Original Research Article

Clinical profile of patients with alcohol use disorder

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Abstract

Introduction: Present study aimed to evaluate the clinical profile of patients with alcohol use disorder and to study the associated derangements in their haematological and biochemical profile.
Materials and methods: A hospital based observational study was conducted in medicine ward of a tertiary care Hospital during January 2016 to June 2017. Study subjects included 150 patients of alcohol use disorder admitted to general medicine ward during the study duration. A similar number of age matched controls were also included. Patients included in study were asked for detailed clinical history and history of alcohol consumption, type, quantity and its duration. Alcohol use disorder was diagnosed as per DSM V criteria. All the study subjects underwent following laboratory tests: complete blood profile, lipid profile and liver function tests.
Results: Out of 150 patients, maximum patients were in the age group 41-60 (46.7%), 46% were in age group 25-40, and 7.3% were in age group 60-80. All patients were male and there was no woman. Most common diagnosis encountered in study patients was liver cirrhosis (38%) followed by anaemia (9.3%). On the basis of discriminant analysis TC, Apo B, and LDL/HDL-c among lipid measures and AST and GGT among liver enzymes emerged as the variables which can significantly discriminate between alcohol dependents and non-dependents.
Conclusion: Heavy alcohol consumption for prolonged periods results in marked derangement of lipid profile and various biochemical and hematological parameters. Combination of more than one marker can be used in non-specialized settings in identifying alcohol-dependent and non-dependent subjects by using limited number of tests. Screening for alcohol use disorder should be done in all adult patients presenting to hospital, to detect alcohol use in its early stages so that interventions can be planned effectively.

Key words

Alcohol Use Disorder, DSM V criteria, Lipid Profile, Liver Function tests, Screening.

Introduction

Alcoholism, also known as alcohol use disorder (AUD) and alcohol dependence syndrome, is major problem in India and is a broad term for any drinking of alcohol those results in problems [1]. It was previously divided into two types: alcohol abuse and alcohol dependence [2, 3]. 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].

DSM V (Diagnostic and Statistical Manual of Mental Disorder) combines alcohol abuse and alcohol dependence for defining Alcohol Use Disorder. DSM V defines 'Alcohol Use Disorder' as presence of at least 2 of 11 criteria during period of past 12 months [4, 5].

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].

Diagnosis is made on the basis of the symptoms and consequences of alcohol consumption. Simple biological measures such as liver function tests are poor indicators of the presence of harmful or dependent drinking. Diagnosis and assessment of the severity of alcohol misuse is important because it points to the treatment interventions required. Acute withdrawal from alcohol in the absence of medical management can be hazardous in people with severe alcohol dependence, as it may lead to seizures, delirium tremens and, in some instances, death [6].

Current practice across the country is varied and access to a range of assisted withdrawal and treatment services varies as a consequence. Services for assisted alcohol withdrawal vary considerably in intensity and there is a lack of structured intensive community-based assisted withdrawal programmes. Similarly, there is limited access to psychological interventions such as cognitive behavioural therapies specifically focused on alcohol misuse. In addition, when the alcohol misuse has been effectively treated, many people continue to experience problems in accessing services for comorbid mental and physical health problems. Despite the publication of the Models of Care for Alcohol by the Department of Health in 2007 (National Treatment Agency, 2007), alcohol service structures are poorly developed, with care pathways often ill defined. In order to address this last point the three pieces of NICE guidance are integrated into a care pathway [6].

With very few studies being carried out till date, in this regards, in the rural Indian setup, our study was planned to evaluate clinical profile of patients with alcohol use disorder in tertiary care hospital.

Materials and methods

A hospital based observational study was conducted in medicine ward of a tertiary care Hospital during January 2016 to June 2017. Study subjects included 150 patients admitted to general medicine ward during the duration of the study, fulfilling the inclusion and exclusion criteria.

Inclusion criteria

- Patients more than or equal to 25 years of age.
- Patients with DSM V score more than or equal to 2 for last year.
- Patients willing to participate in study with consent.

Exclusion criteria

- Age less than 25 years
- Patients with DSM V score less than 2

Methodology

Patients included in study were asked for detailed clinical history and history of alcohol consumption, type, quantity and its duration. Alcohol use disorder was diagnosed as per DSM V criteria [5]. One fifty healthy, age matched males (with no current/ life time history of regular drinking and no family history of alcoholism) were also included as a control group after applying the same exclusion criteria as in the study group. All the study subjects underwent following laboratory tests: complete blood profile, lipid profile and liver function tests.

Data analysis

Sensitivity, specificity, predictive value and diagnostic accuracy were calculated using Epi Info 6.0. Sensitivity was defined as percentage of patients of alcohol dependence correctly identified in the study group and specificity was defined as percentage of normal subjects correctly identified in the control group. Positive predictive value (PV+) represents the true positives in study group & negative predictive value (PV-) represents the true negatives in control group.

Discriminant analysis is essentially an adaptation of regression analysis and was done using the BMDP statistical software. It provides a means to classify any subject into the group it closely resembled. Discriminant analysis was undertaken to assess the power of individual lipid / lipoproteins parameters and liver enzymes to distinguish alcohol dependents from non-dependents. A stepwise discriminant analysis using Wilk's step-wise procedure with a minimum tolerance of 0.001 and F to enter or remove 4 (indicating that a variable would be entered if the ratio between group variance to within group variance for that variable was >4) was used.

Results

Out of 150 patients, maximum patients were in the age group 41-60 (46.7%), 46% were in age group 25-40, and 7.3% were in age group 60-80. All patients were male and there was no woman. Out of total, 140 patients survived (93.3%) while 10 patients died during hospital stay. Most common diagnosis encountered in study patients was liver cirrhosis (38%) followed by anaemia (9.3%) (**Table - 1**).

Table – 1: Distribution of patients according to final diagnosis.

Final Diagnosis	N	%
Cirrhosis	57	38.0%
Alcoholic Hepatitis	5	3.3%
Acute Pancreatitis	8	5.3%
CVA	10	6.7%
Sepsis	1	0.7%
Hypertension	9	6.0%
Alcohol withdrawal	9	6.0%
Gastritis	9	6.0%
Tuberculosis	4	2.7%
Anaemia	14	9.3%
DM	9	6.0%
OP Poisoning	2	1.3%
Fatty liver	2	1.3%
CKD	6	4.0%
Pneumonia	5	3.3%

Out of 57 patients (38%) were diagnosed with cirrhosis, out of which majority had daily intake of alcohol (n=44), <180 ml/day (n=31), total duration for majority being in the range 6-15 years. Similar scenario was encountered in patients diagnosed with alcoholic hepatitis. Amongst pancreatitis patients (n=08) majority had daily intake of alcohol (n=05), country liquor (n=6) with total duration of intake being 6 to 15 years for majority of them (n=6). Out of 9 patients diagnosed with alcohol withdrawal, majority had daily intake of alcohol (n=7), country liquor (n=9), duration being 6-15 years for most of them (n=5). Out of 14 patients with final diagnosis of anaemia, majority were taking

alcohol < 7 days/week (n=9), < 180 ml/day (n=10), country liquor (n=11) with total duration of intake being 6-15 years for majority (n=7) (**Table - 2a, 2b**).

Decreased haemoglobin was encountered in 85.3% patients (n-128), out of these, decreased MCV was seen in 31 patients (24.2%) while increased MCV was seen in 81 patients (54%). Increased bilirubin in 76 patients (50.67%), increased SGOT in 106 patients (70.67%), increased SGPT in 54 patients (36%), and increased INR in 20 patients. All variables (TC, HDL-c, VLDL-c, TG, LDL/HDL-c, ApoA1, ApoA1/ApoB, AST, ALT, GGT, and ADH) except ApoB and LDL-c were significantly higher (P<0.001) in the alcohol dependents as compared to non-dependent subjects. Sensitivity was highest for LDL-c at 94.6 % at which level the specificity was 46%. TC, VLDL-c, LDL/HDL-c, ApoA1 and ApoA1/ApoB had sensitivity exceeding 80%, whereas the specificity was in the range of 25 to 45.8%. Range of PV (+) and PV (-) was 39.6% to 94.7% and 52% to 73.7% respectively. The diagnostic accuracy varied from 44.4% (ApoB) to 69.4% (TC). Among the liver enzymes, the sensitivity was highest for AST (75.3%) followed by GGT (74.2%) at which level the specificity was 88 and 100% respectively. Sensitivity of ADH and ALT was 61% and 67% whereas specificity was 50% and 76% respectively. PV (+) and PV (-) were in the range of 66% to 100% and 51% to 56% respectively. The diagnostic accuracy of all the four liver enzymes ranged from 56 to 85.3%.

Table - 2a: Association of etiology with frequency, quantity and type of alcohol intake.

Final Diagnosis	Frequency		Quantity			Type of Alcohol		
	<7 days	Daily	<180 ml	180-760 ml	>760 ml	Country	English	Both
Cirrhosis (n-57)	13	44	31	22	4	36	7	14
Alcoholic Hepatitis (n-5)	2	3	3	2	0	4	0	1
Acute Pancreatitis (n-8)	3	5	6	2	0	5	1	2
CVA (n-10)	4	6	4	5	1	5	3	2
Sepsis (n-1)	0	1	0	1	0	0	0	1
Hypertension (n-9)	5	4	7	1	1	4	1	4
Alcohol withdrawal (n-9)	2	7	6	3	0	7	1	1
Gastritis (n-9)	2	7	7	2	0	3	3	3
Tuberculosis (n-4)	0	4	4	0	0	3	1	0
Anaemia (n-14)	9	5	10	4	0	11	1	2
DM (n-9)	4	5	5	3	1	7	1	1
OP Poisoning (n-2)	2	0	2	0	0	0	2	0
Fatty liver (n-2)	0	2	0	2	0	2	0	0
CKD (n-6)	4	2	2	4	0	4	0	2
Pneumonia (n-5)	4	1	3	2	0	2	2	1

Discriminant analysis was carried out separately for the lipid/lipoprotein variables and liver enzymes to assess the proportion of correct classification. Among lipids and apolipoproteins: TC, ApoB and ratio of LDL to HDL-c contributed significantly. When all the three variables (TC, ApoB, and LDL/HDL-c) were subjected together for classification, 84.7% of total subjects were classified into correct groups. Among the liver enzymes, only AST and GGT were able to significantly discriminate alcohol dependents and non-dependents. When both AST

and GGT were subjected together for classification, 89.1% could be classified into correct groups (**Table - 3**).

Discussion

Alcohol use is fairly widespread all over the world. It has been estimated approximately 5% of Indian population (of adult males) fulfils the criteria of alcohol dependence syndrome. Alcohol use predisposes subjects to increased risk of coronary disease and changes in lipid profile are associated with increased coronary risk. In understanding the management of atherosclerosis, there has been an increasing interest in measurement of lipoproteins and lipid moieties. The use of lipids and lipoproteins as diagnostic tests revealed high sensitivity for some of the measures including TC, HDL-c, LDL-c, VLDL-c, HDL-c/TC, and ApoA1/ ApoB, but the corresponding specificity was low. This would enable a high-positive pick-up rate but also a low true-negative rate, which is acceptable if these tests are used for screening.

Table - 2b: Association of etiology with duration of alcohol intake.

Final Diagnosis	Total Duration				
	</= 5 yrs	6-15 yrs	16-25 yrs	26-35 yrs	> 35 yrs
Cirrhosis	0	37	17	3	0
Alcoholic Hepatitis	2	4	2	0	0
Acute Pancreatitis	1	6	1	0	0
CVA	0	3	7	0	0
Sepsis	0	0	1	0	0
Hypertension	2	5	1	1	0
Alcohol withdrawal	1	5	4	0	0
Gastritis	1	4	3	1	0
Tuberculosis	0	2	2	0	0
Anaemia	2	7	3	2	0
DM	0	3	4	1	1
OP Poisoning	1	1	0	0	0
Fatty liver	1	1	0	0	0
CKD	1	2	3	0	0
Pneumonia	2	1	1	1	0

Table – 3: Step-wise discriminant analysis of lipid profile and liver enzymes.

Variable	Controls (n)	Cases (n)
Total Cholesterol	0.069 (66)	0.122 (4)
Apo B	0.128 (19)	0.053 (61)
LDL/ HDL	1.50 (85)	0.633 (85)
AST	0.402 (65)	0.63 (5)
GST	0.014 (15)	0.034 (85)

The complex relation between alcohol use, liver function tests and lipid profile has been documented before. Prabhakaran et al. in a community-based survey on the risk factors for coronary heart disease (CHD) in North Indian male population reported the cut-off levels of

lipids (TC200 mg%; HDL-c40 mg%; TG150 mg%), which are the same as ours [7].

Lower levels of LDL-c and ApoB in alcohol dependents as compared to non-dependents in the present study are similar to those reported earlier [8, 9]. Low or subnormal LDL-c has been a consistent finding in chronic alcoholics. In parallel with LDL-c, the ApoB levels are also reduced in alcohol dependents as compared to non-dependents indicating the direct effect of alcohol on LDL metabolism [9]. High levels of ApoA1 and low levels of ApoB along with significantly raised ratio of ApoA1 to B in our study group suggests that apolipoproteins may be better correlates of cardiovascular risk in alcoholics. This is in complete agreement with our earlier findings [10, 11]. Duhamel et al., while speculating the potential role of alcohol to act as inducer of ApoA1 biosynthesis, suggested that distribution of various apolipoproteins especially ApoA1 remains indeterminate [8].

Serum cholesterol has been widely accepted as a risk factor for ischemic heart disease and its value in prevention has been strongly advocated [11]. On step-wise discriminative analysis, emergence of total cholesterol, as the first variable to discriminate alcohol dependents from non-dependents in the present study shows that influence of alcohol on lipid metabolism opens the possibility that the protective effects of moderate alcohol consumption against development of coronary heart disease are to be attributed to transient changes in the lipid metabolism, and that the benefits in alcohol consumption needs to be weighed carefully against its considerable risk in the Indian population [11]. ApoB emerging as the second variable to discriminate alcoholics and non-alcoholics is in agreement with Durrington et al. who (in a case–control study) found that ApoB is more closely associated with ischemic heart disease than any other lipid or lipoprotein variable [12]. However, the same group of researchers subsequently suggested that much, if not all of the genetic component of cardiac ischemia that is not expressed through ApoB or any of the established risk factors, operates through Apo(A) [11].

The role of lipoproteins and lipid profile in defining the alcoholic status of individual has not been extensively explored. In the present study, discriminant analysis using lipoproteins and lipid measures has been used to provide a way to classify subjects into alcohol dependents and non-dependents. It was found that levels of TC, ApoB, and LDL to HDL-c ratio contributed significantly resulting in correct classification in 84.7% cases [12].

Liver is the prime target organ for alcohol induced diseases. Liver enzymes are also important indicators of liver dysfunction, possibly as markers of alcohol dependence. The critical dose at which adverse effects of alcohol emerge differs in the target organ. Recently Dakeishi, et al. reported that hepatocellular injury, as indicated by elevation of AST could emerge only when the alcohol intake is >50 gm/day [13]. This concurs well with our findings where the mean alcohol consumption was 300 g/day and AST levels were also elevated significantly. The AST appears to be the primary marker of hepatocellular injury because it is more specific than other liver enzymes for detecting alcohol induced diseases. Although some information has been developed about alcohol consumption and AST, the threshold of alcohol associated elevation remains controversial [14, 15]. The GGT is the most sensitive indicator of alcohol dependence/hazardous drinking and is the first enzyme to be elevated. The GGT has also been reported to be more sensitive and is more likely to be elevated in regular than in episodic drinkers [16]. The increase in GGT, AST, ALT levels in the study group is in agreement with earlier reports [11].

On step-wise discriminant analysis, emergence of AST as the first variable in correctly identifying alcohol dependents and non-dependents with good diagnostic accuracy is in agreement with the literature [17]. However,

Sorenson et al. suggested that AST has long-term prognostic value [18]. The GGT levels are elevated in approximately 80% of persons with established alcohol dependence, whereas it is increased in as few as 30% of hazardous drinkers [16]. The GGT emerging as the second variable to discriminate alcoholics and non-alcoholics is in agreement with earlier studies. Elevated GGT levels could be in response to hepatocellular damage due to long-term alcohol consumption, as well as its increased synthesis in the liver [11, 16].

It can thus be extrapolated that individuals can be classified with certainty on measures of TC, ApoB, and LDL/HDL-c (among lipid profile) and AST and GGT (among liver enzymes). Accordingly, the subject may be referred to drug dependence treatment Center for detailed alcohol use-related evaluation.

In the present study maximum patients were in the age group 41-60. This finding was corroborated with that of other such studies [19, 20]. But worrying finding was that 2nd most common age group was younger one i.e. 25-40 years. This probably may indicate increased alcohol consumption by young people owing to changing socio-economic status [21]. In the present study maximum patients had hospital stay < 7 days, which was similar to that of finding of other study [22]. In our study all 150 were male and no female and this finding was in contrast with findings of other studies, which reported more number of female patients [19, 21]. This finding may be due to the fact that in this part of country, alcohol drinking is considered as social stigma.

Most common diagnosis was liver cirrhosis, which was corroborated with findings of other such studies [22, 23]. USG findings of the present study corroborated with findings of other studies with most common finding being shrunken liver (cirrhosis) and fatty liver (hepatomegaly) [24]. Majority of the patients consumed country liquor, which was similar to findings of many studies conducted elsewhere [21, 22]. This may be attributed to the fact that majority of the population in this part of country hails from rural background and of low socio-economic strata.

Decreased hemoglobin was found in 85.33% patients, which was similar to other study findings which reported higher incidence of reduced hemoglobin in their study patients [21]. Cirrhosis, alcoholic hepatitis was more associated with frequency of intake (daily) and type of alcohol (country liquor) and no such correlation was found with quantity of alcohol consumed and total duration of alcohol consumption since maximum patients gave history of quantity as <180 ml/day and total duration of alcohol consumption 6 to 15 years as compared to 180 to 650 ml/day and 16 to 25 years, respectively. But on further analysing duration of alcohol consumption, when <5 years group was compared with 6 to 15 years age group, more patients were in 6 to 15 years group, thus indicating that duration of consumption plays a role in development of cirrhosis. Such finding was encountered in other such study [21]. Amongst Child Pugh score findings maximum patients were in grade B followed by grade C and A. Increasing grades indicate increasing mortality. Grades B and C were associated with increased country liquor consumption, 6 to 15 years duration of consumption of alcohol. Most of the patients fall in severe AUD category followed by moderate and then followed by mild AUD category.

Conclusion

One thing is strikingly clear from the present study that alcoholism is affecting most productive age group in our case 25-40 years, so it is of utmost importance to increase awareness about hazards of alcoholism at hospital level and at public places through media to curb this grave disease. Present study has documented the efficiency of TC, ApoB, and ratio of LDL to HDL-c (amongst lipid variables) and AST, GGT (amongst liver enzymes) in discriminating alcohol dependents from non-dependents. These

findings can be extrapolated to non-specialized settings in identifying alcohol-dependent and non-dependent subjects by using limited number of tests. We thus recommend screening for alcohol use disorder in all adult patients presenting to the hospital as early detection of alcoholic use disorder can decrease both morbidity and mortality associated with it.

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