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Liver Function and Platelet Count as an Early Correlate of Delirium Tremens in Patients of Alcohol Dependence Syndrome Admitted in Rehabilitative Care Center

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ABSTRACT

The utility of several laboratory parameters as possible risk factors/predictors for severe AWS has also been investigated. It is extremely important for clinicians to be able to identify individuals at high risk for developing a severe AWS. The study was conducted in tertiary psychiatry center. The first group consists of simple withdrawal and the second group consists of complicated withdrawal with delirium. Socio-demographic details were collected using a semi-structured proforma, results of basic biochemical tests including platelet count and liver function tests (Total Bilirubin, Direct Bilirubin, Indirect Bilirubin, AST, ALT, AST//ALT ratio, GGT) which were performed as a routine in the management of alcohol withdrawal were collected for the study. A total of 402 patients were included in the study. Nearly 26.1% of patients had thrombocytopenia. 43.58% of patients with thrombocytopenia had delirium. 38.3% of patients had total bilirubin more than 1.3 mg/dl of which 44.44% had delirium. About 66.7% of patients had SGOT more than 40IU. 61.5% of patients with higher SGOT levels had delirium. 85.8% of patients had GGT more than 32IU and 87.17% of them had delirium. Platelet counts were significantly lower in patients with delirium/altered sensorium ($p = 0.00$). Further studies can try to elaborate the evidence with larger sample sizes and can also try to assess if these parameters have any role in precipitation of alcohol withdrawal into Wernicke's encephalopathy and Korsakoff's psychosis.

INTRODUCTION

According to the 2019 survey in India, 2.7% of the population is dependent on alcohol which is nearly equal to 2.9 crore people. These people constitute around 18.5% of total alcohol users in India[1]. The alcohol withdrawal syndrome (AWS) occurs in alcohol dependent individuals who abruptly reduce or discontinue their alcohol consumption. The most severe manifestations of the AWS are alcohol withdrawal delirium/ delirium tremens (DT)) and/or seizures. DT occurs 72-96 hours after the last drink.2 DT has been estimated to occur in 5-20% of the individuals who undergo treatment for alcohol withdrawal. Patients with delirium tremens have a high mortality of 20-50% without treatment and 5-10% with treatment[2]. To prevent severe AWS and thus, DT, it is extremely important for clinicians to be able to identify individuals at high risk for developing a severe AWS. In several studies, possible risk factors/predictors for the development of a severe AWS have been investigated. The utility of several laboratory parameters as possible risk factors/predictors for severe AWS has also been investigated.

Berggren *et al*. in tried to evaluate low platelet count as a predictor for the development of delirium tremens in patients with alcohol withdrawal symptoms. They assessed 334 participants and 10 among them developed delirium. 70% of the patients with delirium tremens had thrombocytopenia and it had positive predictive value of 6% and negative predictive value of 99%, with 70% sensitivity and 69% specificity[3]. Eyer *et al*. in tried to frame a model which predicts complicated alcohol withdrawal (withdrawal seizures and delirium tremens) in patients who were having moderate/severe withdrawal symptoms. 827 participants were recruited for the study. Their results showed that lower potassium levels (p = 0.001), lower platelet count (p = 0.001), and prevalence of structured brain lesions (p<0.001) were significant predictors of delirium tremens[4].

Monte *et al*. in tried to evaluate the associations between different clinical variables and delirium tremens in patients with alcohol withdrawal symptoms. They compared 156 patients without DT and 147 patients with DT. The statistical analysis was done with a multi variate logistic regression model. They found that the number of seizures, systolic blood pressure >150 and axillary temp >38 degree Celsius were significant predictors of delirium tremens[5]. Though there have been studies associating low platelet count as predictor for the delirium tremens there is dearth of studies in the Indian population which is why this study was taken up to gather the evidence in this area.

MATERIALS AND METHODS

The study was conducted in tertiary psychiatry center during the period from 1st July 2017 to 31st December 2017. The ethical committee clearance was obtained. All the patients fulfilling the inclusion criteria during the study period were included in this study.

Inclusion Criteria: All in-patients admitted with alcohol-related problems were screened for this study and were enrolled in the study if they fulfilled the following inclusion criteria.

- Patient of age 18 years and above
- A patient who fulfills criteria for alcohol dependence currently in withdrawal according to ICD-10
- Patient or their Nominated representative/informant/family member willing to give written informed consent

Exclusion Criteria: Subjects with any of the following were not included in the study:

- History of any major illness requiring intensive medical/surgical intervention
- Comorbid substance use except tobacco

The detailed information about the design and nature of the clinical study was explained to the patients and their family members/informants. Informed consent was obtained. All patients were first examined by consultant Psychiatrist to confirm the diagnosis of alcohol dependence with the current withdrawal state and they were divided into two groups. The first group consisted of simple withdrawal and the second group consisted of complicated withdrawal with delirium. Delirium was diagnosed when the patients had clinical manifestations of altered sensorium with perceptual abnormalities. Socio-demographic details were collected using a semi-structured proforma, results of basic biochemical tests including platelet count and liver function tests (Total Bilirubin, Direct Bilirubin, Indirect Bilirubin, AST, ALT, AST//ALT ratio, GGT) which were performed as a routine in the management of alcohol withdrawal were collected for the study. All the patients were given appropriate care according to the severity of withdrawal symptoms. The patients were detoxified with tapering doses of lorazepam with appropriate doses of thiamine according to the severity of withdrawal. Other symptomatic treatment was given to patients who needed it. Thrombocytopenia was defined as platelet count less than 1.5lakhs.

Impaired liver function tests were defined as total bilirubin, indirect bilirubin, direct bilirubin, SGOT, SGPT and GGT more than 1.3 mg/dl, 1 mg/dl, 0.3 mg/dl, 40 IU, 40 IU and 32 IU respectively. Statistical analysis was done using SPSS version 25. Socio-demographic and other study variables were analyzed using number and percentage for categorical variables, mean and standard deviation for continuous variables. Among

Table 1: Frequency distribution of study variables between two groups

Study variable	Delirium present	absent
1.Platelet count		
< 1.5	>1.5	51
66	54	231
2. Total Bilirubin		
<1.3	>1.3	65
52	183	102
3. Indirect Bilirubin		
<1	>1	78
39	205	80
4. Direct Bilirubin		
<0.3	>0.3	47
70	146	139
5. SGOT		
<40	>40	45
72	89	196
6. SGPT		
<40	>40	62
55	117	168
7. GGT		
<32	>32	15
102	42	243

Table 2: Comparison of study variables between two groups using Unpaired t-test

	Without DT Mean (SD)	With DT Mean (SD)	p-value
Age	39.82 (9.16)	42.56(9.33)	0.88
Total Bilirubin	1.43 (3.29)	1.63(1.31)	0.83
Indirect Bilirubin	1.15 (4.26)	1.04(0.63)	0.314
Direct Bilirubin	0.59 (1.86)	0.59(0.81)	0.2
SGOT	83.2(91.7)	104.7(124.22)	0.006
SGPT	66.95 (79.95)	72.66(110.1)	0.25
AST/ALT	1.32 (0.67)	1.44(1.004)	0.001
GGT	221.45 (368.19)	268.42(380.14)	0.312

p<0.05 is significant

the different variables, platelet count was normally distributed in both groups and unpaired t-test was used to compare them. Mann-Whitney U test was used to compare all other variables.

RESULTS AND DISCUSSIONS

This is a cross sectional study conducted in a tertiary psychiatry center in Bangalore, Karnataka. This was done to assess if liver function tests and platelet count act as predictor or early correlation for delirium tremens in patients with alcohol withdrawal. A total of 402 patients were included in the study. The average age of presentation was 40.94±9.32 years. Only three female participants were there in 402 patients. Among 402 patients, 285 (70.9%) patients belonged to the 1st group without delirium tremens and 117 (29.1%) belonged to the 2nd group with delirium tremens. (Table 1) depicts the frequency distribution of various study variables in the two groups. Nearly 26.1% of patients had thrombocytopenia. 43.58% of patients with thrombocytopenia had delirium. 38.3% of patients had total bilirubin more than 1.3 mg/dl of which 44.44% had delirium. About 66.7% of patients had SGOT more than 40IU. 61.5% of patients with higher SGOT levels had delirium. 85.8% of patients had GGT more than 32IU and 87.17% of them had delirium. Platelet counts were significantly lower in patients with delirium/altered sensorium (p = 0.00).

This study to evaluate low platelet count and liver function tests as a predictive factor for development of delirium tremens was a cross sectional study conducted in tertiary psychiatry center, Bengaluru. Patients who were admitted in the ward for alcohol dependence currently in withdrawal were recruited for the study. Altered sensorium patients were considered under the group of delirium tremens and other patients were included in the second group. Blood parameters were assessed and analyzed for the study. In our study, 29.1% admitted with alcohol withdrawal developed delirium tremens which is quite similar to Kim *et al*. where the prevalence of delirium was 35.1%[6] but is less compared to study by Kalayasiri who reported delirium in 58.5% of patients[7]. This may be because the patients with mild or moderate alcohol dependence who were admitted for psychosocial interventions were also recruited in our study. Kim et al. also showed low platelet count as a significant risk factor for the prediction of delirium tremens with high diagnostic sensitivity and specificity[6]. Our study showed similar results where low platelet count was present in patients with DT and the difference between two groups was significant(p = 0.00). Nearly 26.1% of patients had thrombocytopenia. 43.58% of patients with thrombocytopenia had delirium. These findings are comparatively lower to findings by Berggren *et al*. which showed that 70% of the patients with delirium tremens had thrombocytopenia[3].

Possible reasons could be the toxic influence of alcohol on the bone marrow resulting in reduced

platelet production[8]. Platelet count difference in two groups was found to be statistically significant with p=0.00 in our study. This finding was similar to Monte *et al*. in who compared platelets in patients with DT and without DT and this difference was statistically significant with p = 0.007[5]. This finding was similar to the study by Harshe *et al*. who reported that the platelet count was comparatively less in the group of delirium tremens than group without delirium. Harshe et al. also followed up on platelet count and it was seen that platelet count showed gradual increase from baseline till 10th day of alcohol withdrawal[9]. The difference in AST and AST/ALT ratio between two groups were statistically significant with p values of 0.006 and 0.001 respectively. This finding was similar to Borah *et al*. in who tried to assess the levels of serum sodium, potassium, magnesium and chloride and liver enzymes and compared their levels in patients with and without delirium. 50 cases in each group were compared. The difference in AST in between two groups was statistically significant with p values of 0.027, however the difference in GGT in between two groups was not statistically significant. The difference between serum potassium and magnesium between two groups was statistically significant with p values of 0.037 and 0.017 respectively[10].

Kalayasiri *et al*. in tried to determine prevalence of delirium tremens in university hospital and tried to find associated factors with delirium tremens. The laboratory parameters which had statistically significant association with delirium tremens were levels of bicarbonate, creatinine and AST. Our study also showed significant association with AST. Unlike our study there was no significant association between platelet count, total bilirubin and delirium tremens in this study[7].

CONCLUSION

Early assessment of liver function and platelet counts can thus help in early recognition of severe AWS and intervention at the earliest, thus decreasing the morbidity and mortality associated with DT. These parameters can also be utilized for psycho education of the patient and their care givers to make them understand the severity of alcohol withdrawal and anticipate the complications. This is one of the few studies in India which have tried to analyze the laboratory parameters as a predictors for development of delirium tremens, however, there are some limitations to this study. Our sample size was small. Another limitation in this study is the number of female patients, which was too low to allow conclusions on gender effects. Further studies can try to elaborate the evidence with larger sample sizes and can also try to assess if these parameters have any role in precipitation of alcohol withdrawal into Wernicke's encephalopathy and Korsakoff's psychosis.

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