



CLINICAL RISK FACTORS ASSOCIATED WITH UNCOMPLICATED AND COMPLICATED WITHDRAWAL SYNDROME IN ALCOHOL DEPENDENT SYNDROME: A CROSS SECTIONAL COMPARATIVE STUDY

Psychiatry

Shashikala I M

Department of Psychiatry, K.Venkatramana Medical College and Hospital, Sullia, Dakshina Kannada, India.

Poonam M.

Department of Psychiatry, K.Venkatramana Medical College and Hospital, Sullia, Dakshina Kannada, India.

ABSTRACT

Background: The alcohol withdrawal is a period of significant clinical risk with high mortality. Identifying the factors which can predict the risk of developing complicated withdrawal can have preventive and therapeutic implications. Thus, the present study is aimed at identifying clinical risk factors associated with the development of complicated withdrawal. **Materials and Methods:** It was a cross-sectional comparative study conducted at a tertiary hospital from MAY- JUNE 2022. Fifty adult inpatients, diagnosed with alcohol dependence syndrome in withdrawal were divided into complicated and uncomplicated withdrawal groups. Socio-demographic and clinical data were collected. For group comparisons, Pearson's Chi-square test and independent sample t-test were used. **Results:** Age at onset of drinking ($P=0.027$), maximum units of drinking ($P=0.013$), and the presence of past history of withdrawal ($\chi^2=5.960$; $P=0.046$) emerged as strong predictors of complicated withdrawal. **Conclusion:** The risk factors found in this study can be easily evaluated by a clinician which helps in identifying patients at risk of developing complicated withdrawal and plan appropriate treatment for them.

KEYWORDS

Alcohol withdrawal syndrome (AWS), delirium tremens, alcohol withdrawal seizures, risk factors

INTRODUCTION

According to recent data published by the World Health Organization (WHO), the total per capita consumption of alcohol by individuals above 15 years of age is 6.2 L of pure alcohol per year, which equals 13.5 g of pure alcohol per day. However, there is a wide variation between the WHO regions and member states. Nearly 5.1% of the global burden of disease is attributable to alcohol consumption, and it causes nearly 3.3 million deaths every year¹. Alcohol-attributable deaths among men amounts to 7.7 % of all global deaths compared to 2.6 % of all deaths among women (WHO).

In alcohol-dependent drinkers, the central nervous system has adjusted to the constant presence of alcohol in the body (neuro-adaptation). When the blood alcohol concentration (BAC) is suddenly lowered, the brain remains in a hyper-excited state, resulting in the withdrawal syndrome. The presentation can be uncomplicated withdrawal and complicated alcohol withdrawal state i.e., delirium tremens and with or without convulsions (ICD10).

The mild withdrawal manifestations starts as early as 3 hours to 12 hours including Agitation/anxiety/irritability, nausea / vomiting/diarrhea, Sweating, Fever, Tachycardia, Systolic hypertension, General malaise and tremors which will reach Peak at 24-48 hours. And the complicated withdrawal i.e., generalized seizures usually presents at around 12-18 hours after the last drink while Delirium tremens occurs within 72- 96 hours after the last drink³. The usual causes of death in complicated AWS are hyperthermia, cardiac arrhythmias, complications of withdrawal seizures, or concomitant medical disorders.

This timeline for occurrence of symptoms of alcohol withdrawal provides us a window of opportunity to halt its progression to complicated alcohol withdrawal syndrome. The available literature documents various predisposing risk factors for complicated AWS e.g., advanced age of the patient, amount and duration of recent alcohol intake, history of withdrawal seizures/delirium tremens, abnormal liver function, co-existing infection, electrolyte abnormalities (e.g. hypokalemia, hypophosphatemia, hypomagnesemia, high blood urea nitrogen), raised mean corpuscular volume and carbohydrate deficient transferrin, low platelets, raised serum creatine phosphokinase levels or medical problems².

The aim of this study is to identify the clinical risk factors that are statistically significant and associated with alcohol withdrawal syndrome in an acute hospital setup population.

MATERIALS AND METHODS

A cross-sectional, observational study was conducted at the Department of Psychiatry in a tertiary care hospital-KVGMCH, Sullia from MAY- JUNE 2022. Ethics committee approval was obtained for

the study. The study population included males and females above 18 years of age who fulfilled the International Classification of Diseases (ICD-10) diagnostic criteria for alcohol dependence syndrome and were currently in the state of alcohol withdrawal at the time of admission. Patients not consenting to the study or having relatives who did not give consent to the patients' participation in the study, with pre-existing medical and surgical co-morbidities, and with other psychiatric disorders were excluded from the study. Total of 50 patients who fulfilled inclusion and exclusion criteria were taken up for the study. Then the patients were divided into two groups; Group A included uncomplicated alcohol withdrawal patients and Group B included patients who were diagnosed with complicated alcohol withdrawal (i.e., delirium and with or without convulsions) and, as per the ICD-10 diagnostic criteria. The socio-demographic data of cases were entered in semi-structured socio-demographic datasheet. And in the clinical datasheet history of amount of alcohol intake which was calculated with reference of one unit of alcohol is 10mL of ethanol or 1L of 1% alcohol, drinking pattern, duration of drinking, last drink, history of any other substance abuse, history of abstinence, present withdrawal state, history of withdrawal features were noted.

All the statistical analysis were performed using SPSS 21.0 version. The data collected in Groups A and B were subjected to statistical analysis with Pearson Chi-square test, t-tests. The P value below 0.05 was considered as significant.

RESULTS

The study included 50 alcohol dependent syndrome patients who belongs to Hindu religion from rural background and daily alcohol use pattern. Out of 50 patients, 31 presented in uncomplicated withdrawal and 19 were in complicated withdrawal state.

The demographic related history and past history of withdrawal status and other substance uses were compared between the two groups in Table 1. Past withdrawal status found to have significant association ($p=0.046$), among them 17 people presented first time with uncomplicated withdrawal and 5 with complicated withdrawal state.

Table 2 represents the comparison of clinical variables between uncomplicated and complicated AWS. The Age at onset of drinking among the complicated AWS was 21.26 ± 5.69 compared to uncomplicated withdrawals was 25.94 ± 7.73 ($p=0.027$). The amount of consumption among complicated withdrawal found to be 27.05 ± 14.91 units of alcohol per day and 16.55 ± 13.41 units per day in uncomplicated AWS ($P=0.013$). The duration of alcohol consumption was 16.63 ± 10.71 years in complicated AWS compared to 17.81 ± 12.14 years in uncomplicated ($P=0.730$). The total weeks of abstinence among the complicated withdrawals was 21.79 ± 21.98 and uncomplicated withdrawal was 37.29 ± 60.06 ($p=0.286$).

The age of onset of drinking and units of consumption found to have

significant association in this study. Though abstinence was not statistically significant, the longer abstinence was seen in uncomplicated withdrawal group.

Table 1: Comparison of socio-demographic factors and alcohol history

Sl. no	Variable	Alcohol withdrawal state Group A n (%) Uncomplicated	Group B n (%) Complicated	Person x2	P value
1.	AGE (years) 18- 35 36-55 >=56	9(29.0) 15(48.4) 7(22.6)	11(57.9) 5(26.3) 3(15.8)	4.160	0.125
2	Sex Male Female	28(90.3) 3(9.7)	18(94.7) 1(5.3)	0.312	0.577
3	Education Illiterate 1-10th std >= 11th std	4(12.9) 23(74.2) 4(12.9)	0(0.0) 16(84.2) 3(15.8)	2.673	0.263
4	Occupation Employed Unemployed	29(93.5) 2(6.5)	18(94.7) 1(5.3)	0.030	0.864
5	Marital status Married Unmarried Divorced/separated/widow	19(61.3) 7(22.6) 5(16.1)	10(52.6) 6(31.6) 3(15.8)	0.520	0.771
6	SES Upper class Middle class Lower class	1(3.2) 12(38.7) 18(58.1)	0(0.0) 6(31.6) 13(68.4)	0.983	0.612
7	Past withdrawal state Uncomplicated Complicated None	13(41.9) 1(3.2) 17(54.8)	8(42.0) 6(32.0) 5(26.0)	5.960	0.046
8	Other substance dependency Tobacco None	21(67.7) 10(32.3)	16(84.2) 3(15.8)	1.661	0.320

Table 2: Comparison of clinical variables

Sl.no	Variables	N	Mean $\pm$ SD	P value
1	Age of onset of drinking (years)			0.027
	Uncomplicated withdrawal	31	25.94 $\pm$ 7.73	
	Complicated withdrawal	19	21.26 $\pm$ 5.69	
2	Duration of alcohol use (years)			0.730
	Uncomplicated withdrawal	31	17.81 $\pm$ 12.14	
	Complicated withdrawal	19	16.63 $\pm$ 10.71	
3	Maximum units of alcohol/day			0.013
	Uncomplicated withdrawal	31	16.55 $\pm$ 13.41	
	Complicated withdrawal	19	27.05 $\pm$ 14.91	
4	Total abstinence period (weeks)			0.286
	Uncomplicated withdrawal	31	37.29 $\pm$ 60.06	
	Complicated withdrawal	19	21.79 $\pm$ 21.98	

DISCUSSION

In the present study, the study samples were selected after detailed evaluation of patients following their admission. Two groups were made depending on the state of withdrawal symptoms at the time of admission. The uncomplicated withdrawal group was followed up for minimum of 10days to check for emergence of delirium and withdrawal seizures, and if so, the patient was reassigned to the other group. Patients who could not initially give a proper history were later interviewed when out of delirium. Assessment of severity of withdrawal symptoms was done by using CIWA-Ar.

In this study, statistically significant differences were observed between the complicated and uncomplicated groups with respect to variables such as age of onset of drinking, maximum units of alcohol and past history of withdrawal symptoms.

This study showed the earlier age of onset of drinking is significantly

associated with complicated withdrawal contrast to previous studies, other studies showed no significant correlation⁴, this may be explained because of the amount of consumption of alcohol is more in younger age group in this study. And the higher units of alcohol consumption is statistically significant with association of complicated withdrawal finding is similar with previous studies^{6,7}. This confirms the explained pathophysiology of excessive quantities of alcohol consumption will up-regulates the N-methyl-D- aspartate receptors causing neuronal hyperexcitability and greater vulnerability for development of delirium and lowering of seizure threshold⁸.

Another significant association found was past history of withdrawal and this finding corroborate with results of previous studies^{10,11} which have found past history of DT and withdrawal fits to be consistent predictors of DT. The Pathophysiological basis of predicting complicated AWS can be explained by the phenomenon of 'kindling'. Kindling is a phenomenon in which a weak electrical or chemical stimulus, which initially causes no overt behavioral responses, results in the appearance of behavioral effects, such as seizures, when it is administered repeatedly. The existence of kindling during withdrawal suggests that even patients experiencing mild withdrawal should be treated aggressively to prevent the increase in severity of subsequent withdrawal episodes. Kindling also may contribute to a patient's relapse risk and to alcohol-related brain damage and cognitive impairment.¹².

The age of the patients was not a significant factor in predicting the complicated AWS in current study. This is in accordance with a number of previous studies, which found no association between age and complicated AWS¹³.

Our study focused on the importance of a relevant clinical history in predicting complicated withdrawal features, and thus early screening of patients with AWS may help to prevent them from developing subsequent withdrawal delirium and seizures. The present study highlights the importance of a focused and detailed clinical history in the treatment of alcohol withdrawal syndrome. The study limitations are smaller sample size and unequal socio- demographic variables distribution and 74% of them had tobacco dependence.

CONCLUSION

The complicated alcohol withdrawal syndrome includes seizures and delirium tremens are medical emergencies which can cause significant illness and death. The prediction of complicated alcohol withdrawal is an important part of alcoholism treatment to ensure to plan appropriate therapies in advance. This study reports that age of onset of drinking, amount of drinking and past history of withdrawal features are statistically significant clinical variables associated with complicated withdrawal. Therefore, goal of treatment in such cases should be prevention of emerging complicated withdrawal by identifying these risk factors followed by attentive medical management in hospital set up.

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