PROSPECTIVE OBSERVATIONAL STUDY OF THE INCIDENCE OF ALCOHOLIC WITHDRAWAL SYNDROME AND THE ROLE OF THIAMINE IN CHRONIC ALCOHOLICS WITH BURN INJURIES

Challuri Anita[1], Avula Krishnaveni[2], Pokkula Ramesh[3], Deepthi Adusumelli[4], Rajit Pokkula[5], Arige Subodh Kumar[6], Erugurala Mahendar[7], Sura Anitha[8]

[1]Associate Professor, Department of Biochemistry, Osmania Medical College, Hyderabad, Telangana, India.
[2]Associate Professor, Department of Obstetrics and Gynaecology, Gandhi Medical College, Secunderabad, Telangana, India.
[3]Associate Professor, Department of Plastic Surgery, Gandhi Medical College, Secunderabad, Telangana, India.
[4]Consultant Plastic Surgeon, Department of Plastic Surgery, Aakar Asha Hospital Hyderabad, Telangana, India.
[5]Medical Student, Telangana.
[6]Professor, Department of Plastic Surgery, Gandhi Medical College, Secunderabad, Telangana, India.
[7]Assistant Professor, Department of Plastic Surgery, Gandhi Medical College, Secunderabad, Telangana, India.
[8]Assistant Professor, Department of Plastic Surgery, Gandhi Medical College, Secunderabad, Telangana, India.

ABSTRACT

BACKGROUND

Chronic alcoholics getting admitted with burn injuries is common. Thiamine is administered in them along with antipsychotics when they develop AWS.

The objectives of this study were- 1. to determine the incidence of "AWS" in chronic alcoholics with burn injuries, and 2. to determine the role of thiamine.

MATERIALS & METHODS

This observational prospective study was done in 62 chronic alcoholic patients with burn injuries in the Department of Plastic surgery, in Gandhi hospital during January 2015 and December 2016. Sample size was taken for convenience.

RESULTS

Amongst the admitted patients, 90.32% were male and 9.67% were female. The mean age of the patients was 43.22 years. The SD was 10.74. 50% of them were laborers. 40.32 % developed "AWS". 32.25% of them were in Group I and 48.38% in Group II. GGT, AST, ALT were elevated and AST: ALT ratio was more than 1 in 51.61% of alcoholics. "AWS", lasted 4.2 days in Group I and 7.14 days in Group II patients; the AST: ALT ratio was greater than one in 60 % and GGT was elevated in 56% in those who developed AWS.

CONCLUSION

AWS was common, the incidence was higher, and recovery was delayed in those who did not receive Thiamine. Though all the liver enzymes were found to be elevated, GGT was elevated the most.

KEY WORDS

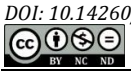
Thiamine, GGT (Gamma Glutamyl Transferase), AST (Aspartate Amino Transferase), ALT (Alanine Amino Transferase), Alcohol Withdrawal Syndrome (AWS), Chronic Alcoholism

HOW TO CITE THIS ARTICLE: Anita C, Krishnaveni A, Ramesh P, et al. Prospective observational study of the incidence of alcoholic withdrawal syndrome and the role of thiamine in chronic alcoholics with burn injuries. J. Evolution Med. Dent. Sci. 2019;8(08):506-511, DOI: 10.14260/jemds/2019/112

BACKGROUND

Most of the burns patients who were admitted were known chronic alcoholics. Development of "alcohol withdrawal symptoms" during their in-patient stay has been observed frequently. "Alcohol withdrawal syndrome" is a set of symptoms that can occur when an individual reduces or stops alcoholic consumption after long periods of use. The withdrawal syndrome is largely a hyperexcitable response of the central nervous system due to lack of alcohol.

'Financial or Other Competing Interest': None.
Submission 08-12-2018, Peer Review 09-02-2019,
Acceptance 15-02-2019, Published 25-02-2019.
Corresponding Author:
Dr. Avula Krishnaveni,
13-6-457/29,
Gayatrinagar, Shivbagh,
Gudimalkar, Hyderabad-500067,
Telangana, India.
E-mail: akveni1010@gmail.com
DOI: 10.14260/jemds/2019/112



Symptoms typical of withdrawal include agitation, seizures and delirium tremens. About 50% of people with alcoholism will develop withdrawal symptoms upon reducing their use. Withdrawal usually begins 6 – 24 hours after the last alcohol intake. It can last for up to one week amongst the chronic alcoholics admitted with burns. Of these, about 3-5% develop "Delirium tremens" or have seizures". It is necessary to identify them and start treatment early. We start Thiamine as early as possible in these patients.[1,2,3] Thiamine (Vitamin B1) is a water-soluble vitamin that is involved in the metabolism of glucose and lipids as well as in the production of glucose-derived neurotransmitters.[4,5] Its deficiency leads to a variety of neurological and cardiovascular symptoms and signs. Early symptoms may include fatigue, weakness and emotional disturbance, whereas prolonged gradual deficiency may lead to a form of polyneuritis (Known as dry beriberi), cardiac failure or peripheral oedema (Wet beriberi).[6]

Severe thiamine deficiency (TD) may result in the development of Wernicke's encephalopathy (WE). The classical signs of Wernicke's encephalopathy are ocular

motility disorders (Nystagmus, Ophthalmoplegia), ataxia and mental changes (Confusion, drowsiness, obtundation, clouding of consciousness, pre-coma and coma), although minor episodes of 'subclinical' encephalopathies are frequent.[7] An appropriate treatment may correct most of these abnormalities; in contrast, the lack of a diagnosis of "WE" may result in serious consequences like mortality which has been reported in 20% and Korsakoff's psychosis (KP) developed in 85% of survivors.[8,9]

Blood levels of the liver enzyme gamma-glutamyl transferase (GGT) is used as a biomarker for heavy drinking. GGT is implicated in alcohol use by keeping intracellular glutathione, the body's most abundant anti-oxidant, at adequate levels to protect cells from oxidative stress resulting during metabolism (e.g. that of alcohol).[10,11]

The association of alcohol use and GGT levels at the population level may then not necessarily reflect a causal effect of alcohol use on GGT, but additionally effects on genes on alcohol use that are shared with those on GGT[12] (genetic pleiotropy; genes influencing multiple traits). GGTis clinically important because of its sensitivity to detect alcohol abuse. GGT is increased in alcoholics even when other liver function tests are within normal limits.[13]

AST rise more than ALT and their ratio being more than one as a good indicator of alcoholism too has been reported.[14,15,16]

Aims and Objectives

1. To determine the incidence of "AWS" in chronic alcoholics with burn injuries, and
2. To determine the role of thiamine.

MATERIALS AND METHODS

This prospective observational study was done in 62 alcoholic patients who sustained burn injuries and were admitted in the Burns ward in the department of plastic surgery, in Gandhi hospital during January 2015 and December 2016. The sample size was limited, and it was decided on convenience. Individuals with history of alcohol intake of more than 80 g of alcohol per day, (120 ml whisky or equivalent) and at risk of developing alcoholic liver disease, were included in the study. Patients were observed for the development of "Alcohol withdrawal symptoms" as they were on alcohol abstinence and they were likely from second or third day of abstinence of alcohol[17]. Patients included in the study were tested for AST, ALT and, GGT levels by testing a blood sample at the time of admission. Incidence, age, gender and occupation too were analysed. It is necessary to identify them and start treatment early. Knowing the importance of Thiamine, we start the drug as early as possible in these patients.[1,2,3] Thiamine (Vitamin B1) is a water-soluble vitamin that is involved in the metabolism of glucose and lipids as well as in the production of glucose-derived neurotransmitters.[4,5] Its deficiency leads to a variety of neurological and cardiovascular symptoms and signs Thiamine was administered based on convenience, as there used to be short supply of it on occasions in the tertiary public sector hospital. Patients were monitored for any symptoms of "Alcohol withdrawal syndrome", and Psychiatric consultation was called for, when the patient developed them, and they were started on Benzodiazepines and Multivitamin supplementation as advised. Patients were monitored for the recovery from Alcohol withdrawal syndrome. Sample size taken for convenience.

Exclusion Criteria

Patients less than 20 years and more than 70 years. Patients with less than 20% burns and more than 60% burns. All electrical and chemical burns. Patients who expired in the middle of the study.

Patients were observed for the development of "Alcohol withdrawal symptoms" as they were on alcohol abstinence and they were likely from second or third day of abstinence of alcohol.[5]

On development of symptom of "Alcohol withdrawal syndrome", Psychiatric consultation was called for, and they were started on Benzodiazepines and Multivitamin supplementation as advised.

Patients were monitored for the recovery from Alcohol withdrawal syndrome.

Statistical Analysis

The data was collected and analysed using standard statistical chi – square test, student t test was used for statistical analysis. $P < 0.001$ – statistically significant. Data was entered in Microsoft excel and analysis was done using SPSS version 22.

RESULTS

Of the total number of patients 56 (90.32%) were male and 6 (9.67%) were female. The mean age of the chronic alcoholics was 43.22 years. The SD was 10.74. Those between 31-50 years of age, constituted the most amounting to 39/62 (62.9%). The mean age of those who developed "Alcohol withdrawal syndrome", was 42.56. The SD was 8.86. Alcohol withdrawal symptoms were most commonly found in the age group 41-50 with 11 (44 %) patients followed by the age group of 31-40 with 8 (32 %). (Table 1).

Laborers amounted to 31 (50 %) patients and were the most common with regard to occupation. (Table 2).

Of the 62 chronic alcoholic patients, 25 (40.32 %) developed alcohol withdrawal symptoms. The chi-square statistic was 1.5549. The p-value was 0.21242. This result is not significant at $p < .01$. The chi-square statistic with Yates correction was 1.1904. The p-value was 0.275241. Not significant at $p < .01$.

It was seen in 10/31 (32.25%) Group I. The same was seen in 15/ 31 (48.38%) amongst Group II patients.

The chi-square statistic was 0.715. The p-value is 0.397787. This result was not significant at $p < .01$. The chi-square statistic with Yates correction was 0.37. The p-value was 0.543007. Not significant at $p < .01$.

The pattern of elevation of the liver enzymes is mentioned below. GGT was elevated in 26/62 patients with chronic alcoholism (41.93 %), Elevation of GGT amongst those who developed 'Alcohol Withdrawal syndrome" was seen in 14 out 25 patients (56%). (Table 3). AST was elevated in 24/ 62 (38.70 %) and ALT in 21/ 62 (33.87 %). AST: ALT ratio of more than one was seen in 32 out of 62 chronic alcoholic patients (51.61%). AST: ALT ratio of more than one was seen in 15 out of 25 patients who developed alcoholic withdrawal symptoms (60 %). (Table 4). Symptoms of alcohol withdrawal lasted 4.2 days in Group I, and 7.14 days in group II patients. The chi-square statistic was 0.6961. The p-value was 0.404107. This result was not significant at $p < .05$. The chi-square statistic with Yates correction was 0.2569. The p-value was 0.61225. Not significant at $p < .05$.

Sl. No.	Incidence of AWS	Number of Patients & %
1	Alcoholics Without AWS	37 (59.70%)
2	Alcoholics Who Developed AWS	25 (40.32%)
Total		**62 (100%)**

Table 1. Showing the Incidence of The Alcohol Withdrawal Syndrome

Sl. No.	AST: ALT Ratio	Chronic Alcoholic Patients	Alcohol Withdrawal Syndrome
1	AST:ALT ratio > 1	32 (51.61%)	15(60%)
2	AST:ALT ratio < 1	30 (48.38%)	10 (40%)
Total		**62 (100%)**	**25 (100%)**

Table 2. Showing AST:ALT Ratio in Chronic Alcoholic Patients and In Those with Alcohol Withdrawal Syndrome

. P < 0.001

Sl. No.	Occupation	Number of Patients & Percentage
1	Labourer	31 (50%)
2	Agriculture	15 (24.19%)
3	Small Business	9 (14.51%)
4	Works in Office	7 (11.29%)
Total		62 (100%)

Table 3. Showing Occupations of Chronic Alcoholic Patients

Sl. No.	Group	No. of Days	SD
1	Group I	4.2 days	8
2	Group II	7.14 days	10
Total			

Table 4. Showing Recovery Period from The Symptoms of Alcohol Withdrawal Syndrome

P < 0.001

Sl. No.	Occupation	No. of Patients	Percentage
1	Labourer	31	50
2	Agriculture	15	24.19
3	Small Business	9	14.51
4	Works in Office	7	11.29
Total		62	100

Table 5. Showing the Occupation of The Admitted Chronic Alcoholic Patients

Sl. No.	AST: ALT Ratio	Alcoholic Patients	Alcohol Withdrawal Patients	'P' value
1	AST:ALT ratio > 1	32 (51.61 %)	15 (60 %)	The chi-square statistic is 0.5046. The p-value is 0.477501. This result is not significant at p <0.05. The chi-square statistic with Yates correction is 0.2234. The p-value is 0.63647. Not significant at p <0.05.
2	AST:ALT ratio < 1	30 (48.38 %)	10 (40 %)	
Total		**62 (100 %)**	**25 (100 %)**	

Table 6. Showing AST:ALT Ratio in Chronic Alcoholic Patients and In Those with Alcohol Withdrawal Syndrome

. P < 0.001

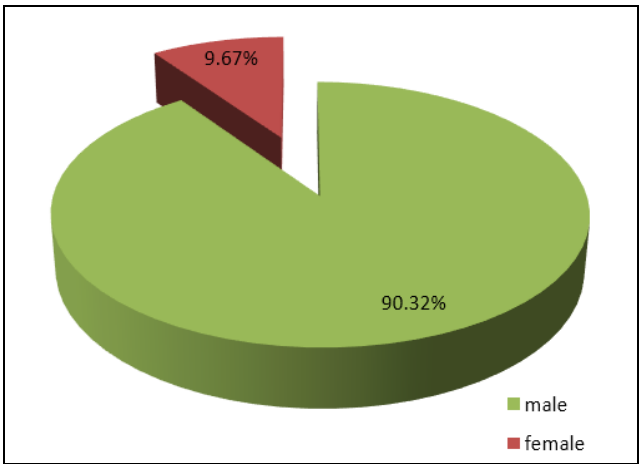


Chart 1. Showing Gender Incidence

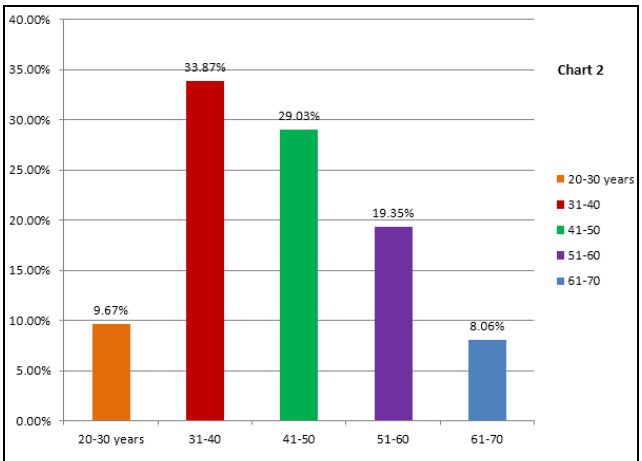


Chart 2. Showing Age Group Incidence

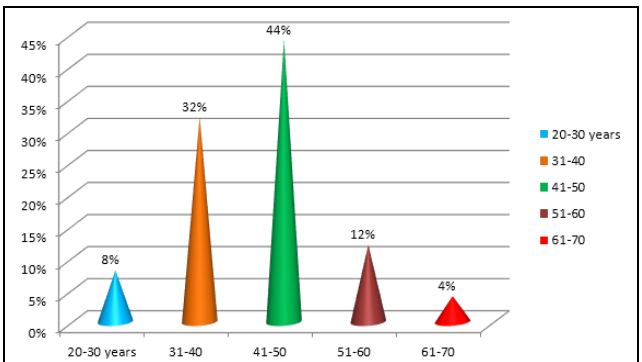


Chart 3. Showing Incidence of Alcohol Withdrawal in Different Age Groups

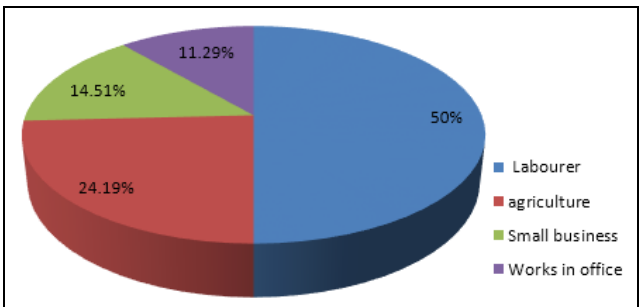


Chart 4. Showing Occupation of Alcohol Patients

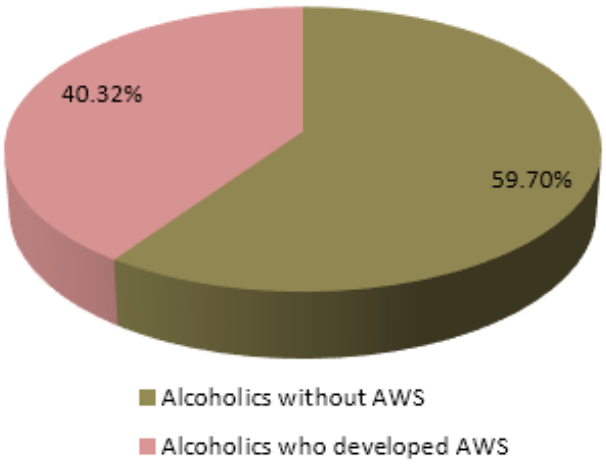


Chart 5. Showing Incidence of Alcohol Withdrawal Symptoms

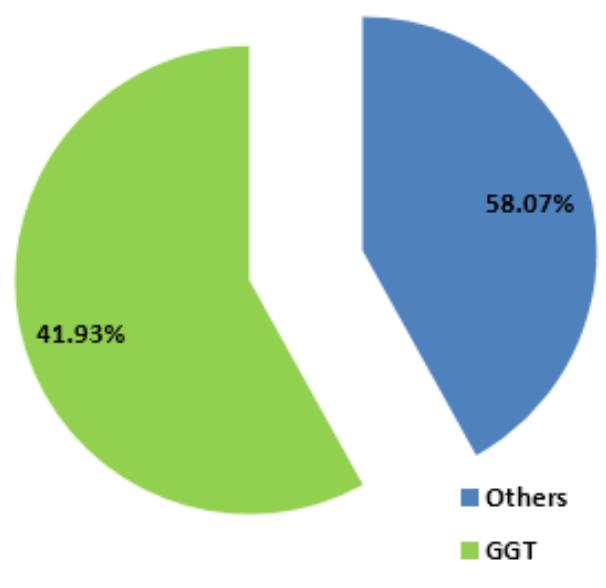


Chart 6. Showing Elevation of GGT Levels in Alcoholic Patients

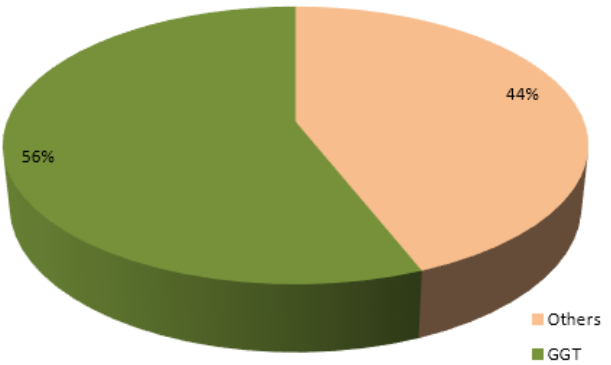


Chart 7. Showing Elevation of GGT Levels in Alcohol Withdrawal Patients

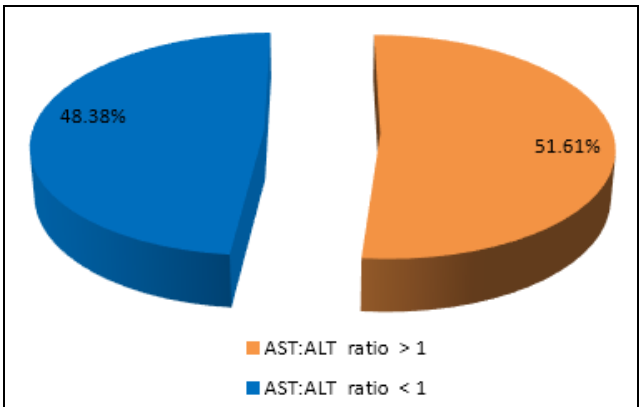


Chart 8. Showing AST: ALT Ratio in Alcoholic Patients

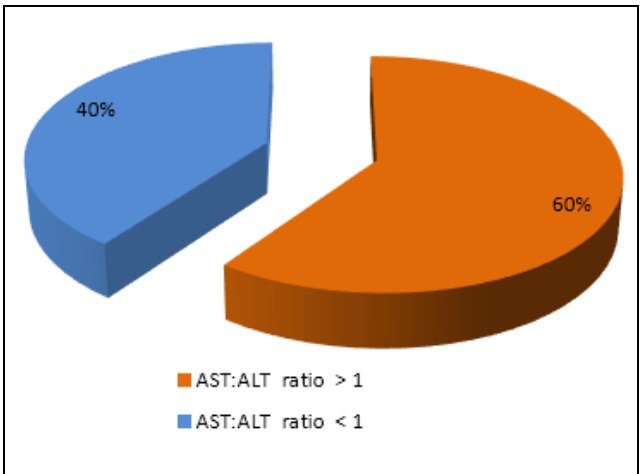


Chart 9. Showing AST: ALT Ratio in Alcohol Withdrawal Patients

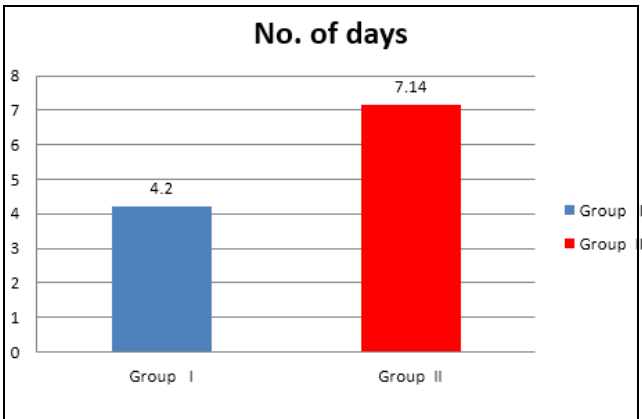


Chart 10. Showing Recovery Period of Alcohol Withdrawal Symptoms

DISCUSSION

This study tried to observe the age, sex incidence of chronic alcoholism, the incidence of development of alcohol withdrawal symptoms, the occupation they were into, the pattern of rise of liver enzymes, their ratios, the outcome of development of alcohol withdrawal syndrome amongst those patients, and the effect of Thiamine in these patients.

Amongst those admitted with burn injuries, those who are chronic alcoholics are common in our set up. On investigations done in these patients, liver enzymes were found to be raised. Development of Alcohol withdrawal symptoms, amongst these patients is a frequent observation,

needing Psychiatry consultation and putting them on Thiamine and Antipsychotics is required.

Symptoms typical of withdrawal include agitation, seizures and delirium tremens.

About 50% of people with alcoholism will develop withdrawal symptoms upon reducing their use. Withdrawal usually begins 6 – 24 hours after the last alcohol intake. It can last for up to one week amongst the chronic alcoholics admitted with burns. Of these, about 3-5% develop "Delirium tremens" or have seizures". It is necessary to identify them and start treatment early. We start Thiamine as early as possible in these patients.[6,7,8] Thiamine (Vitamin B1) is a water-soluble vitamin that is involved in the metabolism of glucose and lipids as well as in the production of glucose-derived neurotransmitters.[9,10] Its deficiency leads to a variety of neurological and cardiovascular symptoms and signs. Early symptoms may include fatigue, weakness and emotional disturbance, whereas prolonged gradual deficiency may lead to a form of polyneuritis (Known as dry beriberi), cardiac failure or peripheral oedema (Wet beriberi).[11]

Severe thiamine deficiency (TD) may result in the development of Wernicke's encephalopathy (WE). The classical signs of Wernicke's encephalopathy are ocular motility disorders (Nystagmus, ophthalmoplegia), ataxia and mental changes (Confusion, drowsiness, obtundation, clouding of consciousness, pre-coma and coma), although minor episodes of 'subclinical' encephalopathies are frequent.[12] An appropriate treatment may correct most of these abnormalities; in contrast, the lack of a diagnosis of "WE" may result in serious consequences like mortality which has been reported in 20% and Korsakoff's psychosis (KP) developed in 85% of survivors.[13,14]

Blood levels of the liver enzyme gamma-glutamyl transferase (GGT) is used as a biomarker for heavy drinking**.** GGT is implicated in alcohol use by keeping intracellular glutathione, the body's most abundant anti-oxidant, at adequate levels to protect cells from oxidative stress resulting during metabolism (e.g. that of alcohol).[15,16]

The association of alcohol use and GGT levels at the population level may then not necessarily reflect a causal effect of alcohol use on GGT, but additionally effects on genes on alcohol use that are shared with those on GGT[17] (Genetic pleiotropy; genes influencing multiple traits).

Although in isolation ALT is not particularly useful as a marker of chronic alcohol abuse or of chronic liver disease, the ratio AST/ALT seems to provide meaningful information[18, 19, 20]. Usually a cut-off value of the ratio > 2 is assumed to reflect an alcoholic aetiology of the liver disease.

Out of 62 Chronic alcoholic admitted patients, labourers amounted the most, the fourth decade men were predominantly affected. 40% developed the withdrawal symptoms. The incidence of withdrawal was higher amongst those who did not receive Thiamine. AST, ALT and GGT were all elevated but that of GGT was more notable and especially amongst those who developed the withdrawal symptoms. The ratio of AST to ALT too was above one in these patients. The symptoms subsided earlier in those who received Thiamine.

The chi-square statistic was 0.0425. The p-value was 0.836664. This result was not significant at $p < 0.01$. A larger comparative study is needed to study the statistical significance.

CONCLUSION

Alcohol withdrawal was predominantly seen more frequently in males of the third and fourth decades who were alcoholics, and the symptoms were seen on the higher side in those who did not receive Thiamine.

Recovery from alcohol withdrawal was found to be faster in those who received thiamine and GGT remains more reliable marker followed by AST.

REFERENCES

[1] Vasudevan DM, Sreekumari S, Vaidyanathan K. Textbook of Biochemistry for medical students. Chapter 23. Clinical enzymology and biomarkers. 6th edn. Jaypee Brothers Medical Publishers (P) Ltd., 2011: p. 270.

[2] Stewart SH, Connors GJ. Ethnicity, alcohol drinking and changes in transaminase activity among heavy drinkers. J Natl Med Assoc 2007;99(5):564-9.

[3] Ashwood ER, Grenache, DG. Liver. Chapter 50. In: Burtis CA, Ashwood ER, Bruns DE, eds. Tietz Textbook of Clinical chemistry and molecular diagnostics. St. Louis, USA: 5th edn. Elsevier Publication 2012: p. 1674.

[4] Das SK, Vasudevan DM. Biochemical diagnosis of alcoholism. Indian Journal of Clinical Biochemistry 2005;20(1):35-42.

[5] Kasper DL, Fauci AS, Hauser SL, et al. Harrison's Principles of Internal Medicine. Vol. 2. 19th edn. New York: McGraw- Hill Education 2015.

[6] Hoyumpa AM Jr. Mechanisms of thiamin deficiency in chronic alcoholism. Am J Clin Nutr 1980;33(12):2750-61.

[7] Agabio R. Thiamine administration in alcohol-dependent patients. Medical council on alcoholism. Alcohol and Alcoholism 2005;40(2):155-6.

[8] Hope LC, Cook CC Thomson AD. A survey of the current clinical practice of psychiatrists and accident and emergency specialists in the United Kingdom concerning vitamins supplementation for chronic alcohol misusers. Alcohol and Alcoholism 1999;34(6):862-7.

[9] Cook CC, Thomson AD. B-complex vitamins in the prophylaxis and treatment of Wernicke–Korsakoff syndrome. British Journal of Hospital Medicine 1997;57(9):461-5.

[10] Singleton CK, Martin PR. Molecular mechanisms of thiamine utilization. Current Molecular Medicine 2001;1(2):197-207.

[11] Thomson AD. Mechanisms of vitamin deficiency in chronic alcohol misusers and the development of the Wernicke–Korsakoff syndrome. Alcohol and Alcoholism Suppl 2000;35(1):2-7.

[12] Reuler JB, Girard DE, Cooney TG. Current concepts. Wernicke's encephalopathy. New England Journal of Medicine 1985;312(16):1035-9.

[13] Thomson AD, Marshall EJ. The natural history and pathophysiology of Wernicke's Encephalopathy and Korsakoff's Psychosis. Alcohol & Alcoholism 2006;41(2):151-8.

[14] Day E, Bentham P, Callaghan R, et al. Thiamine for Wernicke–Korsakoff Syndrome in people at risk from alcohol abuse. The Cochrane Database of Systematic Reviews 2004;(1):CD004033.
[15] Whitfield JB. Gamma glutamyl transferase. Crit Rev Clin Lab Sci 2001;38(4):263-355.
[16] Patel S, O'Gorman P. Serum enzyme levels in alcoholism and drug dependency. Journal of Clinical Pathology 1975;28(5):414-7.
[17] Conigrave KM, Davies P, Haber P, et al. Traditional markers of excessive alcohol use. Addiction 2003;98(Suppl 2):31-43.
[18] Konttinen A, Hartel G, Louhija A. Multiple serum enzyme analyses in chronic alcoholics. Acta Med Scand 1970;188(1-6):257-64.
[19] Wadstein J, Skude G., Changes in amylase, hepatic enzymes and bilirubin in serum upon initiation of alcohol abstinence. Acta Med Scand 1979;205(4):313-6.
[20] Reichling JJ, Kaplan MM. Clinical use of serum enzymes in liver disease. Dig Dis Sci 1988;33(12):1601-14.