Orignal Article

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Prevalence of deviations in hematological and biochemical parameters in patients with Delirium Tremens

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Abstract

Introduction: Delirium Tremens (DTs) is an acute and severe form of alcohol withdrawal which if left untreated could lead to significant mortality. Identification of parameters which may lead to the progression of alcohol withdrawal to delirium tremens will aid in early initiation of appropriate treatment which in turn may help reduce the mortality rates. This study was undertaken to assess the prevalence of haematological and biochemical deviations in Delirium tremens and to assess the corelation between these deviations and severity of delirium tremens.

Materials and Methods: A cross-sectional research was carried out at a Tertiary Care Centre over 6 months. Confusion Assessment Method (CAM) tool was applied as a delirium screening tool for patient selection. After gaining consent, 89 patients who met the criteria for inclusion were enrolled. Demographic and clinical data of the patient was collected and laboratory investigations were recorded. Delirium Index (DI) was applied in conjunction with the Modified Mini-Mental State (3MS) Test as a cognitive screening tool. SPSS-PC -25 version was used for data analysis. The Shapiro-Wilk test was used to investigate normal distribution. The difference in means between the groups was investigated using student t-test or Mann-Whitney U-test. Qualitative data were expressed in frequency and percentage. Spearman correlation coefficient was used to see correlation between different quantitative parameters. Statistics were deemed significant at a $P < 0.05$.

Results: Male gender, older age, unemployment, anemia, thrombocytopenia, hyponatremia, hyperbilirubinemia and raised SGOT were identified as risk factors having a high prevalence in Delirium tremens. Anemia, hyponatremia, hyperbilirubinemia, and raised SGOT and ALP levels were identified as potential risk factors for worsening the severity of delirium tremens.

Conclusions: Assessment of demographic details and deviations in laboratory parameters helps in identification of risk factors for developing Delirium tremens aiding in early intervention which prevents the worsening of the severity of delirium.

Keywords: delirium, alcohol, delirium tremens, investigations, thrombocytopenia, hyponatremia

Introduction

According to ICD-11, Delirium Tremens (DTs) or Delirium induced by alcohol withdrawal is characterized by an acute state of disturbed attention and awareness with specific features of delirium that develops during or soon after alcohol intoxication or withdrawal.[1]

Clinical features of delirium include acute onset and fluctuating course; disturbance of consciousness, arousal, and awareness; disorientation; cognitive disturbances including memory impairment and executive dysfunction; perceptual disturbances; disorganized thinking; delusions; psychomotor agitation(hyperactive delirium); sleep-wakefulness cycle disturbances and disturbances in short-term memory.[1,2]

Delirium Tremens usually develops within 48-72h after cessation of alcohol with an average duration of 3-4 days but may last as long as 8 days.[2]

Approximately, 11.4% of patients in an alcohol withdrawal episode are reported to develop Delirium tremens, which indicates a high prevalence of DTs in patients with alcohol dependance.[3]

In India, a relatively higher mortality of 13.4% has also been reported in patients with DTs.[4]

Several risk factors and predictors for developing Delirium Tremens have been identified which include older age, heavier drinking pattern or higher units of alcohol consumed per day, past history of delirium tremens, lower education status and unemployment[5] as well as medical comorbidities such as Wernicke's Encephalopathy, liver diseases including alcoholic

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hepatitis, alcohol-induced cirrhosis and hepatic encephalopathy which are commonly present with alcohol use as well as cardiac diseases such as cardiomyopathy, ischemic heart disease and hypertension.[2]

Laboratory investigations implicated as predictors of delirium tremens include Low platelet count, hypokalaemia, high blood level of homocysteine, and low blood level of pyridoxine,[6] although research regarding the same in an Indian setting is limited.

In this study, we aim to assess the prevalence of deviations in haematological and biochemical parameters in patients with Delirium Tremens and the correlation between severity of Delirium Tremens and the deviations in haematological and biochemical parameters.

MATERIALS AND METHODS

Inclusion Criteria

Patients who were 18 years and above, admitted in a Tertiary Care Hospital, referred to Department of Psychiatry in Consultation-Liaison and diagnosed as Delirium Tremens or Delirium induced by Alcohol withdrawal (as per the ICD 11 criteria, 2019/2021), with a responsible caregiver providing written, informed consent for participation in study were included in the study.

Exclusion criteria

Patients not fulfilling the inclusion criteria, those who did not have a history of alcohol consumption, or patients whose caregivers were not willing to give an informed consent were excluded from the study.

Data collection

Data collected included:

Sociodemographic profile of patient: (a) Age, (b) gender, (c) education level, (d) employment status, (e) marital status, (f) history of substance consumption (g) Laboratory investigations - Serum Sodium, Hemoglobin, White Blood Cell (WBC) Count, Platelet count and Liver function tests (Total Bilirubin, SGOT/AST, SGPT/ALT and Alkaline phosphatase)

Instruments used

1]The Confusion Assessment Method (CAM) is a standardized delirium screening tool which includes 4 items for the following core features: Acute Onset & Fluctuating Course; Inattention; Disorganized Thinking and Altered Level of Consciousness. Delirium scored as 'present' (1) or 'absent' (0) based the CAM algorithm: presence of acute onset or fluctuating course AND inattention AND EITHER disorganized thinking OR altered level of consciousness. The CAM Long form includes 6 additional items to assess the presence of the following: Disorientation; Memory Impairment; Perceptual Disturbances; Psychomotor Agitation and Retardation and Altered Sleep-Wake Cycle.[7,8]

2] The Modified Mini-Mental State (3MS) Test is a screening tool for cognitive functioning that assesses attention, concentration, orientation, memory, language ability, constructional praxis, abstract thinking, and verbal fluency.[9]

3]Delirium Index (DI) is an observational delirium severity scale which consists of 7 items to assess severity of disturbance in attention, thought, consciousness, orientation, memory, perception, and psychomotor activity. Each item is scored on a scale from 0 (absent) to 3 (present and severe) with total scores between 0-21 with higher scores indicating higher severity.[10,11]

Methodology

This research was cross-sectionally carried out in patients in the inpatient setting of a Tertiary Care Centre over 6 months. Prior approval by the Institutional ethics committee was obtained.

Confusion Assessment Method (CAM) tool was applied as a delirium screening tool for patient selection as per inclusion criteria. 89 patients who met the criteria for inclusion were enrolled in the study after obtaining a written informed consent by a responsible caregiver. Demographic and clinical data of the patient, including detailed substance history was collected using a semi-structured proforma. Laboratory investigations-Serum Sodium, Hemoglobin, White Blood Cell (WBC) Count, Platelet count and Liver function tests (Total Bilirubin, SGOT/AST, SGPT/ALT and Alkaline phosphatase) were recorded. To assess the severity of delirium, Delirium Index (DI) was applied in conjunction with the Modified Mini-Mental State (3MS) Test as a cognitive screening tool.

Data and statistical analysis:

The collected data were transformed into variables, coded and entered in Microsoft Excel. Data were analysed and statistically evaluated using SPSS-PC-25 version.

Normal distribution of different parameters was tested by the Shapiro-Wilk normality test. Quantitative data was expressed in mean±standard deviation and difference between mean of two groups were compared by Mann Whiney U test. Qualitative data were expressed in frequency and percentage. Spearman correlation coefficient was used to see correlation between different quantitative parameters. P' value less than 0.05 was considered statistically significant.

RESULTS AND DISCUSSION

89 patients diagnosed with Delirium Tremens were included in the study out of which (n=87) 97.75% were Males and (n=2) 2.25% were Females, showing a significant male preponderance in patients. (Figure 1) The mean age of patients at the time of presentation was 46.9±13.5 years. (Figure 2) More than half of the patients were married (n=62; 69.6%) and were unemployed/homemakers (n=47; 52.8%). Less than half of the patients belonged to rural backgrounds (n=39;43.8%) and about one-third patients had received education (n=31; 34.8%). (Figure 3)

A study conducted in Spain showed similar findings of a mean age of 54.5 years and male gender having a prevalence of 90.8% in patients studied with Delirium tremens.[12] Previous studies have also reported the significance of both unemployment and lack of education as significant predictors of Delirium tremens.[5] These findings reiterate the significance of sociodemographic history in identifying the risk of progression of alcohol withdrawal to delirium tremens.

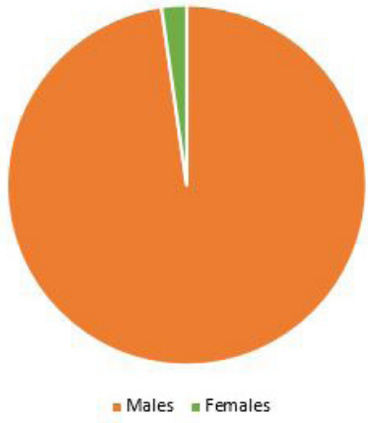

Figure 1 : Percentage-wise distribution by of the patients by gender.

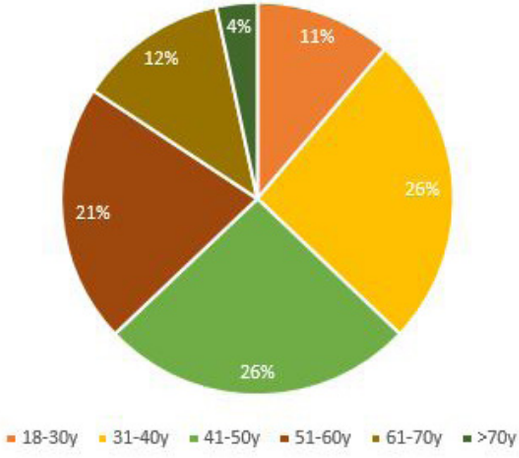

Figure 2 : Percentage-wise distribution by of the patients by age.

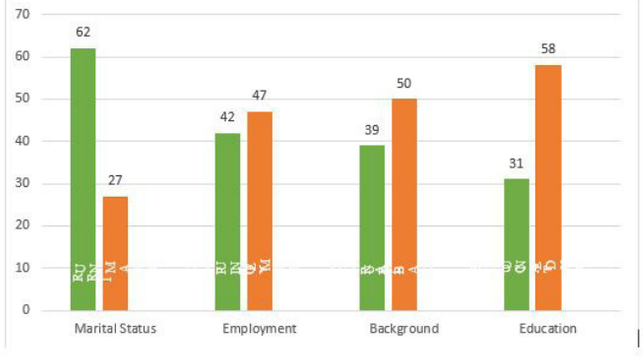

Figure 3: Distribution of sociodemographic data of patients

On applying the Delirium Index to patients included in the study, the items most affected were found to be Attention, closely followed by Orientation and the item least affected was Psychomotor Activity. (Figure 3)

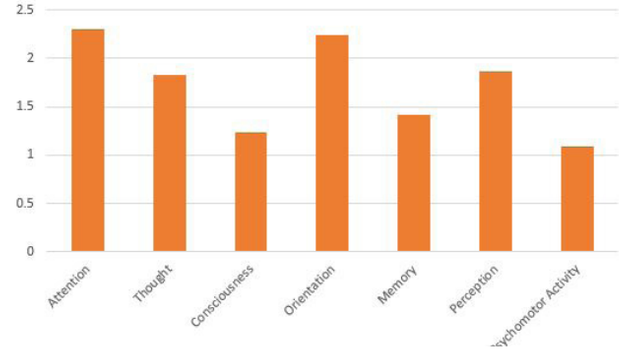

Figure 4: Items affected in Delirium Tremens as per Delirium Index.

Laboratory Investigations of patients were recorded and analyzed. (Table 1) A significantly high percentage of patients having Delirium Tremens were found to have Low hemoglobin or anemia (n=63, 70.8%), raised Total Bilirubin (n=60, 67.4%) and raised SGOT (n=71, 79.8%). Almost half of the patients had Hyponatremia (n=47, 52.8%) and a low platelet count (n=38, 42.7%) (Table 2)

Among the hematological parameters, the high prevalence of low platelet count found in this study is consistent with the findings of previous studies implicating thrombocytopenia as a risk factor for development of severe Delirium tremens.[6,13] Low hemoglobin or Anemia having a significantly high prevalence in Delirium tremens is a finding unique to this study and has not been reported or studied previously.

Among the biochemical parameters, hyponatremia has been observed to have a high prevalence in patients with severe delirium, a finding replicated in this study as well.[14] Other serum electrolytes such as hypochloridemia have also been reported in other studies as risk factors for delirium.[6,14] Deviations in liver function tests, especially ALT have been prominent across the literature on Delirium tremens, as shown by a meta-analysis conducted in 2014[15] in addition to which a high prevalence of raised Serum gamma-glutamyl transferase (GGT) has also been reported in various studies.[12-14]

Table 1: Lab profile found in study subjects (n=89)

	SODIUM (mmol/L)	Hb (gm/dl)	WBC (cells/µL)	PLATELET (cells/µL)	T.BILI (mg/dl)	SGOT (mg/dl)	SGPT (mg/dl)	ALP (U/L)
Mean	133.83	11.496	9.304	162.67	4.901	111.55	60.36	110.58
SD	6.163	2.9068	5.3328	86.294	8.1744	93.676	52.031	54.060
Median	134.00	11.100	8.400	151.00	2.100	94.00	47.00	92.00
IQR	130-137.5	9.3-13.35	5.9-11.3	97.5-218.5	1.05-4.15	43.5-150.5	25.5-79	73-131.5
Minimum	121	4.6	2.2	15	.2	14	6	37
Maximum	154	20.6	36.2	438	45.2	592	286	259

Table 2: Deviations in lab profile found in patients (n=89)

	No. of patients	%
Hyponatremia	47	52.8
Hypernatremia	3	3.4
Low Hb	63	70.8
Raised Hb	2	2.2
Low WBC	7	7.9
Raised WBC	24	27.0
Platelets <150	38	42.7
T. bilirubin >1.3	60	67.4
SGOT >40	71	79.8
SGPT >40	50	56.2
ALP >126	24	27.0

Correlation between laboratory profile of patients and higher severity of Delirium Tremens using the Delirium Index (DI) score was studied using the Spearman correlation coefficient. (Table 8)A statistically significant positive correlation was seen between higher severity of Delirium Tremens and Hyponatremia (Table 3), Hyperbilirubinemia (Table 5), raised SGOT levels (Table 6) and raised ALP Levels (Table 7).A statistically significant negative correlation was seen between higher severity of Delirium Tremens and Hb levels indicating a correlation between Anemia and severity of DTs. (Table 4) This finding is supported by a study conducted in 2010 which reported that anemia was associated with an increase in the risk of mortality.[17]

Table 3: Association between severity of delirium tremens with Sodium level in patients

	Patients with normal Sodium levels	Patients with deranged Sodium levels	p value
Total score on DI	12.26±2.64	13.81±3.18	0.01

Table 4: Association between severity of delirium tremens with Hb level in patients

	Patients with normal Hb levels	Patients with deranged Hb levels	p value
Total score on DI	12.0±3.07	13.48±2.93	0.04

Table 5: Association between severity of delirium tremens with T. Bilirubin level in patients

	Patients with normal T. Bilirubin levels	Patients with raised T. Bilirubin levels	p value
Total score on DI	9.93±1.79	14.60±2.21	<0.001

Table 6: Association between severity of delirium tremens with SGOT level in patients

	Patients with normal SGOT levels	Patients with raised SGOT levels	p value
Total score on DI	11.17±2.59	13.56±2.95	<0.01

Table 7: Association between severity of delirium tremens with ALP level in patients

	Patients with normal ALP levels	Patients with raised ALP levels	p value
Total score on DI	12.57±3.06	14.46±2.50	<0.01

Table 8: Correlation between severity of delirium tremens with lab profile in patients (n=89)

		Total score
Sodium	r value	-.147
	p value	.171
	n	89
Hb	r value	-.258
	p value	.015
	n	89
WBC	r value	-.156
	p value	.146
	n	89
Platelets	r value	-.148
	p value	.166
	n	89
Total Bilirubin	r value	.849
	p value	.000
	n	89
SGOT	r value	.309
	p value	.003
	n	89
SGPT	r value	.102
	p value	.342
	n	89
ALP	r value	.398
	p value	.000
		89

CONCLUSION

Delirium Tremens is a severe form of alcohol withdrawal with a significant mortality as high as 13.4%.[4] Delay in treatment of Delirium tremens potentially increases the risk of development of complications like respiratory depression, arrythmias and cardiogenic shock, liver dysfunction or autonomic hyperactivity which may increase the morbidity and mortality.[16,17] Hence, identifying laboratory parameters which help as predictors of developing DTs as well as identifying risk factors in the patient's sociodemographic profile may help in early identification and management.

The present study observed socio-demographic parameters such as male gender, older age, and unemployment, as well as investigative parameters such as anemia, thrombocytopenia, hyponatremia, hyperbilirubinemia and raised SGOT as factors having a high prevalence in patients of Delirium tremens. This study also observed investigative parameters such as anemia, hyponatremia, hyperbilirubinemia,

and raised SGOT and ALP levels as potential risk factors for worsening the severity of delirium tremens as indicated by higher scores on the Delirium Index (DI).

Hepatic dysfunction in alcohol dependence, as evidenced by the raised bilirubin and liver enzymes in this study, is due to both the primary hepatotoxicity of alcohol as well as secondary factors such as thiamine and other nutritional deficiencies and metabolic disturbances leading to progressive fibrosis known as alcoholic liver cirrhosis along with other hepatic conditions such as chronic hepatitis and hepatocellular carcinoma.[18] Alcoholic liver cirrhosis, in its severe form, may lead to hepatic encephalopathy causing brain dysfunction further predisposing the patient to developing Delirium tremens.

18 Similarly, thrombocytopenia in delirium tremens has also been reported to be mediated by the toxic effects of alcohol on the bone marrow reducing the platelet production.[19]
Several hypotheses have been suggested for the development of hyponatremia in Delirium tremens, although the actual mechanism is poorly understood. Studies have suggested that the imbalance in vasopressin caused by ethanol leads to hyperhydration in chronic alcoholics leading to hyponatremia and other electrolyte imbalances.[14] If untreated, electrolyte imbalances may lead to arrythmias and cardiovascular collapse increasing the risk of mortality in Delirium tremens.[17]

Presence of medical comorbidities and deviations in laboratory parameters also affect the selection of drugs and titration of their doses while treating Delirium tremens. The present study reiterates this significance of medical comorbidities like hepatic impairment and electrolyte imbalance as a risk factor for progression of alcohol withdrawal to severe Delirium Tremens and stresses the importance of assessment of laboratory parameters and the prevalence of their deviations as an essential part of the treatment plan.

ABBREVIATIONS
DI – Delirium Index
DTs - Delirium Tremens
SGOT - Serum glutamic oxaloacetic transaminase
SGPT - Serum glutamate pyruvate transaminase
AST – Aspartate aminotransferase
ALT – Alanine aminotransferase

LIMITATIONS OF THE STUDY

The present study had a few limitations. It was conducted in a small sample limited to patients referred in consultation-liaison psychiatry. Thus, the results cannot be generalized to other group of patients. Future studies should attempt to overcome these limitations.

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