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Association between thrombocytopenia and delirium tremens in alcohol withdrawal syndrome in tertiary care centre

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Abstract

Introduction: Delirium Tremens (DT) is a severe spectrum of Alcohol Withdrawal Syndrome (AWS), which could potentially result in death unless managed promptly and adequately. It has been shown in various studies that alcohol withdrawal is associated with the thrombocytopenia. Almost the studies are from outside the country and limited study are from inside the country. This study aims to explore the association of DT and AWS in terms of platelets count.

Method: This was an analytical cross-sectional study design. This was conducted from December 2022 to December 2023 after the research proposal was approved by the Institutional Review Committee. For this study patients who presented to the Emergency Department with alcohol withdrawal symptoms were enrolled through a non-probability purposive sampling method.

Result: Of the 227 patients enrolled in the study, 16 (7.04%) developed delirium tremens, with all DT cases associated with thrombocytopenia. Thrombocytopenia was present in 183 (80.62%) of the total patients. Notably, 16 (8.7%) of patients with thrombocytopenia experienced the co-occurrence of both DT and thrombocytopenia. The study demonstrated a statistically significant relationship between thrombocytopenia and DT (p=0.042). These findings suggest an association between thrombocytopenia and the development of DT, emphasizing the potential clinical importance of considering thrombocytopenia in the context of DT occurrence.

Conclusion: The study establishes a statistically significant association between thrombocytopenia and Delirium Tremens, as all patients who developed DT had thrombocytopenia.

Keywords: Alcohol Withdrawal Syndrome (AWS), Delirium Tremens, Thrombocytopenia

INTRODUCTION

Delirium Tremens (DT) is a severe spectrum of alcohol syndrome (AWS), which could potentially result in death unless managed promptly and adequately.[1,2]

Studies by Harshe, et al., Kim, et al., and Berggren, et al. indicate that thrombocytopenia, with significantly lower platelet counts, is strongly associated with and potentially predictive of delirium tremens and seizures in alcohol withdrawal.[3-5] Silczuk et al., found that the risk of occurrence of withdrawal seizures or delirium tremens in alcohol withdrawal syndrome increases significantly when the platelet count is less than 119,000/microlitre.[6] Studies show that, in alcohol-dependent people, thrombocytopenia ranges from 3 to 43% in well-fed and healthy individuals and from 14% to 81% of alcoholics requiring hospitalization.[7, 8]

This study aimed at exploring the association of DT and AWS in terms of platelet counts.

METHOD

This was a cross-sectional study. It was conducted in the emergency department of a university hospital of Kathmandu Valley. The study lasted one year, and was conducted from Dec 2022 to Dec 2023, after getting it approved by the Institutional Review Committee (IRC) of Maharajgunj Medical Campus (Ref no: 267(6-11) E2).

Patients diagnosed with alcohol withdrawal syndrome in the emergency department with an age of more than 18 years were included in the study. Patients with hepatic encephalopathy, head injury, under other psychoactive substances, pregnancy, and haematological disorders were excluded from the study. A non-probability purposive sampling method was utilized.

The sample size was calculated using sample formula:
$N= (Z^2 \times P (1-P) /D^2$
Where,
N= no of the subjects required
Z= value of N deviates from the considered level of confidence: 1.96
P= expected prevalence, i.e., 18% (taken from a similar study)[9]
D= margin of error – 5%
N= 227
Applying the values to the above formula, the calculated sample size was 227.

The case proforma/questionnaire designed for the study collected socio-demographic parameters. The DSM-V was used to diagnose withdrawal delirium.[10] Platelet count of below 150000 in a microliter of blood was considered thrombocytopenia.

Data obtained from study participants were put in Microsoft Excel 2013 and analysed in IBM SPSS statistics data editor version 20. Parametric data were reported as mean and standard deviation and compared using Chi-square tests and T-tests. The significance level in the analysis was kept to be 0.05. Management of patients were done according to the detoxification protocol of the centre's Department of Psychiatry & Mental Health. Ethical clearance was obtained from the institutional review committee (IRC).

Patients or caretakers were provided with written informed consent. Consent was taken voluntarily. Confidentiality and privacy were maintained during the research by keeping the information confidential and not disclosing it to anyone other than for research purposes only.

RESULT

There were 227 participants in total. The minimum age was 21, and the maximum was 76, with a mean age of 50.82±11.01 years, a median of 52, and a mode of 50. The study population was mainly male, i.e., 194(85.46%). The age group of the patients who participated in the study is shown in Table 1.

Table 1. Age distribution of participants (n=227)

Age Group (in years)	*f* (%)
21-30	10 (4.4%)
31-40	36 (15.9%)
41-50	60 (26.4%)
51-60	82 (36.1%)
More than 60	39 (17.2%)
Total	227 (100%)

Among the participants in the study, 61(27%) had a history of alcohol withdrawal at any time in the past. The mean±SD of platelets of the patient among the study population was 117096.91±58227.12/mm^3 in a microliter of blood. Similarly, the length of stay of the patient in the hospital was 7.21±3.02 days.

Among the patients with alcohol withdrawal syndrome, delirium tremens was present on 16(7.04%). The patient's place of admission from the emergency department is shown in Table 2.

Table 2. The department of admission of the patient with alcohol withdrawal syndrome (n=227)

Admission	*f* (%)
ICU	5 (2.02)
MICU	7 (3.00)
HDU	87 (38.32)
Ward	128 (56.38)

The association between delirium tremens and thrombocytopenia was calculated and shown in the table 3.

Table 4 elaborates on the association between patient admission and thrombocytopenia. The chi-square value is 37.929, with an odds ratio of 49.576 at 95% C.I of 6.68–367.71, and a significant P value (0.001).

Table 5 elaborates on the association between hospital stay duration and thrombocytopenia. The T-test value was 6.62 at a 95% CI of 2.169-4.005, with a significant P value of less than 0.001.

Table 3. Association between the occurrence of Delirium Tremens and thrombocytopenia (n=227)

Factors	Delirium Tremens *f* (%)	No Delirium Tremens *f* (%)	χ^2	p-value	Odds Ratio	Confidence Interval (CI) 95%
Thrombocytopenia	16 (8.7%)	167(91.3%)	4.139	0.042	8.76*	0.04–0.10
Normal Platelets	0 (0%)	44 (100%)				

* Since one of the frequencies is 0, we used Haldane Correction to calculate the odd ratio

Table 4. Association between Admission of patients in monitoring ward and Thrombocytopenia(n=227)

	Admission *f* (%)		Total	χ^2	p-value	Odds Ratio (OR)	Confidence Interval (CI) 95%
	ICU/MICU/HDU	Ward					
Thrombocytopenia	98 (53.6%)	85 (46.4%)	183 (100%)	37.929	<0.001	49.576	6.68-367.71
Normal platelets	1 (2.3%)	43 (97.7%)	44 (100%)				

Table 5. Association between duration of hospital stay and thrombocytopenia (n=227)

	N	Duration of stay (Mean ± SD)	Student's T-test	p-value	Confidence Interval (CI) 95%
Thrombocytopenia	183	7.81 ± 3.06	6.62	<0.001	2.169- 4.005
Normal platelets	44	4.73 ± 0.69			

DISCUSSION

This study showed that all those patients who developed DT had thrombocytopenia, i.e., 100%, which is somehow similar to the survey conducted by Silczuk, Habrat, et al. among people aged 19-65 years to assess the predictive value of thrombocytopenia in alcohol withdrawal syndrome as a marker of the evolution of complicated withdrawal syndrome: DT which showed that 93.8% of all patients that had thrombocytopenia developed DT (p<0.001).[11]

This study is also similar to the retrospective cohort study conducted by Berggren, Fahlke, et al., which revealed that 83% were males and 17% were females showing male predominance.[5]

There is an association between DT and thrombocytopenia in patients with AWS. A study conducted among 300 patients admitted to the hospital showed that patients with AWS and particularly low platelets levels (below 119000/mL) are more likely to develop complicated AWS.[12] A retrospective cohort study showed that thrombocytopenia is more frequent in patients who develop severe AWS (DT or seizures).[5] A study on the platelet pattern among patients with AWS showed that in a large proportion of patients, platelet counts show a drop below the baseline in the first half of alcohol withdrawal (day 4), followed by a gradual rise until the 10th day of withdrawal.[3] Since the patient was not followed for the whole period of admission in this study, this finding was not possible in our findings. Similarly, a study conducted in India showed that the platelet count is significantly low in DT patients (p<0.05) compared to non-DT patients.[13] There is association of the AWS with the low platelet count at initial presentation.

This study showed that there is association between the complicated withdrawal (DT) and the thrombocytopenia. A survey among the AWS patient showed that among those who developed DT during the treatment period, a significantly higher proportion had thrombocytopenia compared to those who did not, which is similar in contrast to this study.[5] The study conducted by Kim, Bae, et al. concluded that there is an association between thrombocytopenia and DT in alcohol withdrawal with a significant p-value of <0.001, as the patient who developed DT had low platelet counts, similar to this study.[4] Banyal, et al.'s study showed that low platelet count proves significant in predicting complicated AWS, providing clinicians with valuable tools for risk assessment, which is similar to this research.[14]

Similarly, this study found that thrombocytopenia is a predictive factor of delirium tremens because all the patients who developed delirium tremens had thrombocytopenia like a survey conducted by Goodson et al. suggested that a lower initial platelet count was predictive of an incident occurrence of delirium tremens.[15]

The study reports a statistically significant association between thrombocytopenia and the occurrence of Delirium Tremens. While all patients with DT had thrombocytopenia, it is crucial to note that the majority of thrombocytopenic patients did not develop DT. A cohort study of 334 patients found thrombocytopenia (<150 × 10^3/µL) had 70% sensitivity and 69% specificity for predicting DT, though its positive predictive value (PPV) was low (6%).5 Study by Harshe, et al. and Silczuk, et al., showed that platelet counts in DT patients were significantly lower at baseline, and showed transient drops during withdrawal.[3,12] Alcohol's toxic effects on bone marrow suppress platelet production, while splenic sequestration and nutritional deficiencies (e.g., folate) exacerbate thrombocytopenia.[5,12] These factors may synergize with hyperadrenergic states during withdrawal to precipitate DT.[13] This indicates that although thrombocytopenia is associated with DT, it may not serve as an independent predictor.

Likewise, this study showed the association between thrombocytopenia and the disposition of patients with a significant p-value of <0.001, which is similar to the survey conducted by Eyer, et al., among participants diagnosed with alcohol withdrawal, which concluded that considerable predictor at admission for the occurrence of delirium tremens was thrombocytopenia with the significant p-value of 0.001.[16]

Data collection relied on medical records and patient self-reports, was done only at emergency department.

Patients were not followed after admissions in respective departments. Longterm follow-up of the participants would have been important to understand the sustained effects which could not be done in this study.

CONCLUSION

The study establishes a statistically significant association between thrombocytopenia and Delirium Tremens, as all patients who developed DT had thrombocytopenia. Additionally, this research suggests further investigation into the dynamic changes of platelet counts during hospitalization to improve patient care.

DECLARATIONS

Acknowledgement
We would like to thank all the participants of the study.

Conflict of Interest
Author declares no any conflict of interest with others regarding this research work.

Funding
None

Ethical Clearance
Ethical clearance was obtained from IRB of Institute of Medicine-IRC (Reference No :267(6-11) E2).

Consent of the Study
Written informed consent was taken from the participants of the study. If the participants were unable to provide consent, it was taken from next to the keen.

Consent for Publication from Authors
All the authors and the participants consented to the publication of the findings.

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