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Original Article

Psychiatry/Mental Health Section

Psychiatric Comorbidity, Severity of Dependence and Liver Enzymes Dysfunction among Alcohol Dependent Individuals: A Cross-sectional Study from Central Rural India

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ABSTRACT

Introduction: Alcohol Dependence Syndrome (ADS) is a serious health issue all over the world and prominently associated with alcoholic liver disease. Alcohol dependent individuals have high prevalence of psychiatric comorbidities and liver damage among them may further influence associated diagnoses.

Aim: To estimate the prevalence of psychiatric comorbidities among alcohol dependent individuals; to determine association of liver enzymes with psychiatric comorbidities and severity of ADS.

Materials and Methods: A cross-sectional study was conducted on 100 patients of ADS from Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe) Wardha, Maharashtra. They were assessed through semi-structured sociodemographic proforma, Severity of Alcohol Dependence Questionnaire (SADQ), laboratory investigations for hepatic enzymes and Mini International Neuropsychiatric Interview (MINI PLUS). Data were analysed using SPSS 22.0 and considering p-value significant at <0.05.

Results: The prevalence of psychiatric comorbidities among ADS was found to be 49% with Mood disorders (21%) being the most common diagnosis. Prevalence of ADS severity was found to be 10% (mild), 38% (moderate) and 52% (severe) respectively. GGTP (gamma-glutamyl transpeptidase) was significantly associated with psychiatric comorbidities (0.025) while, ALT (0.02), AST (0.023) and GGTP (0.0001) were significantly associated with dependence severity, considering p-value significant at <0.05.

Conclusion: This study suggests that liver enzyme dysfunctions correlated with psychiatric comorbidities and severity of dependence. The liver function profile may alter the mood status of individuals and hence these factors need to be addressed during the management.

Keywords: Alcoholism, Alcohol dependence syndrome, Comorbidity, Hepatic enzymes, Severity

INTRODUCTION

Alcohol abuse/dependence represents a serious health issue. The average alcoholic decreases his or her life span by 10 to 15 years [1,2]. ADS has been associated prominently with liver disease and thyroid dysfunction. Alcoholic liver disease is usually accompanied by hepatitis, cirrhosis and/or hepatocellular cancer [3-5]. The severity of alcohol induced liver damage varied among different individuals and requires one or more additional factors to affect the liver [6]. Alcohol induced liver damage is commonly assessed by the liver enzymes such as ASAT (aspartate-aminotransferase), ALAT (alanine-aminotransferase) and γGT (gamma-glutamyltranspeptidase) [7,8]. Liver cirrhosis and chronic liver disease leads to significant psychological distress on individuals [9,10]. These psychological manifestations are associated with cardiovascular morbidity and autonomic dysregulation [11-13].

Alcohol dependent individuals have high prevalence of psychiatric comorbidity, which is found to be a major contributor to relapse and poses challenges in management [14-16]. Commonly reported comorbidities include unipolar depression, panic disorder, Generalised Anxiety Disorder (GAD), bipolar disorder, Antisocial Personality Disorder (ASPD), Obsessive Compulsive Disorder (OCD), phobia and schizophrenia [17,18]. The number of comorbid diagnosis in a person with ADS may be as high as three [19]. In National Comorbidity Study (NCS), about one third of alcohol dependent respondents had comorbid mood disorder; and prevalence of comorbid major depressive disorder (27.9%) and anxiety disorder (36.9%) were very high [20]. The prevalence of psychiatric comorbidity among ADS was reported to be as high as between 57% and 84% [21-23]. Studies have shown that psychiatric comorbidities are associated with chronic use, treatment resistance, poor compliance and high suicide rates [24,25].

In majority of the alcohol abuse individuals who exhibit the comorbid psychiatric symptoms, symptoms subside after 3-4 weeks of abstinence [26,27]. However, the largely held opinion that liver dysfunction is related to alcohol abuse with psychiatric comorbidity is still controversial and inconclusive. Hence, this study was conducted to estimate prevalence of psychiatric comorbidity among ADS; to find out association between liver dysfunction and psychiatric comorbidities of ADS and to determine association between ADS severity and liver enzymes.

MATERIALS AND METHODS

Study Design, Study Population and Sampling

The observational study was conducted at Department of Psychiatry and De-addiction centre of Acharya Vinoba Bhave Rural Hospital (Jawaharlal Nehru Medical College, DMIMS), Sawangi, in the city of Wardha, Maharashtra over a period of two years (from September 2016 to August 2018). The patients diagnosed with Alcohol dependence syndrome (ADS) as per International Classification of Disease-10th Edition (ICD-10) Diagnostic Criteria for Research (World Health Organisation, 1993) criteria [28], using alcohol for past 12 months, having difficulties in controlling substance taking behaviour, a physiological withdrawal state and evidence of tolerance i.e., increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses; between ages 18 to 65 years; and willing to participate in study were selected through simple random sampling. Those with liver diseases due to illness other than alcoholism, serious physical comorbidities, substance abuse other than alcohol or any other dysfunction interfering with assessment were excluded. The patients were admitted in psychiatric unit and detoxified for alcohol over a period of about two weeks.

The participants were also assessed after detoxification phase at around fourth week of abstinence for psychiatric comorbidities. The approval was taken from Institutional Ethics Committee (DMIMS DU/IEC/2016-2017/3020). The participants were informed about study and written consent was obtained.

Sample Size

The sample size was determined using the standard formula 4 pq/L^2 where p=prevalence of psychiatric morbidities among alcohol dependence individuals, q=100-p and L=allowable error. Considering the 54% of psychiatric morbidities for this research [29], therefore p=54, q=46 and L=20% of p, sample size thus found to be 85. Hence, it was rounded off and subjects' loss to follow-up (10%) when considered, finally sample size of 100 was included.

Instruments

- Semi-structured sociodemographic proforma: The questionnaire includes age, sex, socioeconomic status by Kuppuswamy scale [30], address, occupation, marital status, education status, past history of psychiatric disorder and family history of psychiatric disorder.
- Severity of Alcohol Dependence Questionnaire (SADQ) [31]: The SADQ is a 20-item, self-reported questionnaire designed to measure severity of alcohol dependence syndrome which is self-administered. Items 1 to 16 are scored on a 4-point scale, ranging from "Almost Never" to "Nearly Always," and items 17 to 20 are scored from "Not at all" to "Quite a lot" that lead to a corresponding score of 0 to 3. Thus, the overall score ranges from 0 to 60. The score below 16 suggests mild or none level of alcohol dependence, score 16-30 suggests moderate level of alcohol dependence and score 30+ suggests severe level of alcohol dependence.
- Laboratory investigations for assessment of hepatic enzymes: The levels of ASAT, ALAT, γGT, serum bilirubin and Alkaline phosphatase were measured at the time of detoxification program using diagnostic kits from Olympus diagnostic systems, Hamburg, Germany.
- Mini International Neuropsychiatric Interview (MINI PLUS) [32]: This brief structured diagnostic interview developed by David Sheehan and collaborators aimed at identification of set of DSM IV and ICD-10 mental disorders in multi centre clinical trials and epidemiological studies. It takes approximately 30 minutes to administer. It uses the diagnostic criteria for Axis I and Axis II disorders mentioned in DSM IV and ICD-10. There were two kinds of diagnoses on MINI-PLUS-current and lifetime. The MINI has acceptably high validation and reliability scores and can be administered in short period of time.

STATISTICAL ANALYSIS

The analysis was done by descriptive and inferential statistics. Chi-square test was used to find out association between different variables. Further data were analysed with SPSS version 22.0 and considering p-value <0.05 as significant.

RESULTS

Total 100 patients of Alcohol Dependence Syndrome as per ICD-10 were selected in the present study. There were 99 males and only 1 female with majority of the patients between 26 to 35 years of age (43%) followed by 36 to 45 years (28%), >45 years (19%) and <25 years (10%). There were 81% Hindu, 13% Buddhist and 6% Muslim. Most of the patients were educated upto primary school (50%); employed (75%); and belonged to lower socio-economic status (53%) and nuclear family (53%). Socio-demographic characteristics further reported that majority of them were married (73%) for >10 years (44%) and coming from rural (44%) region. Among study participants 27% and 25% had past and family history of psychiatric disorders, respectively [Table/Fig-1].

Variables	Number (n=100)
Age	
18-25 years	10
26-35 years	43
3) 36-45 years	28
4) >45 years	19
Gender	
Male	99
Female	1
Religion	
Hindu	81
Muslim	6
Buddhist	13
Occupation	
Employed	75
Unemployed	25
Socio-economic status	
Lower	53
Middle	45
Upper	2
Type of family	
Nuclear	53
Extended nuclear	11
Joint	36
Educational status	
Illiterate	1
Primary	50
Secondary	37
Graduate	11
Postgraduate	1
Marital status	
Single	24
Married	73
Divorced	2
Widow	1
Years of marriage	
1-5 years	14
6-10 years	17
>10 years	44
Domicile	
Rural	44
Urban	36
Semi-urban	20
History of psychiatric illness	
Yes	27
No	73
Family History of psychiatric illness	
Yes	25
No	75

[Table/Fig-1]: Socio-demographic characteristics of Alcohol dependent individuals.

The overall prevalence of psychiatric comorbidities as per MINI-PLUS among ADS patients was 49%. Broadly, following diagnostic categories were found: mood disorders-21%, anxiety disorders-13%, adjustment disorders-2%, psychotic disorders-8%, antisocial personality disorder-10% and somatoform disorder-1% [Table/Fig-2].

In the present study, severity of ADS as measured on SADQ revealed 10% mild, 38% moderate and 52% severe levels of

SN	Psychiatric comorbidities (MINI PLUS)	Number (n=100)
1	Major depressive disorder	5
2	Suicidality	4
3	Dysthymia	2
4	MDE with Melancholic features	5
5	Generalised anxiety disorder	4
6	Panic disorder	5
7	Social anxiety disorder	3
8	Obsessive compulsive disorder	1
9	Adjustment disorder	2
10	Schizophrenia	1
11	Substance induced mood disorder	5
12	Substance induced psychotic disorder	4
13	Somatoform disorder	1
14	Delusional disorder	1
15	Antisocial personality disorder	10
16	BPAD I with psychotic features	2

[Table/Fig-2]: Psychiatric comorbidities among ADS.
Mood disorders (Major depressive disorder, Suicidality, Dysthymia, MDE with Melancholic features and Substance induced mood disorder); Anxiety disorders (Generalised anxiety disorder, Panic disorder, Social anxiety disorder, Obsessive compulsive disorder); Adjustment disorders; Psychotic disorders (Schizophrenia, Substance induced psychotic disorder, Delusional disorder, BPAD I with psychotic features)

dependence respectively. While, hepatic enzyme levels at the time of detoxification were found to be higher for ALT (38%), AST (69%), GGTP (79%), Bilirubin (30%) and Alkaline phosphatase (33%), respectively [Table/Fig-3].

Liver Enzymes	Number (n=100)
ALT	
Normal High	62
High	38
AST	
Normal	31
High	69
GGTP	
Normal	21
High	79
BILIRUBIN	
Normal	70
High	30
Alkaline Phosphatase	
Normal	67
High	33

[Table/Fig-3]: Liver enzyme levels among participants.
ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGTP: Gamma glutamyl transferase

The significant difference was reported between GGTP and psychiatric comorbidities among ADS patients ($p<0.05$) whereas, hepatic enzymes such as ALT, AST, Bilirubin and Alkaline phosphatase had no significant difference ($p>0.05$) [Table/Fig-4].

Psychiatric comorbidities	Liver enzymes									
	ALT		AST		GGTP		Bilirubin		Alkaline phos-phatase	
	Nor-mal	High	Nor-mal	High	Nor-mal	High	Nor-mal	High	Nor-mal	High
No comorbidity	34	17	17	34	9	42	35	16	30	21
Major depressive disorder	2	3	0	5	1	4	4	1	4	1
Suicidality	3	1	3	1	3	1	2	2	2	2
Dysthymia	1	1	1	1	1	1	2	0	2	0
MDE with melancholic features	4	1	1	4	0	5	3	2	4	1
Generalised anxiety disorder	2	2	1	3	1	3	3	1	4	0
Panic disorder	2	3	2	3	0	5	5	0	4	1
Social anxiety disorder	1	2	0	3	1	2	1	2	3	0
Obsessive compulsive disorder	1	0	0	1	0	1	1	0	0	1
Adjustment disorder	0	2	0	2	2	0	1	1	2	0
Schizophrenia	1	0	0	1	0	1	1	0	0	1
Substance induced mood disorder	3	2	1	4	0	5	3	2	3	2
Substance induced psychotic disorder	3	1	1	3	0	4	4	0	2	2
Somatoform disorder	0	1	0	1	0	1	1	0	1	0
Delusional disorder	0	1	0	1	1	0	1	0	1	0
Antisocial personality disorder	4	0	2	2	1	3	1	3	3	1
BPAD I with psychotic features	1	1	2	0	1	1	2	0	2	0
Chi-square test	15.53		16.39		28.88		15.01		15.41	
p-value	0.48		0.42		0.025		0.52		0.49	

[Table/Fig-4]: Association of liver enzymes dysfunction with psychiatric comorbidities.

Further the significant difference were found between severity of ADS and hepatic enzymes ALT, AST and GGTP ($p<0.05$) While, Bilirubin and Alkaline phosphatase reported no significant difference ($p>0.05$) [Table/Fig-5].

Liver enzymes	SADQ score			Chi-square test	p-value
	Mild	Moderate	Severe		
ALT					
Normal	9	29	24	12.17	0.002
High	1	9	28		
AST					
Normal	5	15	11	5.14	0.023
High	5	23	41		
GGTP					
Normal	9	6	6	32.13	0.0001, S
High	1	32	46		
BILIRUBIN					
Normal	6	30	34	2.45	0.29
High	4	8	18		
Alkaline Phosphatase					
Normal	9	22	36	3.93	0.13
High	1	16	16		

[Table/Fig-5]: Association of liver enzymes dysfunction with severity of ADS.
ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; GGTP: Gamma glutamyl transferase

DISCUSSION

The present study was a hospital based study and aimed at determining the relationship of liver enzymes with severity of dependence and psychiatric comorbidities among ADS. In the

present study out of 100 patients selected, 99% were males and 1% was female. This may be due the fact that alcohol use by females was socially unacceptable in this region and most of them do not seek treatment openly in the general hospital setting.

The overall prevalence of one or more psychiatric comorbidities among ADS patients on MINI PLUS was found to be 49% and there was more than one psychiatric diagnosis at a time in many patients in this study. This finding is similar to a study by Singh A et al., who reported psychiatric morbidity of 47% among ADS patients [33]. However, some researchers have also reported higher psychiatric morbidities in Alcohol Dependence Syndrome. Vohra AK et al., and Aswal S et al., in their studies reported psychiatric morbidities of 54% and 76.6% in Alcohol dependent patients [15,29]. As per previous literature, the prevalence of psychiatric comorbidity reported to range from 57% to 84% [21-23].

In the present study Mood disorders were found to be the most common psychiatric comorbidities which included Major Depressive Disorder (MDD) (5%), Suicidality (4%), Dysthymia (2%), MDE with Melancholic features (5%), Substance induced mood disorder (5%). Overall 15% had depressive disorders among selected ADS patients which were main Mood disorders. This finding is in accordance with that of Singh A et al., who demonstrated 24% prevalence of Mood disorder with 16% depressive disorders among alcohol dependent patients [33]. Many researchers reported higher prevalence of depression among ADS patients in their literature like Singh HN et al., (26%), Alec R et al., (33%), Cadoret R et al., (39%), Kakunje A (19%) and Shakya DR et al., (18.3%) [14,34-37]. Prevalence of anxiety disorders reported 13% in our study which included Generalised anxiety disorder (4%), Panic disorder (5%), Social anxiety disorder (SAD) (3%), Obsessive compulsive disorder (1%). Previous researchers such as Echeburua E et al., reported 10.1% Panic disorder, 7.6% GAD and 0.6% OCD; Singh HN et al., reported 16% Phobia, 5% Panic disorder, 8% GAD and 2% OCD; Gauba D et al., reported 17.5% Panic disorder, 13.8% GAD, 10% Phobia and 3.8% OCD; while Singh A et al., reported 6% Panic disorder, 3% SAD, 2% GAD, 1% OCD and 2% Mixed anxiety depressive disorder among alcohol dependent subjects in their studies [14,33,38,39].

The present study also reported 8% psychotic disorders which included Schizophrenia (1%), Substance induced psychotic disorder (4%), Delusional disorder (1%), BPAD I with psychotic features (2%) and 10% ASPD. Almost similar finding was mentioned by Singh A et al., in his research [33]. Whereas others such as Singh HN et al., demonstrated 4% Schizophrenia spectrum disorder and 8% Personality disorder; Aswal S et al., reported 2% Schizophrenia and 21% ASPD; Gauba D et al., reported 2.5% Schizophrenia and 15% ASPD in patients of alcohol dependence [14,29,39]. The differences in prevalence of psychiatric comorbidities may be due to factors like the context (whether the study is conducted in inpatients, outpatients or community sample), stage of illness (whether the evaluation was done during active use or remission), the tools used (whether a structured interview schedule was used or not) and differences in sample size [18,33].

Further, our study demonstrated severe level of dependence (52%) in most of the participants whereas; others reported moderate level (77%) and severe level of dependence in majority of alcohol dependent subjects in their respective research [33,40]. Most of the patients had increased serum levels of AST (69%), GGTP (79%) and Alkaline phosphatase (33%) while, serum levels of ALT (62%) and Bilirubin (70%) were normal at the time of detoxification in present study. This finding is confirmed by previous studies which reported elevated levels of ALT, AST and GGTP levels in alcohol dependent individuals upon admission [9,41]. Our results also found significant correlation between SADQ scores and liver enzymes such as ALT, AST and GGTP. Pradeep RJ et al., also reported significant association between total SADQ scores and ALT; and correlation of withdrawal relief drinking sub-score of SADQ with total bilirubin and AST/ALT ratio [42]. This supports the idea that severity of dependence is associated with the liver dysfunction. The above differences in results could be attributed to heterogeneity of the population under study and tools used for measurement.

The significant correlation was obtained between GGTP and psychiatric comorbidities with high levels among MDD, MDE with Melancholic features, Panic disorder and Substance induced mood disorder in present study. It has been found that increased serum levels of hepatic enzymes upon admission were significantly reduced at the end of detoxification phase. In addition the psychological symptoms were found to be improved after detoxification period in alcohol dependent individuals [9]. Liappas IA et al., found statistically significant correlation between ASAT and Hamilton Depression Rating Scale (HDRS) upon admission; ASAT and Hamilton Anxiety Rating Scale (HARS) at the end of detoxification; and γGT levels and HARS at the end of detoxification period. Gauba D et al., also reported significant association between psychiatric morbidity and mean GGTP-value only. This suggests that liver function profile is related to mood status of alcohol dependent patients, in the sense that liver damage is enhanced and mood deteriorates as the alcohol consumption increases [39,43]. It has been hypothesised that co-occurrence of liver cirrhosis may affect the Hypothalamic Pituitary Thyroid axis (HPT) dysfunction in alcohol abuse. Alcohol abuse frequently produces considerable reductions in triiodothyronine (T3) levels and modest decrease in serum thyroxine (T4) levels. Many alcohol abusing individuals have an increased thyroid hormones binding capacity, evidenced by increased thyroxin-binding globulin level and decreased T3 uptake level. Thyroid hormone dysfunctions found to influence mood symptoms of affected individuals. Thyroid abnormalities in alcohol dependent persons can possibly reflect the influence of liver disease [43]. There is a paucity of research on association of liver enzymes with psychiatric comorbidities and dependence severity among alcohol dependent individuals which is addressed in this research.

LIMITATION

The limitations of our study are that it was a hospital based cross-sectional study and only inpatients were included and hence the results cannot be generalised. The sample size was small and other personality disorders were not assessed. These issues need to be addressed in future research with bigger sample size, control groups, inclusion of other laboratory parameters such as T3, fT3, T4, fT4, TSH and more structured interviews.

CONCLUSION

The prevalence of psychiatric comorbidities among ADS was found to be high comparable to previous research. Mood disorders were found to be most common psychiatric diagnosis. The statistically significant association was found between hepatic enzymes and SADQ scores; and between psychiatric morbidities and hepatic enzymes suggesting that liver function profile may alter the mood status of ADS patients. Hence, these factors need to be taken into consideration at the time of managing alcohol dependent persons for relapse prevention, to improve poor compliance, better outcome and policy making in patients suffering from alcoholism.

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