used as a measure of mortality in a period of 3 months in transplant patients among end-stage chronic liver disease and precedent for liver allotment [23].An altered scoring system with addition of serum sodium termed as MELD-Na score was prospective as an alternative to the MELD score and was implemented for liver allotment in 2016, since hyponatremia is a robust predictor of mortality among waiting list liver transplantation candidates. The adequency of MELD-Na was shown to be only somewhat superior to that of MELD in candicates for transplantation [24].

An MDF score more than equal to 32 illustrates severe form of disease with a 1month mortality rate up to 30-50%. Patients with an elevated mDF and/or with encephalopathy that received corticosteroid therapy, showed a 28-day mortality of 6 % in the treatment group correlated to 35 % in the placebo group. DF has an inadequate specificity of <40 % to 62% and sensitivity of 67-100% for short term mortality [25].

5. CONCLUSION

In conclusion, there has been a gradual increase in the number of hospitalized patients with ALD and with its related complications. From this study, we found that hazardous alcohol consumption is more typical in adult males Age wise distribution of ALD showed, elder study participants with advanced stage of disease. This study does not correlate between Quantity, Type of alcohol beverage and frequency of alcohol consumption as this is an observational study. We found that patients attending hospital with moderate to severe disease severity. Among 200 patients of data collected 121 patients attended with poor prognosis of disease. The Spectrum of disease is mostly affecting productive age groups of males. From our study we determined the prevalence of various forms of ALD and predicting severity of disease with help of prognostic markers. The outcome of the study establishes most of the common facts about ALD.

ABBREVIATIONS

CNS-Central nervous system, WHO- World Health Organisation, ALD-Alcoholic liver disease, CLD- Chronic liver disease, CAGE- Cut Down,Annoyed,Guilty and Eye opener, , AUDIT-C- Alcohol use Disorder Identification test Consumption, MELD-Na-Model for end stage liver disease-sodium,AUD-Alcohol use disorder, MDF- Maddrey's Discriminant function, AFL- Alcoholic fatty liver, ASH-Alcoholic steatohepatitis, AH- Alcoholic Hepatitis, ALC- Alcoholic Liver Cirrhosis, ACLF-Acute on chronic liver failure,HCC- Hepatocellular Carcinoma, DCLD-Decompensated chronic liver disease, LDLT-Living donor liver transplant,GGT- Gamma-glutamyl transferase, MCV-Mean corpuscular volume, AST- Aspartate aminotransferase, ALT- Alanine transaminase, INR- International normalized ratio, CPS- Child pugh score,ALP-Alkaline phosphatise,PT-Prothrombin time,TBIL-Total bilirubin, ALB-Albumin, HGB-Hemoglobin, DF-Discriminant function.

ETHICAL STATEMENT The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This research was approved by our IRB (IRB number: AIG/IEC-Post BH&R 10/12.2020-01). The informed consent was obtained from all the study participants.

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