



## TITLE OF THE MANUSCRIPT: “FACTORS ASSOCIATED WITH DELIRIUM TREMENS-A CROSS SECTIONAL STUDY”

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### ABSTRACT

**Background:** Delirium Tremens (DT) a severe complication of alcohol dependence occurring in approximately 5-20% of patients and has high morbidity and mortality. Research till date has showed various clinical, laboratory and drinking related variables as risk factors for DT but there is always a question of what makes certain individuals vulnerable for DT.

**Aim:** The current study aims to look at the factors associated with delirium tremens among inpatients with DT.

**Methods:** A total of 63 patients presenting with Delirium tremens in Drug naïve state were included in the study after excluding other causes of delirium. Blood samples were collected after obtaining informed consent to estimate Serum electrolyte levels, bilirubin, liver enzymes, platelet counts and mean corpuscular volume before initiating treatment. CIWA-Ar and SADQ were administered.

**Results:** Mean & standard deviation values of different parameters are observed as; serum sodium ( $141.26 \pm 4.49$ ), serum potassium ( $3.43 \pm 0.546$ ), serum chloride ( $100.69 \pm 4.43$ ), serum calcium ( $9.02 \pm 0.87$ ) and serum magnesium ( $2.03 \pm 0.57$ ). Mean CIWA-Ar score was  $18.5 \pm 4.88$ . There was a positive correlation between severity of alcohol dependence and severity of alcohol withdrawal (p-value 0.000).

**Conclusion:** The present study has shown that few delirium tremens patient have a considerable number of changes in serum electrolytes, liver enzymes, bilirubin, platelet counts and MCV levels but no statistical significance was found when compared among different age and CIWA-Ar cluster groups. Serum SGOT levels of DT patient is significantly high especially in younger age group.

**Keywords:** Delirium Tremens, Serum electrolytes, Severity of alcohol dependence, Severity of alcohol withdrawal.

## INTRODUCTION

Alcoholism is among the most common psychiatric disorders observed in the western world. Alcohol is a potent drug that causes both acute and chronic changes in almost all neurochemical systems and it can cause serious psychological symptoms including depression, anxiety and psychosis. Long term, escalating levels of alcohol consumption can produce tolerance and cessation of use can precipitate a withdrawal syndrome usually marked by insomnia, feelings of anxiety and hyperactive autonomic nervous system.<sup>1</sup>

Alcohol use is associated with tolerance and progressive increased consumption has led to various physical, psychological and social problems. Alcohol dependence is one of the many manifestations and is still elusive in terms of its causation as why only few people get dependent and develop complications like delirium tremens and seizures. Research in this field has helped us understand some risk factor and vulnerability of certain people to develop dependence and its complications, but much research is still required. Although mild withdrawal symptoms like insomnia and tremors are seen, a substantial proportion of patients develop more severe symptoms like seizures and delirium tremens.<sup>2</sup>

Delirium tremens (DT) or alcohol withdrawal delirium (AWD) is a severe complication of alcohol dependence and it occurs in approximately 5-20% of patients who develop withdrawal and is associated with high morbidity and mortality rate.<sup>2</sup> DT is a short lived, but occasionally life threatening, toxic confusional state with accompanying somatic disturbances. It is usually a consequence of absolute or relative withdrawal of alcohol in severely dependent patients with a long history of use. Onset may also be preceded by withdrawal convulsions and prodromal symptoms like insomnia, tremulousness and fear.<sup>3</sup>

Research till date has implicated various clinical, laboratory and drinking related variables as the risk or predictive factors for developing DT. There is always a question of what makes certain individuals vulnerable to a severe withdrawal state as compared to others. The current study aims to look at various factors like levels of serum electrolytes, bilirubin, liver enzymes, platelet count and mean corpuscular volume among patients with delirium tremens and to find the relationship between severity of alcohol withdrawal and these laboratory parameters.

## MATERIALS AND METHODS:

It was a cross-sectional observational study conducted in the Department of Psychiatry after the ethical approval from the institution. The study period was one and a half year from December 2019 to October 2021.

Sample was taken from a tertiary care teaching hospital where all cases of DT presenting to hospital in drug naïve state fulfilling the criteria mentioned below were taken.

### Inclusion Criteria

1. Patients who presented to OPD/casualty with delirium tremens and willing for admission.
2. Age between 18 to 65 years of both sexes.
3. Patients &/or caregiver who agreed for the study and gave informed consent for the study.
4. Cases who met DSM 5 criteria<sup>4</sup> for alcohol withdrawal delirium.

### Exclusion criteria

1. Early discharge before delirium resolves.
2. Delirium due to other causes- sepsis, stroke, head injury, neuro-infections, toxic ingestion or exposure, thyrotoxicosis, diabetic ketoacidosis, hepatic encephalopathy, seizure disorder, renal disorders and metabolic acidosis.
3. Benign or malignant brain tumour, head injury or neurosurgical interventions, blood dyscrasias in the past will be excluded from the study.
4. Patients who presented with alcohol withdrawal seizures.
5. Pre-existing illness known to cause electrolyte changes like uncontrolled diabetes mellitus, uncontrolled hypertension, parathyroid disorders, renal disorders, pancreatitis due to other causes

except alcohol and patients on drugs like diuretics, laxatives or antacids as per the assessment of the treating physician.

6. Other substance use disorders other than tobacco.

7. Patients testing positive for COVID-19.

Sample size-

Sample size calculated using the formula: -

$$n = \frac{Z^2 \sigma^2}{\epsilon^2 \mu^2}$$

Mean and SD were 3.17 and 0.611 respectively.<sup>5</sup>

$$= 3.84 \times (0.611)^2 / (0.05)^2 \times (3.17)^2$$

Minimum sample is estimated to be 60.

All patients presenting to casualty/Psychiatry OPD with history and clinical examination suggestive of alcohol withdrawal delirium fulfilling DSM 5 criteria<sup>4</sup> were taken. After obtaining written informed consent from the attender &/or patient for the study, sociodemographic details and clinical data were collected using semi structured proforma. Blood was collected from intravenous route in drug naive status, at first contact of patient to the hospital (before administering thiamine, fluids, benzodiazepines) and estimation of serum electrolytes (Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, Mg<sup>2+</sup>, Ca<sup>2+</sup>) bilirubin, hepatic enzymes, platelets and MCV was done at clinical biochemistry and hematological laboratory of the hospital. To rule out other cause of delirium detailed history and examination, relevant investigations and neuroimaging was done. Clinical Institute Withdrawal Assessment of Alcohol Scale, revised scale (CIWA-Ar)<sup>6</sup> was applied every day to see the severity of alcohol withdrawal (CIWA <8) until no or minimum withdrawal symptoms persists. Severity of alcohol dependence (SAD-Q) was applied after recovery before discharging the patient from hospital.

## RESULTS

Forty three percent (43%) of the subjects were between 41-50 years, 23.8% of our patients were above 50 years. Mean age of our subjects was 44 ± 9.74 years. Men constituted 95.23% of the sample. 85.7% were from rural area and belonged to Hindu religion. 63.49% were married and 20.63% were unmarried. Most of them were educated, 33.3% had studied up to high school and 35% had a degree. Only 3.17% of the subjects were unemployed and 38.09% of them had their income between 3,908-11,707 per month. 46.03% of them belonged to lower middle socioeconomic status & 36.5% to upper lower according to Kuppuswamy system of classification. 87.3 % of patients were living with their family and 84.12% had a nuclear family.

It was found that 43.47% of patients started consumption of alcohol due to peer pressure and around 37.68% started because of curiosity. Craving (55.42%) followed by withdrawal symptoms (22.89%) and coping with stress (18.07%) where the factors associated with maintenance of alcohol consumption. Average units of alcohol consumed per day by 71.04% of patients were between 11-30units. Mean years of alcohol consumed by the patients were 22.52 ± 9.21 years, 39.68% of patients had been consuming alcohol for 16-25years and 26.9% for around 5-15years. 63.49% of patients usually drank alone at their houses while 26.9% consumed alcohol in the company of their friends. 55.55% had regular pattern of consumption of alcohol while 39.68% had regular with bingeing pattern of alcohol consumption. Brandy (42.85%) followed by whiskey (30.15%) was the most common beverage consumed by the patients. 49.2% of the sample consumed both tobacco and alcohol.

Mean age of onset of alcohol drinking was 21.63 ± 5.1, around 79.36% of the patients started drinking before 25 years and 23.8% of patients had past history of withdrawal seizures but patients presenting with current history of withdrawal seizures and/or developing seizures following admission to the hospital were excluded from the study. Mean hours from last consumption of alcohol to presentation to hospital is 56.95±37.84 hours (2.37±1.57 days). 38.09% of patients presented to hospital with delirium tremens 48hours after last consumption of alcohol and 30.15% of them presented between 25-48hours of last consumption of alcohol. 7.93% of patients had diabetes mellitus and hypertension, 12.69% of patients had hypertension but were in well controlled state with medications. Family history of medical/psychiatric illness had more than one response in most of the patients, 16.04% had family h/o chronic medical conditions like diabetes mellitus and hypertension, 58.02% of them had

family history of alcohol consumption among first degree relatives. 9.87% of patients had family history of psychiatric disorder and history of completed suicide in the family.

**Table 1: Comparison of Socio-demographic and Clinical variables with severity of alcohol withdrawal on CIWA-Ar (N=63)**

| Variable                             | Categories         | CIWA-Ar  |        | Chi-Square                              | P-value      |
|--------------------------------------|--------------------|----------|--------|-----------------------------------------|--------------|
|                                      |                    | Moderate | Severe |                                         |              |
| Age                                  | 21-40              | 12       | 9      | 32.91<br>(Yate's<br>Correction)         | 0.374        |
|                                      | 41-50              | 10       | 17     |                                         |              |
|                                      | 51-65              | 2        | 13     |                                         |              |
| Gender                               | Male               | 23       | 37     | 0.030<br>(Yate's<br>Correction)         | 0.826        |
|                                      | Female             | 1        | 2      |                                         |              |
| Marital status                       | Single             | 7        | 6      | 1.995<br>(Yate's<br>Correction)         | 0.638        |
|                                      | Married            | 13       | 27     |                                         |              |
|                                      | Separated/divorced | 3        | 4      |                                         |              |
|                                      | Widow/Widower      | 1        | 2      |                                         |              |
| Socioeconomic status                 | Upper              | 0        | 0      | 4.450<br>(Fisher<br>Exact Test)         | 0.694        |
|                                      | Upper middle       | 5        | 5      |                                         |              |
|                                      | Lower middle       | 12       | 17     |                                         |              |
|                                      | Upper lower        | 6        | 17     |                                         |              |
|                                      | Lower              | 1        | 0      |                                         |              |
| Age at first drink                   | <25years           | 20       | 30     | 21.37<br>(Yate's<br>Correction)         | 0.314        |
|                                      | >25years           | 4        | 9      |                                         |              |
| Substance use                        | Alcohol            | 16       | 15     | 7.14                                    | <b>0.020</b> |
|                                      | Alcohol & Tobacco  | 8        | 24     |                                         |              |
| Years of alcohol consumption         | 5-15years          | 8        | 9      | 24.97                                   | 0.348        |
|                                      | 16-25years         | 13       | 12     |                                         |              |
|                                      | 26-35years         | 3        | 11     |                                         |              |
|                                      | 36-45years         | 0        | 5      |                                         |              |
|                                      | >46years           | 0        | 2      |                                         |              |
| Units of alcohol consumption per day | <10units           | 4        | 8      | 34.39<br>(Yate's<br>Correction<br>Test) | <b>0.014</b> |
|                                      | 11-20units         | 10       | 14     |                                         |              |
|                                      | 21-30units         | 8        | 13     |                                         |              |
|                                      | 31-60units         | 2        | 4      |                                         |              |
| Last drink before admission          | <12hours           | 3        | 4      | 16.87<br>(Exact<br>Test)                | 0.209        |
|                                      | 13-24hours         | 3        | 8      |                                         |              |
|                                      | 25-48hours         | 7        | 12     |                                         |              |
|                                      | >49hours           | 11       | 15     |                                         |              |
| Beverage of preference               | Wine               | 2        | 0      | 5.38<br>(Fisher<br>Exact Test)          | 0.549        |
|                                      | Beer               | 1        | 1      |                                         |              |
|                                      | Rum                | 1        | 4      |                                         |              |
|                                      | Whiskey            | 7        | 12     |                                         |              |
|                                      | Brandy             | 9        | 18     |                                         |              |
|                                      | Toddy              | 2        | 3      |                                         |              |
|                                      | Vodka              | 2        | 1      |                                         |              |
| Frequency of drinking                | Regular            | 17       | 18     | 6.13<br>(Yate's<br>Correction)          | 0.044        |
|                                      |                    | 5        | 20     |                                         |              |

|                                                            |                                                                                                                       |                             |                             |                                 |              |
|------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------|-----------------------------|-----------------------------|---------------------------------|--------------|
|                                                            | Regular with<br>intermittent<br>Bingeing<br>Bingeing                                                                  | 2                           | 1                           |                                 |              |
| Co-morbid illness                                          | Diabetes Mellitus<br>Hypertension<br>Diabetes Mellitus & Hypertension                                                 | 4<br>2<br>0                 | 1<br>6<br>5                 | 11.55<br>(Fisher<br>Exact Test) | <b>0.013</b> |
| Drug History                                               | OHA<br>Antihypertensives<br>OHA &<br>Antihypertensives                                                                | 2<br>2<br>0                 | 0<br>5<br>5                 | 6.75<br>(Fisher<br>Exact Test)  | 0.056        |
| Family history<br>(multiple<br>response in 18<br>patients) | Chronic<br>medical/surgical<br>disorder<br>Suicide attempt<br>Completed suicide<br>Substance use<br>disorders<br>None | 3<br>4<br>1<br>1<br>13<br>2 | 5<br>9<br>1<br>6<br>17<br>0 | 5.65                            | 0.34         |

**Table 2: Levels of Serum Electrolytes in delirium tremens**

| Age                  | Sodium<br>[mean (SD)] | Potassium<br>[mean (SD)] | Chloride<br>[mean (SD)] | Calcium<br>[mean (SD)] | Magnesium<br>[mean (SD)] |
|----------------------|-----------------------|--------------------------|-------------------------|------------------------|--------------------------|
| 21-40years<br>(n=21) | 140.76 (4.78)         | 3.41 (0.57)              | 100.33 (4.80)           | 9.34 (0.63)            | 2.06 (0.52)              |
| 41-50years<br>(n=27) | 141.59 (4.76)         | 3.44 (0.58)              | 101.18 (4.66)           | 8.9 (0.95)             | 2.01 (0.51)              |
| 51-<br>65years(n=15) | 141.4 (3.75)          | 3.46 (0.46)              | 100.33 (3.57)           | 8.78 (0.93)            | 2.04 (0.54)              |
| Mean $\pm$ SD        | 141.26 $\pm$ 4.4      | 3.43 $\pm$ 0.546         | 100.69 $\pm$ 4.43       | 9.02 $\pm$ 0.87        | 2.03 (0.57)              |
| ANOVA                | 0.985                 | 0.921                    | 0.914                   | 0.142                  | 0.870                    |

**Table 3: Levels of Bilirubin and Hepatic enzymes in delirium tremens**

| Age                  | SGOT [mean<br>(SD)] | SGPT<br>[mean<br>(SD)] | Total<br>Bilirubin<br>[mean (SD)] | Direct<br>Bilirubin<br>[mean (SD)] | Indirect<br>Bilirubin<br>[mean (SD)] |
|----------------------|---------------------|------------------------|-----------------------------------|------------------------------------|--------------------------------------|
| 21-40years<br>(n=21) | 172.81 (147.92)     | 92.80<br>(75.67)       | 1.366 (1.066)                     | 0.58 (0.61)                        | 0.78 (0.60)                          |
| 41-50years<br>(n=27) | 108.51 (75.09)      | 67.40<br>(55.31)       | 1.52 (1.60)                       | 0.711 (0.90)                       | 0.81 (0.71)                          |
| 51-<br>65years(n=15) | 115.533 (85.35)     | 63.73<br>(48.94)       | 1.82 (2.10)                       | 0.74 (0.91)                        | 1.08 (1.24)                          |
| Mean $\pm$ SD        | 131.61 $\pm$ 109.26 | 75 $\pm$ 61.92         | 1.54 $\pm$ 1.57                   | 0.67 $\pm$ 0.80                    | 0.866 $\pm$ 0.837                    |
| ANOVA                | <b>0.018</b>        | 0.316                  | 0.306                             | 0.199                              | 0.385                                |

**Table 4: Levels of platelets and mean corpuscular volume in patients with DT**

| Age               | Platelets [mean (SD)] | MCV [mean (SD)] |
|-------------------|-----------------------|-----------------|
| 21-40years (n=21) | 1.90 (0.64)           | 93.36 (9.51)    |
| 41-50years (n=27) | 1.57 (0.68)           | 88.69 (21.90)   |
| 51-65years (n=15) | 1.87(0.92)            | 94.68 (8.78)    |

|               |                 |                   |
|---------------|-----------------|-------------------|
| Mean $\pm$ SD | 1.75 $\pm$ 0.73 | 91.67 $\pm$ 15.96 |
| ANOVA         | 0.075           | 1.00              |

61.90% of the sample had severe alcohol withdrawal and 38.09% of them had moderate withdrawal. Mean CIWA-Ar score of the sample was  $18.5 \pm 4.88$ . 61.90% of the subjects had moderate dependence and 30.15% had severe dependence. Mean SADQ score of the sample was  $25.50 \pm 7.23$ .

**Table 5: Relationship between the CIWA-Ar scores and serum electrolytes levels**

| CIWA-Ar            | Sodium<br>[mean (SD)] | Potassium<br>[mean (SD)] | Chloride<br>[mean (SD)] | Calcium<br>[mean (SD)] | Magnesium<br>[mean (SD)] |
|--------------------|-----------------------|--------------------------|-------------------------|------------------------|--------------------------|
| Mild               | 0                     | 0                        | 0                       | 0                      | 0                        |
| Moderate<br>(n=24) | 141.25 (4.96)         | 3.41 (0.59)              | 100.54(4.72)            | 9.22(0.77)             | 2.12 (0.63)              |
| Severe<br>(n=39)   | 141.28 (4.25)         | 3.45 (0.51)              | 100.79 (4.30)           | 8.89 (0.92)            | 2.07 (0.53)              |
| ANOVA              | 0.503                 | 0.616                    | 0.836                   | 0.338                  | 0.856                    |

**Table 6: Relationship between the CIWA-Ar scores and levels of bilirubin and hepatic enzymes levels**

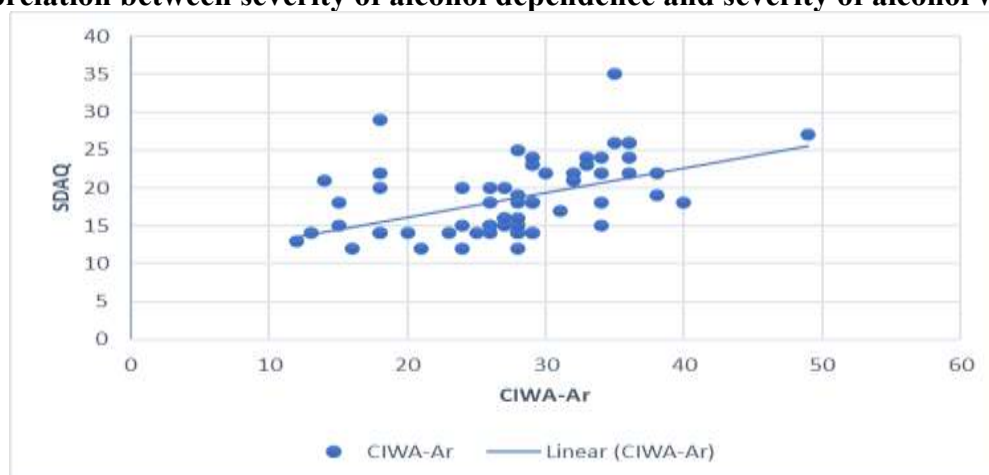
| CIWA-Ar            | SGOPT [mean (SD)] | SGPT [mean (SD)] | Total Bilirubin [mean (SD)] | Direct Bilirubin [mean (SD)] | Indirect Bilirubin [mean (SD)] |
|--------------------|-------------------|------------------|-----------------------------|------------------------------|--------------------------------|
| Mild               | 0                 | 0                | 0                           | 0                            | 0                              |
| Moderate<br>(n=24) | 133.375 (100.327) | 85.25 (73.73)    | 1.6125 (1.89)               | 0.666 (0.88)                 | 0.94 (1.088)                   |
| Severe<br>(n=39)   | 130.538(115.682)  | 68.69(53.46)     | 1.497 (1.361)               | 0.67 (0.77)                  | 0.81 (0.64)                    |
| ANOVA              | 0.870             | 0.667            | 0.587                       | 0.220                        | 0.854                          |

**Table 7: Relationship between CIWA-Ar scored and levels of Platelets and Mean corpuscular volume**

| CIWA-Ar         | Platelets [mean (SD)] | MCV [mean (SD)] |
|-----------------|-----------------------|-----------------|
| Mild            | 0                     | 0               |
| Moderate (n=24) | 1.700(0.67)           | 89.7 (13.67)    |
| Severe (n=39)   | 1.788 (0.78)          | 92.89 (17.28)   |
| ANOVA           | 0.987                 | 0.976           |

**Table 8: Relationship between severity of alcohol dependence (SADQ) with severity of alcohol Withdrawal (CIWA- Ar)**

| Correlations                                                 |                     |              |              |
|--------------------------------------------------------------|---------------------|--------------|--------------|
|                                                              |                     | SADQ         | CIWA Ar      |
| SADQ                                                         | Pearson Correlation | 1            | 0.478**      |
|                                                              | Sig. (2-tailed)     |              | <b>0.000</b> |
|                                                              | N                   | 63           | 63           |
| CIWA Ar                                                      | Pearson Correlation | 0.478**      | 1            |
|                                                              | Sig. (2-tailed)     | <b>0.000</b> |              |
|                                                              | N                   | 63           | 63           |
| **. Correlation is significant at the 0.01 level (2-tailed). |                     |              |              |

**Fig 1: Corelation between severity of alcohol dependence and severity of alcohol withdrawal****DISCUSSION:**

This study was a sincere attempt to evaluate the factors and biochemical changes in DT. At the end of one and half year of data collection, around 86 patients with DT admitted in IP care were evaluated. 8 patients were excluded from the study due to early discharge and 4 patients had presented with both withdrawal seizures and delirium tremens hence were excluded, remaining 11 patients were excluded because of uncontrolled hypertension (on diuretics), uncontrolled diabetes mellitus, hypothyroidism and acute pancreatitis with multiple episodes of vomiting which would affect the parameters selected. The mean values of different electrolytes were observed as; serum sodium ( $141.26 \pm 4.49$ ), serum potassium ( $3.43 \pm 0.546$ ), serum chloride ( $100.69 \pm 4.43$ ), serum calcium ( $9.02 \pm 0.87$ ) and serum magnesium ( $2.03 \pm 0.57$ ). Although serum potassium and calcium levels were found in lower levels in few patients, no significant difference for serum ions was found among various age clusters (table no 2). Similarly, no significance was found when patients were grouped according to alcohol withdrawal severity on CIWA-Ar (table no 5), this finding may be because of the stringent criteria in selection of study sample. A study by Wetterling T et al<sup>7</sup> showed significantly lower levels of serum electrolyte levels in patients with complicated withdrawal when compared with patients having uncomplicated withdrawal.

Like as discussed above most of the literature available till now shows differences in the study methodology like retrospective nature, small sample size and involvement of patients fulfilling alcohol dependence criteria and/or uncomplicated withdrawal. DT group seen in most of studies involves patient who gradually developed DT following admission to hospital and were not in drug naïve state. The comparison done between these groups in some studies does show significant hypokalaemia, hypomagnesemia, thrombocytopenia<sup>5,8,9,10,11</sup> in DT group compared with uncomplicated withdrawal group unlike our study where the sample comprised only of patients presenting with DT in drug naïve state to hospital. Even though serum potassium, calcium and platelets were decreased and SGOT, SGPT, MCV and bilirubin values were elevated in few patients with DT we didn't find any significant difference between different age or CIWA-Ar clusters.

Similar finding could be seen in a study by Borah J et al<sup>5</sup> where no significant difference is found in different age clusters for mean values of electrolytes and hepatic enzymes in DT group which is similar to our study except that we found significant high values of SGOT values among younger age group.

A study by Chandini et al<sup>10</sup> showed no significant changes in electrolytes and platelet count in DT group, but found significant elevation in SGOT values like current study.

Our study also showed that SADQ and CIWA-Ar scores were positively correlated ( $r=0.478$ ;  $p$ -value 0.000) indicating that high alcohol dependence (SADQ score) correlated with severe alcohol withdrawal (high CIWA-Ar score). (table no 8). Study by Aswathy G et al<sup>12</sup> done to find the association between severity of alcohol dependence on SADQ and severity of alcohol withdrawal on

CIWA-Ar found that 50% of patients who developed DT had moderate severity, 43.4% had mild and 6.52% had severe alcohol dependence. Lower values seen in their study might be because of their lower sample size in DT group (n=46).

## CONCLUSION:

In this descriptive cross-sectional study- factors associated with delirium tremens, we found that few delirium tremens patient have a considerable number of changes in serum electrolytes, liver enzymes, bilirubin, platelet counts and MCV levels but no statistical significance was found when compared among different age and CIWA-Ar cluster groups which were similar to the existing literature, even though few patients had individually shown lower levels of potassium, calcium and magnesium, this finding may be because of the stringent criteria in selection of study sample. We had included patients with no comorbid medical illness that would affect the serum electrolytes and also blood investigations were done before starting the patient on fluids, thiamine and lorazepam. Most of the patients presented to hospital within 3-4 days of last drink (mean 2.37) and vomiting- one of the withdrawal symptom was absent in most of the patients which might explain the normalcy seen in the sample. The significant changes found in other studies mentioned above might be because of the varied methodology, inclusion of patient with withdrawal seizures, uncomplicated withdrawal and of the comorbid medical illness in their study samples.

## LIMITATIONS:

- a) As the study was done only on inpatients in a tertiary hospital, factors found can be over or underestimated when compared with general population.
- b) We had only one study group, having a comparison group of subjects with uncomplicated withdrawal could have helped us in better comparison.

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