



**ORIGINAL RESEARCH PAPER**

**Psychiatry**

**CORRELATION BETWEEN DEPRESSIVE SYMPTOMS AND GAMMA GLUTAMYL TRANSFERASE IN ALCOHOL DEPENDENCE PATIENTS**

**KEY WORDS:** Depression, Alcohol dependence , GGT , Correlation

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**ABSTRACT**

**Background :** As many as 80% of alcoholic men and women complain of depressive symptoms and at least one third meet the criteria for a major depressive episode. Biological monitoring of alcohol usage is important in evaluation of prevention efforts and alcoholism treatment programs.

**Objectives :** To find correlation between depressive symptoms and GGT levels in Alcohol dependence patients.

**Material and methods :** The study was conducted over a period of seven months between July 2017 to January 2018, among patients fulfilling the inclusion criteria and admitted in the deaddiction ward at a tertiary treatment centre. The study group consisted of persons with alcohol dependence. Two matched control groups were chosen. Blood samples were collected on admission and on the 21<sup>st</sup> day of deaddiction. Psychiatric rating scales like AUDIT, ASI , Clinical Institute Withdrawal Assessment scale-Alcohol (revised), Montgomery-Asberg Depression Rating Scale were administered . Statistical analysis was done using SPSS 11 .

**Results :** Most of the cases, 46.67% were in the 31 to 40 year group. The mean age of cases was 34.7 years. On admission 80% of alcohol dependents had depressive symptoms and it reduced to 36.67% after de-addiction. The mean GGT value for alcohol dependents on day 0 was 52 with S.D. of 24.49. The difference between the cases and control groups was statistically significant. There was positive correlation between MADRS scores and levels of GGT on day 21.

**Conclusion :** Depressive symptoms were present in 90% of alcohol dependents prior to deaddiction and was reduced to 36.67% after abstinence. There was a positive correlation between MADRS scores and levels of GGT on day 21. About 43% of alcohol dependents had increased levels of GGT.

**INTRODUCTION**

As many as 80% of alcoholic men and women complain of depressive symptoms and at least one –third meet the criteria for a major depressive episode. Alcohol confounds the diagnostic picture of depression, interferes with treatment compliance, completion and response to medications or therapy, increases the risk of suicidal or violent behaviors, increases the rate of costly medical and psychiatric health service utilization and is a factor in hospitalization (Liskon B et al, 1982).

Lifetime alcohol abuse or dependence increases the risk of major depression by a factor of approximately 2 to 7. Secondary depression of recent onset was present in 2% -18% of persons meeting criteria for alcohol use disorders. About 42% of alcoholics have clinically significant levels of depression on admission as inpatient for de-addiction compared with only 6% after 4 weeks of completed de-addiction (Brown SA et al, 1988).

**GGT AS A BIOCHEMICAL MARKER OF ALCOHOLISM**

Reliable biological tools for assessing alcoholism and harmful alcohol consumption is an utmost necessity for the success of efforts to prevent and treat alcohol induced damage to both individuals and to society (Anders Helander et al, 1997). Biological monitoring of alcohol usage is also important in evaluation of prevention efforts and alcoholism treatment programmes (Fuller RK et al, 1988).

Providing feedback to patients under treatment based on their biomarker values and changes in them during the course of treatment can enhance motivation, a key component in recovery from alcohol problem (Allen JP et al, 2003).

Traditional alcohol biological markers are of an indirect nature because they suggest heavy alcohol consumption by detecting the toxic effects that alcohol may have on organ systems. Included in this group are the blood-based measures of gamma glutamyl transferase (GGT). Biological methods also overcome the interviewer bias and the recall bias inherent in questionnaires.

Screening tests depend upon honesty and recalling abilities of patients. As a consequence, a need for laboratory markers as objective tests, arise (Mussheff F et al, 1988).

The present study was conducted to find the correlation between depression in persons with alcohol dependence with GGT .

**METHODOLOGY :**

The study was conducted over a period of seven months between July 2017 to January 2018 on every 3<sup>rd</sup> patient fulfilling the inclusion criteria and admitted in the deaddiction ward at a tertiary care centre in Chennai. The institutional ethical committee's approval was obtained before conducting the study.

**STUDY GROUP :**

The study group consisted of persons with alcohol dependence. The inclusion criteria were

- Age 20 to 50 years
- Male gender.
- Patients fulfilling the criteria for alcohol dependence according to ICD-10.
- Patients admitted in the deaddiction ward at IMH.
- Patients who had consumed alcohol within the last 72 hours of initial assessment.

The exclusion criteria were

- Concomitant substance dependence other than alcohol
- Co-morbid medical complication
- Gross cognitive impairment
- Previous history of psychosis
- Presence of psychosis.
- Use of hepatotoxic medication
- Female gender

Two control groups were selected. The first control group consisted of the first or second degree male relatives who do not meet the criteria for alcohol abuse or dependence. The second control group consisted of the non-relatives of the patients who do not meet the criteria for alcohol abuse or dependence. They consisted of parents of mentally retarded children, who attend the Special clinic at the centre . The exclusion criteria for both the above groups were those with major medical illness, history of psychosis, presence of psychosis, gross cognitive impairment and female gender.

The need for including two control groups was to minimize the genetic influence. The cases were selected from 65 patients of alcohol dependence who were screened using Alcohol Use

Disorder Identification Test (AUDIT) questionnaires and meeting the criteria for alcohol dependence according to ICD-10. Among the 65 patients, 10 patients did not have first or second degree male relatives who were willing to participate in the study. Another 8 patients were on medication for co-morbid medical illness. About 7 patients were not willing to participate in the study and about 5 patients dropped out of the study. Two patients were diagnosed to have psychosis and were excluded from the study. Three patients had co-morbid substance abuse and were not included in the study. The remaining 30 patients constituted the study group. The diagnosis was confirmed by two consultants.

Blood samples were collected on admission observing all aseptic precautions and on the 21<sup>st</sup> day of deaddiction. 5 ml of venous blood was collected and transferred immediately to a sterile container to which anticoagulant has been added. The laboratory facilities at the tertiary care centre were utilized for the study.

The measurement of serum GGT were done using semi-autoanalyser with commercially available reagent kits. Gamma glutamyl transferase was determined using Kinetic (Szasz) method. The normal values are 7-34 U/L.

The following tests were carried out to the controls only once. The case were assessed twice, once on admission day and then on day 21 of de-addiction treatment.

**INSTRUMENTS USED**

1. Proforma for sociodemographic data
  2. Alcohol Use Disorders Identification test (AUDIT)
  3. Addition Severity Index (ASI)
  4. Clinical Institute Withdrawal Assessment scale-Alcohol (revised) CIWA-Ar.
  5. Montgomery-Asberg Depression Rating Scale (MADRS)
- Socio- demographic information like education, occupation, mode of income, marital status, type of family and religion were collected in the proforma for socio-demographic data sheet for both cases and controls.

**AUDIT :**

AUDIT questionnaire has ten questions which objectively measures the alcohol use behavior in a 0 to 4 scale with a total score of 40. The individuals scoring more than 8 were included in the study.

**Addiction Severity Index (ASI) :**

The ASI serves as a qualitative measure of symptoms and functional impairment due to alcohol or drug disorder. It covers demographics, alcohol use, drug use, psychiatric status, medical status, employment, legal status, and family and social issues. It has 142 items in varying formats. Very good to excellent reliability has been demonstrated for the overall composite score, with somewhat lower reliability for severity ratings in each area. Validity has also been demonstrated based on correlation with other measures and discrimination of patient from non patient populations. ASI was administered to cases on admission (day 0) and once to controls.

**Montgomery Asberg Depression Rating Scale (MADRS)**

The MADRS developed by SA.Montgomery and M. Asberg is a rating scale for the assessment of depression. The MADRS focuses on symptoms such as sadness, tension, lassitude, pessimistic thoughts and suicidal thoughts.

**Clinical Institute Withdrawal Assessment Scale for Alcohol-revised version (CIWA-Ar)**

The CIWA-Ar is a 10-item scale which can be completed in 5 minutes. The CIWA-Ar can be used as a baseline against which withdrawal severity can be measured over time. CIWA - Ar was administered to the cases on day 0 (day of admission) and day 21 (day of discharge).

The subjects and informants were independently interviewed and the control groups were matched for age, marital status and social status.

**STATISTICAL ANALYSIS :**

1. Data analysis was done using 'SPSS-11' statistical software. Methods used were Student t test , Chi-square test, Other statistical methods whenever needed

**RESULTS :**

Table 1 describes the distribution of cases and controls among various age groups. Most of the cases, 46.67% were in the 31 to 40 year group. In the control group- relatives 40% were in the 41-50 group. The control group non-relatives 43.33% were in the 31-40 group. There was no significant statistical difference in the distribution of age among the three groups. The mean age of cases was 34.7 years, that of relatives was 35.43 years and non-relatives was 35.76 years. There was no significant statistical difference in the mean age among the three groups.

**Table 1: Comparison of age distribution in cases and controls.**

Age group	Groups				Chi-square	p-value
	Alcohol Dependents	Relatives	Non relatives	Total		
	n(%)	n(%)	n(%)	n	3.137	0.535
20-30	8 (26.67)	10(33.3)	9(30.0)	27		
31-40	14 (46.67)	8(26.67)	13(43.33)	35		
41-50	5(26.67)	12(40.0)	8(26.67)	28		

In all three groups, the majority have been educated upto secondary school or less. No significant statistical difference was found between the groups. Most of the cases (46.67%) were skilled workers. The control group of relatives had 56.67% unskilled workers while control group of non-relatives had 43.33% skilled workers. The differences were not statistically significant. The marital status of the three groups were analysed. The married group constitutes the largest one among all the three groups. Among cases 20% were separated. There was no significant statistical difference between the three groups.

**Table 2 : Comparison of composite score of ASI for individual domains in cases and control group**

Domains of ASI	Alcohol Dependents		Relatives		Non-relatives		F value	p value
	Mean	S.D.	Mean	S.D.	Mean	S.D.		
CSM	.20	.13	.18	.12	.16	.17	.685	.507
CSI	.40	.13	.24	.11	.16	.12	35.993	.00
CSE	.33	.19	1.9	.42	2.03	.52	329.462	.00
CSL	.00	.00	.00	.00	.00	.00	.00	.00
CSP	.57	.20	.10	.17	.06	.18	72.598	.00
CSDA	3.3	.91	.04	.08	.07	.13	375.003	.00

- CSM -composite score for medical status
- CSF -composite score for employment status
- CSF -composite score for family/social status
- CSL -composite score for legal status.
- CSP -composite score for psychiatric status
- CSDA -composite score for drug and alcohol status

The composite score was calculated for each domain in the ASI using the prescribed formula and compared between the two groups. Significant difference was found in all domains except medical. As the logarithm of value (=infinity) was interfered more frequently while calculating composite score for legal status, the mean of which became zero, the significance for legal status had to be omitted.

**Table 3 : Comparison of MADRS scores of alcohol dependence on Day 0 and Day 21**

MADRS Scores	Mean	S.D.	Paired 't' test	p value
Day 0	22.63	9.20	7.52	<0.001
Day 21	6.63	7.05		

Table 3 shows the mean MADRS scores of alcohol dependents on day 0 (day of admission) and day 21 (day of discharge). The mean MADRS score on day 0 was 22.63 with S.D. of 9.20. The mean

score on day 21 was 6.63 with S.D. of 7.05. This was statistically significant. On admission 80% of alcohol dependence had depressive symptoms and it reduced to 36.67% after deaddiction.

**Table 4 : Comparison of MADRS scores on day 21 among alcohol dependents and day 0 among controls.**

Groups	MADRS mean	S.D.	ANOVA F value	P value
Alcohol dependents	6.63	7.05	5.9	0.004
Relatives	3.70	3.73		
Non-relatives	2.37	2.81		

Table 4 compares the MADRS scores of cases and controls. The mean MADRS score of alcohol dependents is 6.63 and S.D. of 7.05. The mean score of controls-relatives is 3.70 with S.D. of 3.73. The mean score of controls non-relatives is 2.37 and S.D. 2.81. The difference between control groups is not statistically significant while the difference between cases and control groups is statistically significant.

**Table 5 : Comparison of CIWA-Ar scores of alcohol dependents on day 0 and day 21**

CIWA-Ar Scores	Mean	S.D.	Paired t test	p value
Day 0	5.77	3.72	8.70	<0.001
Day 21	1.00	1.53		

The table 5 compares the CIWA-Ar scores on alcohol dependents on day 0 and day 21. The mean score was 5.77 with S.D. of 3.72. On day 21, the mean was 1.00 with S.D. of 1.53 on day 21. The values were statistically significant.

**Table 6: Comparison of GGT values of all three groups**

Groups	Mean	S.D.	t value	p value
Alcohol dependents	52	24.49	117.1881	<0.001
Relatives	3.30	1.68		
Non-relatives	3.37	1.90		

Table 6 compares the GGT value of all three groups. The mean GGT value for alcohol dependents on day 0 was 52 with S.D. of 24.49. the mean GGT value of relatives was 3.30 with S.D. of 1.68. The mean GGT value of non-relatives was 3.37 with S.D. of 1.90. The difference is statistically significant. About 43% of alcohol dependents have increased GGT values.

**Table 7 : Correlation between MADRS scores and GGT values of Alcohol dependents**

	GGT (Day 0)	GGT (Day 21)
MADRS(Day 0)	0.064 (Pearson's correlation)	0.738 (Pearson's correlation)
MADRS(Day21)	0.058 Sig.(2tailed)	0.760 Sig.(2tailed)

Table 7 shows the correlation between MADRS scores and GGT values of alcohol dependent patients. Correlation was tested using Pearson's correlation and 2-tailed test. There was positive correlation between MADRS scores and levels of GGT on day 21.

**DISCUSSION :**

This study was done primarily to correlate the depressive symptoms of alcohol dependent persons with levels of gamma glutamyl transference, the biological marker of alcohol.

In the present study, persons suffering from alcohol dependence did not differ in the socio demographic profiles from the two control groups. Also, 90% of alcohol dependents have depressive symptoms. Even after three weeks of abstinence 36.67 % continued to have depressive symptoms. The mean MADRS score on day 21 was 6.63 with S.D. of 7.05 among cases. This was a statistically significant finding. In spite of the fact that, in some persons, antidepressants would have been administered during deaddiction treatment.

These findings were higher than that of Weissman et al (1980) who reported that depressive symptoms were present in 59% of alcoholics in a study done on 61 alcoholics.

Brown SA et al (1988) used DSM III diagnostic criteria and reported that 42% of 191 alcoholics had depressive symptoms.

Herz et al (1990) reported depressive symptoms in only 16% of the alcoholics according to DSM III.

The differences may be due to various diagnostic approaches, differences in the samples or the willingness of the individuals for deaddiction treatment.

After 3 weeks of abstinence, 36.37% had depressive symptoms. This was in agreement with Brown et al (1995) who reported that three weeks of abstinence from alcohol was necessary for remission of depressive symptoms in 54 male alcohol dependents. 42% had depressive symptoms at intake but only 6% remain clinically depressed of week 4. Davidson KM (1995) reported diagnosis of major depression in 66% of inpatient alcoholics.

In a study conducted by Martin et al (2001) on 133 alcohol dependent men 15% has depressive symptoms.

This is in agreement with Schuckit MA et al (1997) who asserted that in the majority of cases, the depressive symptoms remit within four weeks of abstinence.

**Gamma Glutamyl Transferase in alcohol dependents :**

In the present study, GGT, values of all the three groups were compared. About 43% of alcohol dependents had increased GGT. There was a significant difference in the GGT values of cases and controls. This was similar to the findings of Johanna Hietala et al (2005) who showed that GGT values in heavy drinkers with >40 grams of alcohol per day was significantly higher than moderate drinkers and abstainers. Also L.Papoz et al (1982) found significant correlation between daily alcohol intake and GGT and MCV values.

Furthermore, Klopocka (2007) reported that liver function tests were determined by gastric PH, H. Pylori infection, smoking besides the hepatotoxic effect of alcohol drinking.

In the present study, higher depression in alcohol dependents were present with high levels of GGT at the start of deaddiction. After three weeks of deaddiction there was a significant lowering of depression and anxiety symptoms and also lowering of GGT levels.

This was in agreement with the study of Ioannis A. Liappas et al (2006) who reported improved depression and anxiety profile in 100 alcohol dependents after four weeks of deaddiction which was accompanied by markedly reduced hepatic enzyme levels to almost normal levels. Furthermore, the statistical correlation between enzyme levels and psychopathology suggests that liver function profile is related to mood status of alcohol dependent individuals, in the sense that as the consumption of alcohol increases, liver damage is enhanced and the mood of the individual deteriorates.

The findings of this study are clinically more relevant as earlier treatment could prevent and lower the psychopathology associated with alcohol dependence like depression.

**CONCLUSIONS :**

The present study assessed the depressive symptoms of 30 persons with alcohol dependence and also measured their levels of G.G.T and compared the results with suitably matched controls taken from the relatives of the above patients as well as non relatives.

Depressive symptoms were present in 90% of alcohol dependents prior to deaddiction and was reduced to 36.67% after abstinence. This was statistically significant.

Depressive symptoms were more in alcohol dependents compared to controls even after three weeks of abstinence. There was a

positive correlation between MADRS scores and levels of GGT on day 21.

Patients of alcohol dependence had more rates of family history of alcohol dependence than non-alcohol dependent individuals. This difference was statistically significant.

About 43% of alcohol dependents had increased levels of GGT.

#### LIMITATIONS OF THE STUDY

1. Factors which may influence the levels of GGT like smoking and body weight were not included as variables.
2. The use of antidepressants and anxiolytics may have influenced the remission rates.
3. The study was hospital based and its findings could not be generalized to the population.
4. The female gender was not included in the study.
5. The results of other liver function tests which may have detected alcoholic liver disease were not included in the study.

#### RECOMMENDATIONS

1. Biological markers of alcoholism in female population could be investigated.
2. The role of newer biological markers of alcoholism like carbohydrate deficit transferin (CDT) could be investigated in our population.

**Conflict of interest:** nil

**Funding:** Nil

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