

## Alcohol Related Seizure A Hospital Based Study from North East India

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### Abstract

### Original Research Article

Alcohol is one of the leading causes of death and disability globally affecting both the central and peripheral nervous system. Alcohol related seizure is a common medical emergency in Neurology and Psychiatry department and is responsible for 20-30% of seizure admission. **Materials and Method:** A prospective study carried in a referral centre in North East India for duration of one year. Seizure patients who fulfil the definition of alcohol related seizure were included. Routine blood work, an electroencephalogram (EEG) and a required neuro imaging was done. Patient's data were collected and analysed. **Results:** Thirty-four male patients were included with mean age of presentation was  $40.79 \pm 11.85$  years. The mean duration of alcohol intake was  $12.82 \pm 8.48$  years with a range of 3-40 years. The gap between last binge of alcohol and onset of seizure was <24 hours in 10 patients (29.4%); 24-48 hours in 18 patients (52.9%) and >48 hours in 6 patients (17.6%). The mean Alcohol Use Disorders Identification Test (AUDIT) score was  $22.8 \pm 6.97$  and mean Clinical Institute Withdrawal Assessment for Alcohol (CIWA) score was  $16.47 \pm 7.9$ . The mean MMSE score in all alcohol related seizure cases was  $26 \pm 2.0$  and was found to be inversely correlated with duration of alcohol intake (Pearson's coefficient = -0.29). Focal epileptiform changes in EEG was seen in two patients (5.8%), generalized spike and wave seen in one patient (2.9%) and generalized theta slowing seen in 9 patients (26.4%). Presence of an abnormal EEG, a positive past history of seizure related to alcohol and an AUDIT score >20 is significantly associated with recurrence of seizure. **Conclusion:** Alcohol related seizure can reoccur; Presence of abnormal EEG, past history of similar illness and AUDIT scores of >20 can predict recurrent seizure in these patients. **Keywords:** Alcohol Related Seizure, AUDIT Score, and Electroencephalogram.

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## INTRODUCTION

Alcohol related seizures has been known since Hippocratic times but still are perhaps the most complex and perplexing complication of alcoholism. [1, 2] The term of 'alcoholic epilepsy' was proposed in 1881 from Echevarria, and re-discovered in 1967 from Victor and Brausch. In 1983, Devetag *et al.* suggested the division of convulsive activity or seizure types among alcoholics in four types: (a) solitary convulsive seizures; (b) convulsive seizures in the setting of withdrawal syndrome or due to massive intake of ethanol; (c) seizures related to the presence of other potentially epileptogenic diseases and (d) alcoholic epilepsy, a disorder per se. [3] Alcohol is responsible for one third of seizure-related admissions. [4,5,6] In adults with a first generalized seizure, chronic alcohol abuse was found to be the principal cause in 20% of cases and

a cofactor in an additional 17% of patients. [7] The typical alcohol withdrawal seizure is a primarily generalized tonic-clonic seizure (GTCS) [8,9] but partial onset may be more common than previously recognized. [6] The seizure may be a single or a few multiple attack over a short time, over 90% of convulsive attacks occurred between 7 and 48 hours after cessation of drinking and <3% had status epilepticus. [10] Excessive alcohol use is a well-known precipitant of idiopathic generalized epilepsy (IGE) and some proportion of late onset IGE may present as alcohol related seizures (ARS).

With this in mind, studying alcohol related seizure would be beneficial to understand the clinical spectrum and type of seizure related with alcohol. Correlating the EEG changes with seizure semiology to

know the outcome of these patients and to know the etiological role of alcohol in ARS and generation of idiopathic epileps.

## MATERIALS AND METHODS

A prospective study carried out in a referral centre in North East India over a period of one year where all patients of alcohol withdrawal seizure were taken into consideration. Ethical clearance was received from the ethical committee.

Alcohol-related seizures are defined as seizures in patients with AUDIT scores  $\geq 8$  which is a cut-off by which both sensitivity and specificity for hazardous drinking has been reported greater than 90% [11, 12]. Patients with prior history of active epilepsy, recent head injury (within 1 week) prior to seizure, any other provoking causes i.e. stroke, CNS infections, hypoglycemia, dyselectrolytemia and other substance abuse were excluded. Patients with other paroxysmal events as pseudo seizures, syncope or those who refuse to give consent were also excluded.

We obtained a detailed history regarding the seizure semiology, associated clinical history and alcohol intake history were included. The seizure type, duration of seizure and any other associated factors or focal neurological deficit was noted. A past history of seizure or similar alcohol related seizure was inquired. Family history and a past history of febrile seizure were also noted. The alcohol history consisted of total duration of alcohol intake, frequency of alcohol intake, type of alcohol used, amount consumed per day, recent change in drinking habits, amount of alcohol consumed in the bout preceding the seizure and time interval between last bout and seizure. As patients frequently underreport true levels of alcohol consumption, therefore, whenever possible, a relative or friend was asked about the alcohol intake. History of consumption of other legal or illegal pharmacological agents may influence the tendency to have seizures (e.g. benzodiazepines, antipsychotics, antidepressants, or stimulant drugs) is also ruled out.

A detail general physical and neurological examination including mini mental status examination (MMSE) when feasible was noted. These patients were subjected to Alcohol Use Disorders Identification Test (AUDIT) score and Clinical Institute Withdrawal Assessment for Alcohol, Revised (CIWA-Ar) score. AUDIT score is a structured questionnaire that has been developed to reveal and grade excessive alcohol consumption as well as alcohol overuse and dependence. The questionnaire is brief and reliable. The AUDIT is a 10-item questionnaire which requires a 2–3 min interview and provides a fine-pitched grading (0–40) of alcohol use and overuse. CIWA-Ar survey consists of 10 items and can be administered rapidly at the bedside in about 5 minutes. The 10 items include nausea and vomiting, anxiety, tremor, sweating,

auditory disturbances, visual disturbances, tactile disturbances, headache, agitation, and clouding of sensorium. Zero to 7 points is assigned to each item, except for the last item, which is assigned 0-4 points, with a total possible score of 67. The CIWA-Ar will help us to know severity of withdrawal symptoms if any.

A routine haematological and biochemical investigations for liver (serum bilirubin, alanine transaminase [ALT], aspartate aminotransferase [AST], gamma-glutamyl transferase [GGT], ammonia levels) and renal functions (serum urea and creatinine) was done for every patient. Serum electrolytes, sodium, potassium, calcium and magnesium, random blood sugar level, were carried out in all patients at the time of presentation. All patients were screened for Human immunodeficiency virus (HIV) I and II, Hepatitis B and C. Electroencephalogram (EEG) recordings were carried out on a 24-channel digital electroencephalography (EEG) acquisition system with the scalp electrodes placed according to the international 10-20 system. A computed tomography or magnetic resonance imaging of the brain was done in all patients to rule out head injury and any other provoking cause for seizure like subdural hematoma, neurocysticercosis, intracranial space occupying lesion etc.

The data were collected and analysed using SPSS (version 25). Descriptive statistics were noted. The correlation of alcohol abuse or abnormal EEG, CIWA score and AUDIT score with seizure or its recurrence, correlation of years of alcohol abuse with MMSE was also considered.

## RESULT AND OBSERVATIONS

A total of 34 cases of alcohol related seizures were studied, which included 34 male and no female patient. The mean age of presentation was  $40.79 \pm 11.85$  years with a range of 21 to 75 years. Maximum (35.2%) cases were in the age range of 31-40 years, no patients note in the 61-70 age group and 2.9% only cases were observed in the age group of >71 years.

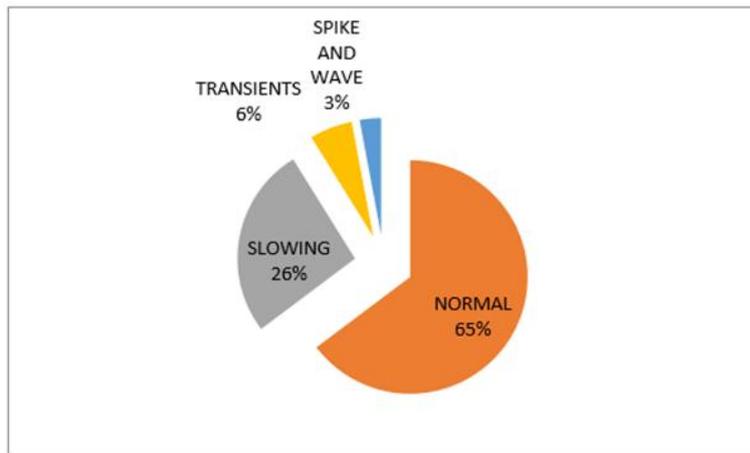
The mean duration of alcohol intake was  $12.82 \pm 8.48$  years with a range of 3-40 years. A long-term alcohol consumption >5 years was seen in 30 patients (88%), among which twelve patients have cerebral atrophy on Neuroimaging. The gap between last binge of alcohol and onset of seizure was <24 hours in 10 patients (29.4%); 24-48 hours in 18 patients (52.9) and >48 hours in 6 patients (17.6%) as shown in figure 2. The maximum gap which was seen was three months in one patient, one-week gap seen in 3 patients and minimum gap was 9 hours seen in one patient. Maximum (47.1 %) cases consumed Indian Made Foreign Liquor (IMFL) mainly whisky, followed by 14.7% cases consumed home-made liquor and 38.2% cases consumed both IMFL and home-made liquor.

The most common seizure semiology note was generalized tonic clonic seizures (GTCS) seen in 91 % and rest 2.9 % cases had focal seizures. Two patients (5.8%) presented with status epilepticus. Withdrawal symptoms were present in twenty-two (64.7%) cases and tremor was the most common withdrawal symptom. Four cases (11.8%) had a positive family history of seizures and one (2.9%) patient had a past history of febrile seizures. A past history of seizure related to alcohol was seen in 25 patients (73.5%) out of the 34 patients.

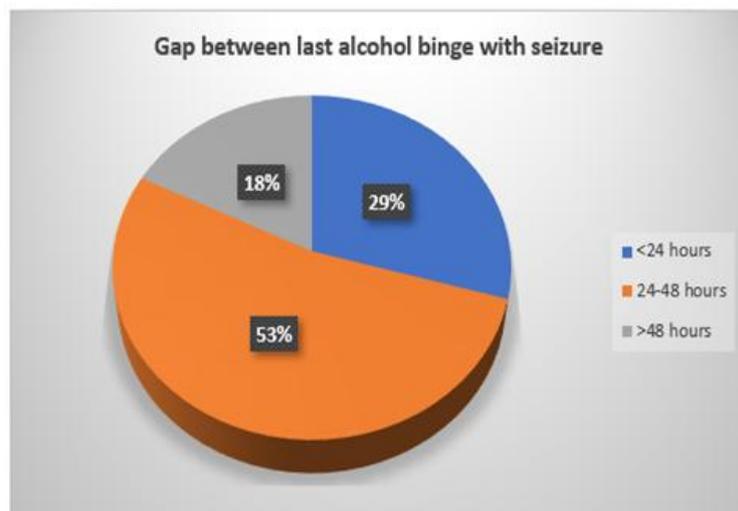
The mean AUDIT score was  $22.8 \pm 6.97$ . Only five (14.7%) cases had AUDIT score lesser than 10, while five (14.7%) had AUDIT score ranging from 10 to 20 and twenty-four (75%) cases had AUDIT score more than 20 (table 1). The mean CIWA score was  $16.47 \pm 7.9$  with the minimum score of 5 maximum score of 35. A CIWA score of  $>10$  was significantly associated with withdrawal symptoms (Table-2). The mean MMSE score in all alcohol related seizure cases

was  $26 \pm 2.0$ . MMSE score was found to be inversely correlated with duration of alcohol intake (Pearson's coefficient -0.25).

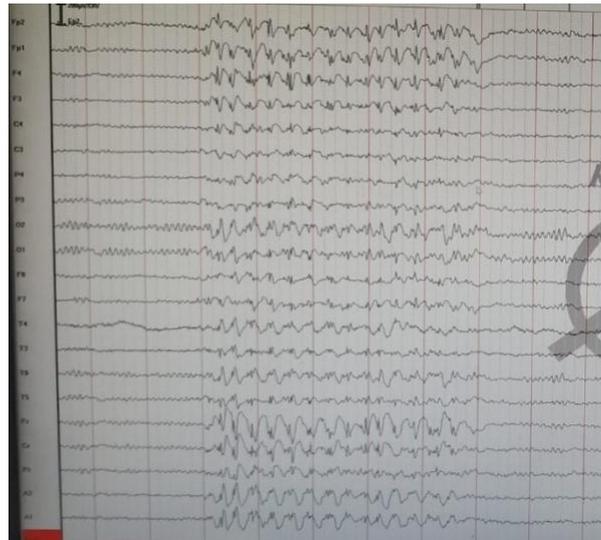
Out of all 34 cases of alcohol related seizures, focal epileptiform changes (image 2) in EEG was seen in two patients (5.8%), generalized spike and wave (image 1) seen in one patient (2.9%) and generalized theta slowing (image 3) seen in 9 patients (26.4%) as shown in figure 1. On performing Neuroimaging, 23.5% cases had evidence of cerebral atrophy on CT scan and 17.6% on MRI brain. Recurrence of seizure on follow up in these patients was seen in twenty patients (58 %). Most of these recurrences of seizure were related to alcohol again except for one patient who continue to have seizure despite stopping alcohol. Presence of an abnormal EEG, a positive past history of seizure related to alcohol and an AUDIT score  $>20$  is significantly associated with recurrence of seizure (Table-3).



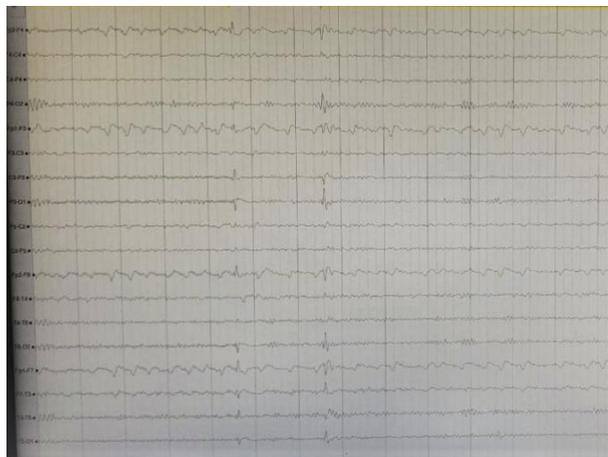
**Fig: 1- PIE Chart Showing the Various EEG Finding**



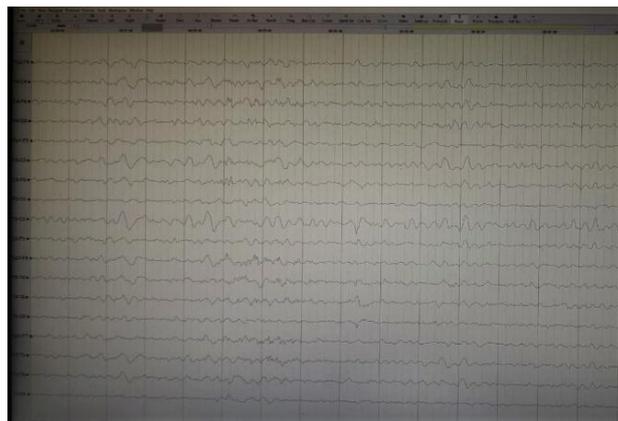
**Fig: 2- Duration gap between last binge and onset of seizure**



**Image 1: EEG showing generalised spike and wave discharge**



**Image 2- EEG showing sharp focal transients**



**Image 3- EEG showing theta slowing**

**Table-1: Descriptive statistics of variable from study**

	N	Minimum	Maximum	Mean	Std.Deviation
Age	34	21	75	40.79	11.850
Years of alcohol abuse	34	3	40	12.82	8.487
MMSE	34	22	29	26.18	2.081
CIWA Score	34	0	35	16.47	7.906
Audit Score	34	7	37	22.82	6.970
Valid N (Listwise)	34				

**Table-2: Correlation Between CIWA Score with occurrence of Withdrawal symptoms**

		Withdrawal symptoms		Total
		Present No. of cases (%)	Absent No. of cases (%)	
CIWA	<10	1(2.9%)	8(23.5%)	9(26.4%)
	10-20	12(35.2%)	3(8.8%)	15(44.1%)
	12-30	7(20.5%)	1(2.9%)	8(23.5%)
	>30	2(5.8%)	0(0%)	2(5.8%)
<b>The p-value is .002513. The result is significant at p&lt;.05.</b>				

**Table-3: Correlation of the Various Findings with recurrence of Seizure**

Findings	Present of Seizure Reoccurrence	No Seizure Reoccurrence	Total	P Value
Abnormal EEG	10	2	12	0.03198 significant
Normal EEG	10	12	22	
Present past history of seizure	19	7	26	0.008448 significant
Absent past history of seizure	1	7	8	
Withdrawal symptoms present	14	8	22	0.440068 not significant
Withdrawal symptoms Absent	6	6	12	
Positive family history of seizure	2	2	4	0.702665 not significant
Negative family history of seizure	18	12	30	
Audit score <10	1	4	5	0.012181 significant
Audit score 10-20	1	4	5	
Audit score >20	18	6	24	
<b>The result is significant at p &lt;.05: chi-square test</b>				

## DISCUSSION

About two billion people worldwide consume alcoholic beverages and one-third (nearly 76.3 million) is likely to have one or more diagnosable alcohol use disorders. [13] In India the estimated numbers of alcohol users in 2005 were 62.5 million, with 17.4% of them (10.6 million) being dependant users [14] and 20-30% of hospital admissions are due to alcohol-related problems. [15] Raekha Prasad [16] reported that more than half of all alcohol drinkers in India falling into the criteria for hazardous drinking, alcohol abuse is emerging as a major public-health problem in the country. Reddy and Chandrashekar observed a greater prevalence in rural areas in comparison to urban areas (7.3 v/s 5.8 /1000 population) against the overall prevalence of alcoholism (6.9/1000) in the country. Almost all studies have reported higher use rates among men varying from 26 % to 72 %.[17,18] Prevalence of alcohol dependence remains stable across time between 5-7% in men and 2-3% in women [17] Alcohol consumption which forms an important risk factors for various diseases has been shown to be associated with epilepsy. [19] Alcohol may act in several ways to produce seizures in patients with or without underlying foci. Partial or absolute withdrawal of alcohol after a period of chronic intake may lead to glutaminergic over activity. Binge drinking can cause an acute alcohol-related metabolic disorder (e.g., hypoglycemia, hyponatremia) leading to acute symptomatic seizures. It can create a situation leading to cerebral trauma or can precipitate seizures in patients with idiopathic or posttraumatic epilepsy. Persistent heavy intake of alcohol without alcohol withdrawal can also cause

seizures. [20] Alcohol acts on the brain through several mechanisms that influence seizure threshold. These include effects on calcium (Ca<sup>2+</sup>) and chloride (Cl<sup>-</sup>) flux through the ion-gated glutamate, N-methyl aspartate (NMDA) and gamma-aminobutyric acid (GABA) receptors. During prolonged intoxication, the CNS adapts to the effects of alcohol, resulting in tolerance; however, these adaptive effects seem to be transient, disappearing after alcohol intake is stopped. [21] ARS present at varied times after abstaining from drinking. Many patients do not have overt withdrawal symptoms at the time of seizures. There is a general tendency to consider all seizures in alcoholics as withdrawal related but many studies have shown that not all seizures can be attributed to alcohol withdrawal alone.

In our study, we evaluated 34 cases of alcohol related seizures and all of them were males. The mean age note was 40.79 ± 11.85 years with a range of 21 to 75 years which is similar as compared to other studies. Recently, Sandeep et al evaluated clinical profile of patients with nascent alcohol related seizures in 100 cases in south India. [22] in that study all cases were male; the average age of cases was 43.7 years. Bajaj *et al*. [23] found history of seizures in 120 cases out of 320 cases with alcohol dependence and found that the mean age of presentation was 35.5 years. In north east India, there is tradition of making liquor from rice at home. However, in urban areas IMFL has replaced the home-made liquor, thus, the availability of alcohol at home and its social acceptability might be the reason for exposure to alcohol at an earlier age as the youngest age

in our study was 21 years. However, the maximum number of patients was of the age group 31-40 years.

The mean duration of alcohol intake was  $12.82 \pm 8.48$  years with a range of 3-40 years. These patients mostly consumed Indian Made Foreign Liquor (IMFL) mainly whisky (47.1%) followed by 14.7% cases consumed home-made liquor and 38.2% cases consumed both IMFL and home-made liquor. Mean AUDIT score was  $22.8 \pm 6.97$ . Only five (14.7%) cases had AUDIT score lesser than 10, while five (14.7%) had AUDIT score ranging from 10 to 20 and twenty-four (75%) cases had AUDIT score more than 20. Sandeep et al [14] found that mean duration of alcohol intake was 17 years, mean AUDIT score was 21.9, nearly 76% cases were in the habit of consuming rum.

In our study, maximum (91%) cases had generalized tonic clonic seizures (GTCS) and rest 2.9 % cases had focal seizures. Two patients (5.8%) presented with status epilepticus, these patients had an abnormal EEG and recurrence of seizure on follow up. A family history of seizure was note in 4 patients (11.7%) and a history of febrile seizure was seen in 1 patient. A past history of similar type of alcohol relates seizure was note in in 25 patients (73.5%). Sandeep et al. found, generalized tonic clonic seizures (GTCS) in 88% while partial seizures in 12 % cases, none of them presented with status epilepticus, family history of seizures was present in 8 % of cases and clustering at presentation occurred in 22 cases (22%). [22] A recurrence of seizure was seen in twenty (58.8%) on follow up of these patients who were included in the study. A positive past history of seizure related to alcohol and an AUDIT score  $>20$  is significantly associated with recurrence of seizure (Table-3). Schaumann et al. studied the incidence of seizures in first-degree relatives of cases of alcohol related seizures and found an odds ratio of 2.45 in relatives of patients with alcohol induced seizures. [24] The gap between last binge of alcohol and onset of seizure was  $<24$  hours in 10 patients (29.4%); 24-48 hours in 18 patients (52.9) an  $>48$  hours in 6 patients (17.6%). The maximum gap which was seen was three months in one patient, one-week gap seen in 3 patients and minimum gap was 9 hours. Withdrawal symptoms were present in twenty-two (64.7%) cases and tremor was the most common withdrawal symptom. Two patient's had AUDIT score of  $< 8$ , these patients did not have withdrawal symptoms or recurrence of seizure during follow up. An abnormal EEG suggestive of idiopathic generalized epilepsy (IGE) was seen in one patient while the other one had theta slowing. Recurrence of seizure was related to alcohol in most of the patients except for one patient who persistently had seizure despite discontinuation of alcohol. This could indicate the potential role of alcohol itself in inducing seizures, rather than the withdrawal state. Hence this group of patients can potentially be considered to have alcohol induced seizures rather than withdrawal seizures. Our

findings were also supported by Sandeep [22] *et al.* who found that out of their 100 cases, 85 cases developed withdrawal symptoms. 78 cases had their first seizure between 6 and 48 hours and 14 cases had seizures within 6 hours of alcohol intake. 8 cases out of the 14 had no withdrawal symptoms at all and the mean duration of alcohol intake in this subgroup of eight was significantly lower than those who had withdrawal symptoms ( $P=0.013$ ). One young male in this subset had EEG abnormalities suggestive of IGE. As far as alcohol withdrawal seizures are concerned, figures vary widely. Studies conducted by Earnest and Yarnell [4] and Hillbom [25] shows that alcohol withdrawal accounted for 59% and 31% of seizures respectively. According to Victor and Brausch in their study, 88% of seizures encountered were related to alcohol withdrawal alone. [10] Murthy et al found that only 28% of seizures could be confidently attributed to alcohol withdrawal and family history of seizure was obtained in 25% of patients with ARS. [26] Bajaj et al. could attribute only 27.5 % seizures to withdrawal. [23]

Among the IGE syndromes, [27] IGE with GTCS has high probability to present to the clinician initially as ARS. An abnormal EEG with findings classical of IGE helps us in differentiating them. In the present study, out of all 34 cases of alcohol related seizures, 12 patients (35.2%) ha an abnormal EEG; focal spike and sharp transients in EEG was seen in two patients (5.8%), generalized spike and wave seen in one patient (2.9%) and generalized theta slowing seen in 9 patients (26.4%). Only one patient had an EEG finding similar to IGE but no recurrence of seizure was noted in this patient. However, an abnormal EEG finding could predict the recurrence of seizure (Table-3) and help us in choosing patients who may need anti epileptics.

Available evidence shows a strong and consistent association between duration of alcohol consumption and cerebral atrophy. In our study, 23.5% cases had evidence of cerebral atrophy on CT scan and 17.6% on MRI brain. These patients have a long-term alcohol consumption  $>5$  years in 12 patients while two patients had an exposure of  $<5$  years. While Sandeep et al. suggested that patients with cortical atrophy had a significantly higher mean duration of alcohol intake compared to those who had no atrophy. Evidence of cerebral atrophy in patients with ARS portends an increased risk for developing clustering. [22] Dam *et al.* observed that 74% of long-term heavy alcohol users with epilepsy had cerebral atrophy as a consequence of chronic alcohol intake. [28] Lusins et al. suggested that the only factor that correlated to a significant degree with cerebral atrophy was the duration of problem drinking. [29] Bajaj et al. noted cortical atrophy in 75% cases, predominantly in the frontal, parietal and temporal regions. [23] The mean MMSE score in all alcohol related seizure cases was  $26 \pm 2.0$ . MMSE score was found to be inversely correlated with duration of alcohol intake (Pearson's coefficient = -0.29).

It is well-known that as the duration of alcohol intake increases the chance of developing epilepsy or unprovoked seizure increases. The kindling hypothesis proposed by Ballenger and Post states that repeated ethanol withdrawal, including natural withdrawal during sleep over the years, in chronic alcoholics lead to the gradual lowering of the epileptogenic threshold.[30] In our study, presence of an abnormal EEG, a past history of alcohol related seizure and a high AUDIT score is associated with recurrence of seizure. However, the duration of alcohol intake worsens the brain functions causing cerebral atrophy and a lower MMSE.

## CONCLUSION

Alcohol is a known risk for developing seizure or lowering the epileptogenic threshold. Certain factors like a status epilepticus presentation, an abnormal EEG or a similar past history of withdrawal seizure may indicate a high chance of recurrence in the future in this subgroup. EEG may have a role in identifying those patients who may require antiepileptic but needs to assess with a large sample size.

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