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A study of thrombocytopenia in patients with alcohol withdrawal and its association with clinical complications

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Abstract
Background: The aim of the study is to evaluate thrombocytopenia in alcohol withdrawal symptoms (AWS) as a predictive marker for non-severe alcohol withdrawal symptoms (nAWS) to severe alcohol withdrawal symptoms (sAWS) and its relationship with liver enzymes.
Methodology: A 3 months (forty-three patients) prospective study during June 2023 to August 2023 was carried out in patient admitted at B. J. Medical College with complains of symptoms related with alcohol withdrawal. Detailed history and evaluation regarding alcohol dependence along with laboratory parameters like CBC, LFT, RFT at regular intervals was carried out. On achieving the diagnostic criteria of alcohol withdrawal symptoms patients was treated and discharge.
Result: During the treatment period out of 43 patients, 9 (21%) were having complains of sAWS out of which 7 had reduced platelet counts and remaining 34 (79%) were having complains of nAWS. Liver enzyme (Alanine transaminase (ALT)) was higher in 28% (12/43) of patients ranging from (42-178 IU/L) which was a significant risk factor ($p<0.05$) for severe alcohol withdrawal symptoms and there was no association of potassium level with sAWS.
Conclusion: Thrombocytopenia is more frequent in patients with sAWS and it shows reverse thrombocytosis during the course of treatment.

Keywords: Thrombocytopenia, alcohol withdrawal symptoms, reverse thrombocytosis

Introduction
The alcohol withdrawal syndrome (AWS) occurs in alcohol-dependent individuals who abruptly reduce or discontinue their alcohol consumption. Symptoms of AWS range from mild signs of autonomic hyperactivity, anxiety and psychomotor agitation, to severe complications such as withdrawal seizures (WS) and delirium tremens (DT). However, its severity and course cannot be reliably predicted during an initial routine clinical assessment because symptoms might differ strongly between individual patients and subsequent withdrawal episodes. WS and DT typically develop with latency, and evidence on how to translate indicators of such poor outcomes into clinical practice is limited. Although most patients experience only mild withdrawal symptoms and has self-limiting course.

Delirium tremens has been estimated to occur in ~5–20% of the patients who undergo treatment for alcohol withdrawal and the mortality rate may be in the range of 5–15%. However, with appropriate detection and treatment, including the use of benzodiazepines, the mortality rate falls in the range of 1% or less.

Blood-derived markers demonstrated predictive value with higher gamma-glutamyl transferase and increased alanine transaminase to severe AWS, and lower platelet count and potassium to both WS and DT. On the basis of such results, screening tools for risk assessment at admission were developed.

Evidence suggests that platelet count in patients with DT was in thrombocytopenic range ($<150 \times 10^9$/L) whereas it was within normal limits in ND group. Most authors hypothesized that chronic alcohol consumption, heavy alcohol intake, recent binging, and comorbid liver cirrhosis, nutritional deficiency may be the causative factors for thrombocytopenia during alcohol withdrawal. Thus, we planned this study to evaluate the stability of platelet count during the course of alcohol withdrawal and its relationship if any with serum liver enzymes.

Aims
- To evaluate the platelet count during the course of alcohol withdrawal symptoms
- To evaluate the relation of serum liver enzymes and alcohol withdrawal symptoms

Material and Methodology
45 patients diagnosed with alcohol dependence and presenting within 12 hrs of their last consumption and admitted at B. J. Medical College and Hospital, Ahmedabad, during June 2023 to August 2023 were included in study.

Inclusion Criteria
1. Age 18-60 years.
2. Preferred Blood examination

Exclusion Criteria
1. Taking anti-platelet/anti-coagulant or anti-psychotic drugs
2. Diagnosed as hepatic cirrhosis or Liver failure.
3. History of cerebrovascular stock, traumatic brain injury or peripheral vascular disease.

From 45 patients one had history of Liver failure and one was under age (17 years) so they were excluded from study.
On the admission of patients (n-43) routine investigation (CBC), renal function tests and liver function tests were carried out. Patients were put on tablet Lorazepam 8mg/day or tablet Chlordiazepoxide 100mg/day and tablet Thiamine 100mg 8 hourly or injection Optineurin 1500 IU/day and were under strict observation by on duty resident. Dose of Lorazepam and chlordiazepoxide was adjusted according to clinical status. CBC for platelet count was sent on alternate days (day 3, day 5, day 7) till patient got discharged.
Demographic and numerical data was collected and plotted in MS Office Excel. Variants were assessed with Chi-square test and 2 x 2 cross-tables analysis. Pearson's correlation was used to study relationship between platelet count, liver enzymes (Alanine transaminase) and alcohol consumption details. Statistical significance was assumed at $p<0.05$.

Observation and Result
Sample of 43 patients all being males with mean age of 34.81 years (ranging from 23-57 years) were assessed. Among which 9 patients (21%) were having complains of sever alcohol withdrawal symptoms (sAWS) out of which 7 had reduced platelet counts and remaining 34 (79%) were having complains of non-sever alcohol withdrawal symptoms (nAWS).

Table 1: Platelet count with severity of symptoms

Platelet counts	Number of patients	
	nAWS (34)	sAWS (9)
Normal (29)	27	2
Reduced (14)	7	7

From above table 1 we get P-value <0.05 which indicates strong association of reduced platelet counts with severity of alcohol withdrawal symptoms like WS/DT in patients as compared to ones having normal platelet counts.
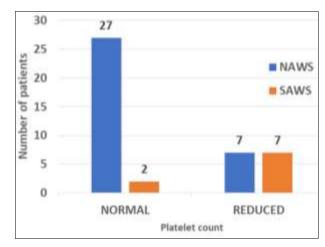

Fig 1: Platelet count with severity of symptoms

Table 2: ALT levels with severity of symptoms

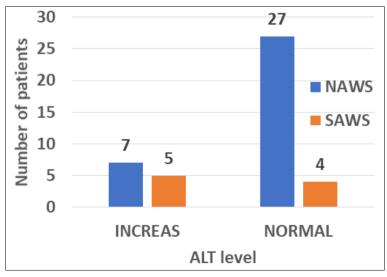| ALT level	Number of patients	
	nAWS (34)	sAWS (9)
Increase (12)	7	5
Normal (31)	27	4

Fig 2: ALT levels with severity of symptoms

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Above table 2 shows 72% (31/43) were having normal levels of liver enzyme (Alanine transaminase) whereas they were higher in 28% (12/43) of patients ranging from (42-178 IU/L) which was found to be a significant risk factor (*p*<0.05) for severe alcohol withdrawal symptoms, and there was no association of potassium levels with severe AWS (X^2-0.3, P>0.05).

From figure 3 and 4 it is observed that among 43 patients 22 (51%) who consumed country liquor (CL) 3 of them presented (13.6%) with severe AWS and 21 (49%) who consumed Indian-made foreign liquor (IMFL) 6 of them presented (28.6%) with severe AWS. This states that sAWS were more commonly associated with IMFL.
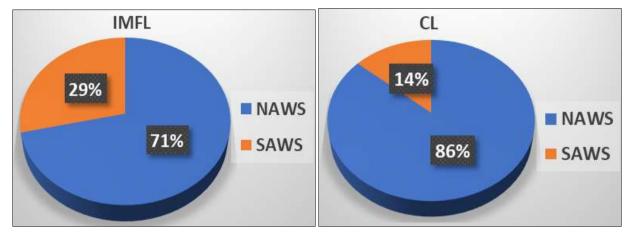

Fig 3 & 4: Type of liquor with severity of symptoms

Table 3: Duration of alcohol consumption and severity of symptoms

Duration of alcohol consumption	Number of patients	
	nAWS (34)	sAWS (9)
<10 years (21)	18	3
>10 years (22)	16	6

Above table 3 indicates that nearly 42% of patients (18/43) were consuming alcohol since <10 years and 58% of patients (25/43) since >10 years. Thus, the P-value being >0.05 shows no association between duration of alcohol consumption and severity of symptoms.

Platelet affecting factors
Platelet counts are unaffected by:
1. with or without increase ALT (X^2- 0.39),
2. with duration of consumption of alcohol like <10 years and >10 years (X^2-0.011) and
3. Type of alcohol consumption like country liquor (CL) or Indian-made foreign liquor (IMFL) (X^2-0.23).

Discussion
In present study, we found that thrombocytopenia is more frequently associated with alcohol depended patients who developed severe alcohol withdrawal symptoms. The result of study replicates findings of previous studies (Andrzej *et al*., 2019, ulf beggren *et al*., 2009) [1, 2]. The platelet count is not stable during the course of withdrawal. It gradually rises till the end of withdrawal symptoms and subsides, this phenomenon is called Reverse Thrombocytosis (RT) seen in all patients with or without sever AWS. The development of thrombocytopenia can be a result of toxic influence on the bone marrow and due to cumulative hepatotoxic effect of alcohol. Along with thrombocytopenia, severe AWS may also due to functioning of platelets. (Berggren *et al*., 2000). In this study, level of the of the liver function enzyme like ALT were elevated in patients with severe AWS and patients with thrombocytopenia had average ALT level (Andrzej *et al*., 2019) [1]. This laboratory parameter is marker of excessive alcohol consumption and use as

predictive marker for sever AWS (ulf beggren *et al*., 2009) [2]. Some study show serum K^+ (potassium) level significantly lower in individual with sever AWS and postulate predictive effect of low serum K^+ and sAWS. But in present study, show average variation in serum K^+ level in individual with sAWS which is replicated by multiple regression analysis (Lee *et al*., 2005) [7].

Limitation of this study arise because of small number of sample size and a smaller number of patients presented with severe alcohol withdrawal symptoms. Gender wise analysis cannot be assessed because only male patients with appropriate clinical history were part of our study. The data obtained from the consumers may be less reliable because of patients are not willing to give history regarding amount of consumption, duration of consumption and take defensive posture and not reveal some content due to fear of society and legal issue.

In addition, the knowledge of cause and nature of thrombocytopenia in alcohol withdrawal patients allow clinician to make more rational decision with respect to patient symptoms like: avoiding platelet transfusion, corticosteroid therapy etc.

Conclusion
We can conclude that thrombocytopenia and serum level of ALT that have strong association with severity of alcohol withdrawal symptoms. Reserve thrombocytosis is also observed in patient on alcohol withdrawal treatment. Platelet count is not affected by type of liquor, serum level of ALT and duration of alcohol consumption.

Conflict of Interest
Not available

Financial Support
Not available

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