

Severity of Dependence and Alcohol Withdrawal Delirium

Aswathy G¹, Jithu VP²

1. Department of Psychiatry, Government Medical College, Kozhikode, Kerala, India.

2. Department of Psychiatry, Government Medical College, Kozhikode, Kerala, India.

Corresponding author: Jithu VP

Abstract :

Background: It has always been an enigma as to what makes certain individuals vulnerable to a severe alcohol withdrawal state as compared to others. There is paucity of literature in India concerning the relationship between severity of dependence and occurrence of alcohol withdrawal delirium. The present study intends to assess the relation between severity of dependence and delirium and to explore other risk factors.

Materials and Methods: Study setting- Deaddiction centre, Government medical college, Kozhikode; Study design-cohort study. Participants-126 patients diagnosed with Alcohol withdrawal. Age group- 18-65. Patients with co-morbidities like Diabetes Mellitus, Hypertension, Epilepsy, Head injury, intellectual disability and comorbid or past psychiatric illness were excluded. Study tools : socio-demographic proforma, DSM 5, SADQ, CAM. Duration- 9 months

Results : Average daily use in the last one week prior to admission was 472.3 ml. SADQ Scores revealed 76, 46 and 4 patients with mild, moderate and severe dependence respectively. 26%, 50% and 75 % of patients with mild, moderate and severe dependence as per SADQ Scores developed delirium showing statistically significant association for SADQ Scores with development of delirium (p value 0.008). 64% of patients who consumed more than 500 ml developed delirium while only 31 % of patients who consumed <500 ml developed delirium (p value 0.04). 35 patients with delirium had history of deaddiction treatment (49.3%) while 11 patients with delirium had no history of deaddiction treatment(20%)(p value 0.001). While 56.4% of patients who developed delirium had past history of delirium, 27.6% had no past history of delirium.(p value 0.002)

Conclusions : SADQ Scores are predictive of development of alcohol withdrawal delirium. Development of delirium is significantly associated with average amount of alcohol use in the week prior to admission, past history of deaddiction treatment and delirium tremens.

Keywords: Alcohol dependence; Delirium tremens; Alcohol withdrawal.

Date of Submission: 20-05-2021

Date of Acceptance: 05-06-2021

I. Introduction

Alcohol is one of the most common drugs of abuse with enormous social and economic impact worldwide. The World Development Report found that the alcohol related disorders affect 5-10% of the world's population each year. Global alcohol consumption has increased in recent decades with most or all of this increase occurring in developing countries. Both average volume of alcohol consumption and patterns of drinking vary dramatically between regions with average volume of drinking being highest in Europe and North America and lowest in the Eastern Mediterranean and SEAR-D regions (Bangladesh, Bhutan, DPR Korea, India, Maldives, Myanmar and Nepal (1).

Alcoholism is a progressive disease in which the individual has been unable to quit drinking and continues to drink even after knowing its harmful effects (2). Alcohol Use Disorder (AUD) is a common health hazard globally. The average alcohol dependent person decreases his or her lifespan by 10-15 years representing a significant issue with increasing morbidity and mortality in the population(3-7). The harmful use of alcohol is one among the five risk factors for disease, disability and death throughout the world. Alcohol consumption causes death and disability relatively early in life and in the age group of 20 - 39 years, almost 25 % of the total deaths can be attributed to alcohol (8). The inclusion of harmful use of alcohol as an indicator under the health goal in the UN 2030 Agenda for Sustainable Development illustrates the importance of harmful use of alcohol as a development issue (9).

Although India is regarded as a traditional "dry" country, it is the dominant producer of alcohol in the South-East Asia region. ICMR bulletin estimated 62 million alcoholics in India. National level per capita consumption of pure alcohol per year in Indian males above 15 years is 4.3 litres which is against a global per capita consumption of 6.13 litres (10). Kerala is a state where alcohol consumption is more than the national average with a per capita consumption of around 8.3 litres (11). National Family Health Survey (NFHS-4) has found that 37% of males and 1.6% of females drink alcohol in Kerala (12).

In patients suffering from AUD, alcohol withdrawal symptoms appear after a significant reduction or complete discontinuation of alcohol consumption and this usually occurs within 1-3 days after the last drink (13). The withdrawal symptoms are caused by specific changes in brain neurophysiology after various periods of usually heavy drinking (14). In the mild form of withdrawal, tremor, hyperactivity, sweating, tachycardia and sleep disturbances are present. In the severe alcohol withdrawal, especially when untreated, hallucinations, seizures and delirium may occur. The most severe complication of alcohol withdrawal syndrome is alcohol withdrawal delirium, which may be preceded or complicated by seizures.

Delirium Tremens is a short lived but an occasionally life threatening toxic confusional state with accompanying somatic disturbances and always represents one of the psychiatric emergencies. Delirium Tremens occurs in approximately 5% to 10% of individuals with alcohol withdrawal and usually presents between 48 and 96 hours after last alcohol use (15). Patients with delirium are a danger to themselves and to others because of unpredictability of their behaviour.

It has always been an enigma as to what makes certain individuals vulnerable to a severe withdrawal state as compared to others. The most commonly identified risk factors included past history of delirium tremens, seizures, presence of acute somatic comorbidity especially infections, presence of early withdrawal symptoms and genetic predisposition(16). Most studies have evaluated the relative importance and capacity of physical signs as important predictors of alcohol withdrawal delirium. There is paucity of literature in India, especially in Kerala concerning the relationship between severity of dependence and occurrence of alcohol withdrawal delirium and whether we can predict the development of alcohol withdrawal delirium from the dependence pattern and its severity. My study aims to look into this association of dependence and delirium and explore various variables associated with this.

II. Materials And Methods

This Cohort study was carried out on patients of Department of Psychiatry at Government Medical College, Kozhikode, Kerala for a period of 9 months from January 2017 to September 2017. All consecutive adult subjects in the age group 18-65 years who got admitted during the study period with alcohol use disorder in withdrawal state without perceptual disturbances were included in the study.

Study design: Cohort Study.

Study location: Deaddiction treatment centre of Department of Psychiatry, Government Medical College, Kozhikode, a tertiary care centre in North Kerala.

Study duration :9 months from January 2017 to September 2017.

Sample size :126 patients

Sample size calculation: Formula: $n = 4pq/d^2$; $p = 10\%$; $q = 90$; $d = 5$ $n = 140$.

subjects and selection methods : Consecutive patients who got admitted with alcohol use disorder in withdrawal state without perceptual disturbances were included in the study

Inclusion criteria :

1. Patients fulfilling the diagnostic criteria of alcohol withdrawal according to DSM 5.
2. Age between 18-65 years.
3. Patient or relative giving informed consent.

Exclusion criteria:

1. Severe medical or surgical illness interfering with formal assessment of mental status.
2. Previous history of epilepsy/head injury/diabetes mellitus.
3. Patients with mental retardation.
4. Past history of psychiatric illness/ Comorbid psychiatric illness except nicotine dependence syndrome.

Procedure methodology

Study subjects were patients admitted with alcohol related disorders and alcohol withdrawal symptoms without delirium, fulfilling inclusion and exclusion criteria. Their sociodemographic profile and clinical details were collected using the proforma created. Using DSM-5 criteria, alcohol withdrawal was diagnosed. Patients were treated with lorazepam as per their alcohol use and the clinical assessment, along with parenteral or oral thiamine given twice daily and multivitamins. Patients with alcohol withdrawal were given the SADQ to assess the severity of dependence. These patients were screened for delirium on alternate days using CAM questionnaire for 10 days. If delirium was observed as indicated in CAM, diagnosis of delirium was confirmed by DSM 5 criteria. Thus on serial screening we got patients with withdrawal symptoms who developed delirium and those who did not develop delirium. The SADQ scores of all these patients were looked into and analyzed and thus the data was used to test the hypothesis regarding severity of dependence and alcohol withdrawal delirium. The Assessment Tools used were a Semi structured data sheet to collect the socio-demographic and

clinical details of the patients, The Diagnostic and Statistical Manual for Mental Disorders- V (DSM-5) criteria for diagnosis of alcohol use disorder and alcohol withdrawal syndrome, Severity of Alcohol Dependence Questionnaire (SADQ) – Malayalam version – to assess the severity of dependence, Confusion Assessment Method (CAM) – to identify delirium. DSM -5 criteria for substance use disorders by American Psychiatric Association combines the DSM- IV categories of alcohol abuse and alcohol dependence into a single disorder as Alcohol Use Disorder measured on a continuum from mild to severe. SADQ is a short, easy-to-complete, self-administered, 20-item questionnaire designed to measure severity of dependence on alcohol as formulated by Edwards & Gross (1976) and Edwards (1978). The original SADQ as first described in 1979 and further refined in 1983 is designed purely for use with populations of problem drinkers attending treatment facilities of various kinds. There are five subscales with four items in each: Physical Withdrawal, Affective Withdrawal, Withdrawal Relief Drinking, Alcohol Consumption, and Rapidity of Reinstatement. Each item is scored on a 4-point scale, ranging from “Almost Never” to “Nearly Always,” resulting in a corresponding score of 0 to 3. Thus the total maximum score possible is 60 and the minimum is 0. Maximum score is 60 and scores greater than 30 correlate with clinicians’ ratings of “severe alcohol dependence.” Test-retest reliability is 0.85. Clinical utility of the instrument is that it can be used for prediction of likelihood of achieving control drinking goal; prediction of withdrawal severity; differential diagnosis of primary or secondary phobic anxiety state (17). CAM Questionnaire is a standardized evidence-based tool that enables clinicians to identify and recognize delirium quickly and accurately in both clinical and research settings. The CAM includes four features found to have the greatest ability to distinguish delirium from other types of cognitive impairment. The CAM was designed and validated to be scored based on observations made during brief but formal cognitive testing, such as brief mental status evaluations. The tool identifies the presence or absence of delirium. Screening of delirium is done by presence of acute onset and fluctuating course in abnormal behaviour throughout the day and inattention along with either disorganised/ incoherent thinking or altered level of consciousness.

Statistical analysis

Degree of association between the relevant variables were found out using Chi –square test for qualitative variables and mean for quantitative variables. Data analysis was carried out using the Statistical Package for Social Sciences (SPSS) VERSION 18.0.

III. Result

The study included 126 patients with alcohol use disorder in withdrawal without perceptual disturbances at the time of admission.

Table 1 : Relationship between Severity of Alcohol dependence score (SADQ) and Development of Delirium.

SADQ SCORE	DELIRIUM	NO DELIRIUM	TOTAL
1.Mild (4-19)	20 (26%)	56 (74%)	76
2.Moderate (20-30)	23 (50%)	23 (50%)	46
3.Severe (31-44)	3 (75%)	1 (25%)	4
TOTAL	46	80	126

Pearson Chi Square value is 9.575, Degree of Freedom is 2, p value = 0.008 Table shows that when the severity of dependence increases, chances of developing delirium also increases. 26 % and 50 % of patients with mild and moderate dependence developed delirium respectively, while 75% of patients with severe dependence went into delirium.

Table 2: Relation between average use of alcohol in the week prior to the admission and the development of delirium

AVERAGE USE	DELIRIUM	NO DELIRIUM
>500 ml	14 (64%)	8 (36%)
<=500 ml	32 (31%)	72 (69%)

Pearson Chi Square is 4.35 with degree of freedom of 2 with p value of 0.04 Table shows that 64% of the patients who consumed more than 500ml of alcohol developed delirium, while only 31 % of the patients with less than or equal to 500ml of alcohol consumption developed delirium. The result was statistically significant with p value of 0.04.

Table 3 :Relation between past history of deaddiction treatment and development of delirium.

H/O DEADDICTION Rx	DELIRIUM	NO DELIRIUM
H/O Treatment in the past	35 (49.3%)	36 (50.7%)
No History of treatment in the past	11 (20%)	44 (80%)

Pearson Chi Square is 11.48 with degree of freedom of 1 and p value of 0.001 Table shows that patients with a past history of de-addiction treatment has more chances of developing delirium. The result is statistically significant with a p value = 0.001.

Table 4 : Relation between past history of withdrawal delirium and development of delirium.

PAST H/O OF DELIRIUM	DELIRIUM	NO DELIRIUM
Past History of Delirium	22 (56.4%)	17 (43.6%)
No past history of delirium	24 (27.6%)	63 (72.4%)

Pearson Chi Square is 9.652 with degree of freedom of 1 with a p value of 0.002 Table shows that patients with past history of delirium has more chances of developing delirium. The result is statistically significant with a p value of 0.002.

IV. Discussion

This cohort study was conducted in 126 patients to look into severity of dependence and the relation with the development of delirium.

77.8% of the patients were married , 19.8% were single, and the rest were widowers and one divorcee. Married status can be considered as a protective factor in the case of AUD as reported by Liang et al (18). But this study reveals that married people have more association with AUD as was

seen in a study by Saffer et al (19). This is contrary to economic theory which expects marriage to have a negative effect on alcohol consumption. Mahal et al argues that marital status reflects economic strength (20). Unmarried people in rural India are likely to be young and atleast some of them will not have enough money to purchase alcohol until their peers encourage them to buy it.

SADQ scores of the 126 patients shows that 76 patients fall under mild dependence, 46 under moderate dependence and 4 under severe dependence.46 developed delirium while 80 did not develop delirium.

Factors found to have a positive association with the development of delirium was the severity of dependence, average use of alcohol the week prior to admission, past history of deaddiction treatment and past history of delirium tremens/seizures.

23 patients with mild dependence, 20 with moderate and 3 with severe dependence developed delirium, with a total of 46 out of the 126 going into delirium. From the results it can be inferred that as the severity of dependence increases, the chances of delirium increases which is evident as 26% ,50% and 75% of mild, moderate and severe dependence respectively going into delirium similar to the reports of Cushman and Griffin et al(21). Through the scores from SADQ we can assess the level of dependence in the patient. The results shows that 75% of the patients with severe dependence went into delirium , giving a positive correlation to this study that with the SADQ score we can predict the development of delirium. The result is statistically significant with a p value of 0.008 proving the hypothesis. There are studies about the clinical predictors of delirium by Palmstierna (22) . But in this study, only the symptoms of dependence were taken into consideration and finally proved to be significant in the development of delirium.

The chances of developing delirium increases with years of alcohol use and that too in dependence which is substantiated by the studies of Saitz et al(23).

64% of the patients with > 500ml of alcohol use went into delirium. This correlation was statistically significant with a p value of 0.04. This is in accordance to the studies by Cushman et al (24), Wojnar et al (25).

Becker et al (26) says that multiple detoxifications done through deaddiction programmes can lead onto increased sensitivity for withdrawal symptoms.56.3% of the patients had undergone detoxifications in the past in this study which makes them prone for withdrawal symptoms.

10. 76 % of the delirious patients had a history of deaddiction treatment in the past which is showing the importance of kindling , ie : increased sensitivity to withdrawal symptoms and complications due to multiple detoxification experiences as studied by Becker(27), Kraemer et al (25),Ballenger (28). This finding was statistically significant with a p value of 0.001 indicating the importance of taking into consideration deaddiction treatment in the past as a significant predictor of delirium/ seizure in the future. 56.4% of the patients, ie: 22 patients with a positive history of delirium tremens in the past went into delirium which shows that it is an important risk factor. Ferguson et al says that history of delirium tremens is one of the strongest predictor of complicated alcohol withdrawal syndrome in the future(27). According to Kraemer, self-reported

history of delirium tremens is an independent correlate of severe alcohol withdrawal syndrome (29). This is an important predictor for delirium and it was found to be statistically significant with a p value of 0.002.

The major limitation of the study is that the sample was selected from patients seeking treatment at a tertiary care hospital. It is likely that such patients have more severe dependence compared to the general population. Hence, the findings may not be generalized to patients in the community. Clinical parameters of the patients were not considered in assessing the risk factors for developing delirium which can very much contribute. Though the sample size was calculated to be 140, data collection and analysis could be done only in 126 patients in the set study period.

V. Conclusion

Development of delirium could be predicted from the SADQ scores which is a measure of the severity of alcohol dependence in patients with AUD.

Statistically significant association was found between development of delirium and SADQ score, average use of alcohol in the week prior to admission, past history of deaddiction treatment and past history of delirium tremens.

No statistically significant association was found between development of delirium and age of the patient, educational and occupational status, marital status, years of alcohol use, time since the last use of alcohol, medical comorbidities like HTN, CAD, TB, Asthma, family history of AUD and marital discord.

References

- [1]. World Health Organisation. The world health report 2002 - Reducing Risks, Promoting Healthy Life. 2002
- [2]. Hoffman P, Tabakoff B. Alcohol dependence: A commentary on mechanisms. Vol. 31. 1996. 333 p.
- [3]. Rehm J, Mathers C, Popova S, Thavorncharoensap M, Teerawattananon Y, Patra J. Global burden of disease and injury and economic cost attributable to alcohol use and alcohol-use disorders. *Lancet Lond Engl*. 2009 Jun 27;373(9682):2223–33.
- [4]. Rehm J, Zatonksi W, Taylor B, Anderson P. Epidemiology and alcohol policy in Europe. *Addict Abingdon Engl*. 2011 Mar;106 Suppl 1:11–9.
- [5]. Rehm J, Shield KD, Gmel G, Rehm MX, Frick U. Modeling the impact of alcohol dependence on mortality burden and the effect of available treatment interventions in the European Union. *Eur Neuropsychopharmacol J Eur Coll Neuropsychopharmacol*. 2013 Feb;23(2):89–97.
- [6]. Bagnardi V, Rota M, Botteri E, Tramacere I, Islami F, Fedirko V, et al. Light alcohol drinking and cancer: a meta-analysis. *Ann Oncol Off J Eur Soc Med Oncol*. 2013 Feb;24(2):301–8.
- [7]. Room R, Babor T, Rehm J. Alcohol and public health. *Lancet Lond Engl*. 2005 Feb 5;365(9458):519–30.
- [8]. WHO/Alcohol Factsheet 2015
- [9]. WHO Forum on Alcohol, Drugs and Addictive Behaviours :Global developments in alcohol policies: progress in implementation of the WHO global strategy to reduce the harmful use of alcohol since 2010
- [10]. Ray R. The extent, pattern and trends of drug abuse in Indian -National survey. Ministry of social justice and empowerment ,Government of India and United Nations office on drugs and crime .UNDOC.2004.,P.85-111
- [11]. WHO .WHO Regions country profile. Global status report on alcohol and health 2014. 2014 :166
- [12]. International institute for population services(IIPS) and Macro international. 2015-2016. National Family health survey(NFHS-4), India : kerala. Mumbai :IIPS
- [13]. Elholm B, Larsen K, Hornnes N, Zierau F, Becker U. Alcohol withdrawal syndrome: symptom-triggered versus fixed-schedule treatment in an outpatient setting. *Alcohol Alcohol Oxf Oxfs*. 2011 Jun;46(3):318–23.
- [14]. McKeon A, Frye MA, Delanty N. The alcohol withdrawal syndrome. *J Neurol Neurosurg Psychiatry*. 2008 Aug;79(8):854–62.
- [15]. Victor M, Brausch C. The role of abstinence in the genesis of alcoholic epilepsy. *Epilepsia*. 1967 Mar;8(1):1–20.
- [16]. Wetterling T, Kanitz RD, Veltrup C, Driessen M. Clinical predictors of alcohol withdrawal delirium. *Alcohol Clin Exp Res*. 1994 Oct;18(5):1100–2.
- [17]. Stockwell T, Murphy D, Hodgson R. The severity of alcohol dependence questionnaire: its use, reliability and validity. *Br J Addict*. 1983 Jun;78(2):145–55.
- [18]. Liang W, Chikritzhs T. Brief report: marital status and alcohol consumption behaviours. *J Subst Use*. 2012 Feb 1;17(1):84–90.
- [19]. Chaloupka FJ, Grossman M, Saffer H. The effects of price on alcohol consumption and alcohol-related problems. *Alcohol Res Health J Natl Inst Alcohol Abuse Alcohol*. 2002;26(1):22–34
- [20]. Mahal A What works in alcohol policy ? Evidence from rural India *Polit Wkly* 2000;35(45):3959-68
- [21]. Cushman P. Delirium tremens. Update on an old disorder. *Postgrad Med*. 1987 Oct;82(5):117–22.
- [22]. Palmstierna T. A model for predicting alcohol withdrawal delirium. *Psychiatr Serv Wash DC*. 2001 Jun;52(6):820–3.
- [23]. Saitz R, O'Malley SS. Pharmacotherapies for alcohol abuse. Withdrawal and treatment. *Med Clin North Am*. 1997 Jul;81(4):881–907.
- [24]. Marshal MP. For better or for worse? The effects of alcohol use on marital functioning. *Clin Psychol Rev*. 2003 Dec;23(7):959–97.
- [25]. Kraemer KL, Mayo-Smith MF, Calkins DR. Independent clinical correlates of severe alcohol withdrawal. *Subst Abuse*. 2003 Dec;24(4):197–209.
- [26]. Becker HC, Diaz-Granados JL, Hale RL. Exacerbation of ethanol withdrawal seizures in mice with a history of multiple withdrawal experience. *Pharmacol Biochem Behav*. 1997;57(1–2):179–83.
- [27]. Becker HC. Alcohol Dependence, Withdrawal, and Relapse. *Alcohol Res Health*. 2008;31(4):348–61.
- [28]. Ballenger JC, Post RM. Kindling as a model for alcohol withdrawal syndromes. *Br J Psychiatry J Ment Sci*. 1978 Jul;133:1–14.
- [29]. Duka T, Gentry J, Malcolm R, Ripley TL, Borlikova G, Stephens DN, et al. Consequences of multiple withdrawals from alcohol. *Alcohol Clin Exp Res*. 2004 Feb;28(2):233–46.