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TREATMENT PATTERNS AND PREDICTORS OF RELAPSE IN PATIENTS WITH ALCOHOL WITHDRAWAL SYNDROME: A HOSPITAL-BASED STUDY

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ABSTRACT

Background: Alcohol Withdrawal Syndrome (AWS) is a significant clinical challenge requiring effective inpatient management and post-discharge care. Understanding treatment patterns, relapse predictors, and outcomes can guide optimal therapeutic strategies.

Materials and Methods: This hospital-based observational study assessed treatment patterns, relapse rates, and associated factors in patients with AWS. Data on demographics, treatment regimens, clinical outcomes, and post-discharge adherence were analyzed. Comparisons between benzodiazepine and non-benzodiazepine treatment groups were performed using appropriate statistical methods.

Results: Among 136 patients, benzodiazepines were the primary treatment (72.1%), while 27.9% received non-benzodiazepine alternatives. The mean CIWA-Ar score at admission was higher in the benzodiazepine group (16.1 ± 5.0) than in the non-benzodiazepine group (13.5 ± 5.6, $p=0.027$). Medication adherence ($p<0.001$), participation in rehabilitation ($p<0.001$), and strong social support ($p<0.001$) were significantly associated with lower relapse rates. Patients with higher baseline CIWA-Ar scores ($p=0.002$), previous withdrawal episodes ($p<0.001$), and psychiatric comorbidities ($p=0.019$) were at greater risk of relapse. Common complications included delirium tremens (15.4%) and seizures (11.8%).

Conclusion: Effective management of AWS requires individualized treatment approaches, adherence monitoring, and post-discharge rehabilitation. Benzodiazepines remain the mainstay of treatment, but non-benzodiazepine alternatives may have a role in selected cases. Strengthening social and psychological support is essential for relapse prevention.

Keywords: Alcohol Withdrawal Syndrome, Benzodiazepines, Rehabilitation, Treatment Patterns, CIWA-Ar Score.

INTRODUCTION

Alcohol withdrawal syndrome (AWS) is a well-recognized complication of alcohol dependence, affecting approximately 50% of individuals with alcohol use disorder (AUD) who suddenly reduce or stop alcohol consumption.[1] AWS manifests in a spectrum of symptoms, ranging from mild tremors, anxiety, and insomnia to severe complications such as alcohol withdrawal seizures (occurring in 10–15% of cases) and delirium tremens (DT), which has a reported mortality rate of 5–15% if untreated.[2,3] The risk of severe withdrawal is higher in individuals with a history of prior withdrawal episodes, prolonged heavy alcohol use, and coexisting medical conditions.[4]

Management of AWS typically follows established guidelines, with benzodiazepines being the first-line treatment due to their efficacy in preventing seizures and DT.[5] However, treatment approaches vary widely across healthcare settings. Studies indicate that 20–30% of patients receive adjunctive therapies

such as anticonvulsants (e.g., carbamazepine, valproate) and α2-adrenergic agonists (e.g., clonidine) to manage withdrawal symptoms, particularly in cases where benzodiazepines are contraindicated.[6] Furthermore, evidence suggests that up to 40% of hospitalized AWS patients receive inadequate symptom monitoring or suboptimal dosing regimens, leading to increased risk of complications.[7]

Post-discharge care is crucial in preventing relapse, yet it remains a neglected aspect of AWS management. Studies indicate that nearly 60% of patients resume alcohol use within six months of discharge if not enrolled in structured rehabilitation or outpatient follow-up programs.[8] Pharmacological interventions such as naltrexone, acamprosate, and disulfiram, combined with behavioral therapies, have been shown to reduce relapse rates significantly, but adherence remains suboptimal, with only 30–40% of patients continuing prescribed treatment beyond three months.[9] In India, where AUD prevalence is estimated at 4.6% among men and 0.6% among women, AWS-related hospitalizations are increasing, yet data on treatment patterns and post-discharge care remain scarce.[10,11]

This study aimed to assess the management of AWS in hospitalized patients, evaluate adherence to guideline-based treatment, and identify gaps in post-discharge care. By analyzing real-world treatment patterns, the findings may inform evidence-based interventions to optimize inpatient management and long-term recovery strategies.

MATERIALS AND METHODS

Study Design and Setting

This hospital-based, observational study was conducted in the department of Psychiatry, a tertiary care center in North India, for a period of 2 years from June 2022 to May 2024. The study aimed to assess the treatment patterns of alcohol withdrawal syndrome (AWS) during hospitalization and post-discharge, focusing on adherence to clinical guidelines, variations in pharmacological management, and follow-up care. The institution serves a diverse population, including both urban and rural patients, providing a comprehensive representation of AWS treatment practices in a real-world setting.

Study Population

The study included adult patients aged 18 years and above who were diagnosed with AWS based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria and admitted for inpatient management. Patients with severe hepatic encephalopathy, chronic psychiatric illnesses requiring ongoing antipsychotic therapy, or neurological disorders that could mimic or confound withdrawal symptoms were excluded. Additionally, patients who left against medical advice before completing treatment were not considered for post-discharge follow-up.

Sample Size and Sampling Technique

The study included 136 patients, determined based on an estimated prevalence of AWS-related hospital admissions to ensure adequate statistical power for detecting treatment pattern differences. A confidence level of 95% and an appropriate margin of error guided the sample size calculation. Consecutive sampling was used, enrolling all eligible AWS patients admitted during the study period until the target sample size was reached.

Data Collection

Patient data were collected prospectively using a structured case record form. Baseline demographic information, including age, sex, socioeconomic status, history of alcohol use, duration of dependence, and previous withdrawal episodes, was recorded. The severity of AWS was assessed using the Clinical Institute Withdrawal Assessment for Alcohol Scale, Revised (CIWA-Ar) at the time of admission and monitored throughout hospitalization [12]. Laboratory parameters, including liver function tests, complete blood count, and electrolyte levels, were documented to assess the impact of alcohol dependence and withdrawal on systemic health.

Treatment details were recorded, including the type, dosage, and duration of benzodiazepine therapy, use of adjunctive medications such as anticonvulsants (carbamazepine, valproate), α2-adrenergic agonists (clonidine, dexmedetomidine), and antipsychotics (haloperidol, olanzapine). The frequency of symptom monitoring, adjustments in treatment regimens, and adherence to AWS management guidelines were analyzed. The study also documented complications such as seizures, delirium tremens, and need for intensive care unit (ICU) admission.

Post-discharge follow-up was conducted at one month and three months through outpatient visits or telephonic interviews. Patients were assessed for relapse using self-reported alcohol consumption and validated screening tools. Medication adherence was evaluated by verifying prescription refills and self-reported compliance. Additionally, participation in rehabilitation programs, psychiatric follow-up, and engagement in psychosocial interventions were documented. Patients who failed to attend follow-up visits were contacted telephonically, and reasons for non-adherence were recorded.

Outcome Measures

The primary outcomes of the study included adherence to established AWS treatment protocols, the proportion of patients receiving benzodiazepine-based therapy, the frequency of adjunctive medication use, and the rate of post-discharge relapse. Secondary outcomes included factors associated with medication adherence, participation in rehabilitation services, and predictors of successful abstinence at three months. The study also explored hospital-related factors influencing variations in AWS management, such as physician

preference and availability of addiction psychiatry services.

Statistical Analysis

All collected data were entered into SPSS version 20.0 for analysis. Continuous variables were summarized as means ± standard deviations (SD) and compared using independent t-tests. Categorical variables were expressed as frequencies and percentages, with bivariate comparisons conducted using the chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee (IEC). Written informed consent was obtained from all participants before data collection. Confidentiality of patient information was maintained, and all data were anonymized before analysis. The study adhered to ethical principles outlined in the Declaration of Helsinki, ensuring that participants received appropriate medical care regardless of their decision to participate.

RESULTS

Among 136 AWS patients, 98 (72.1%) received benzodiazepines and 38 (27.9%) non-benzodiazepines. The mean age was 42.6 ± 8.4 years, with no significant group differences. Males comprised 94.1%, and most were married (74.3%) and employed (58.1%). The benzodiazepine group had higher daily alcohol consumption (9.7 ± 3.4 vs. 8.2 ± 2.8 units, p=0.048) and more previous withdrawal episodes (38.8% vs. 23.7%, p=0.091). Comorbidities (43.4%) were similar between groups. The benzodiazepine group had a significantly higher CIWA-Ar score (16.1 ± 5.0 vs. 13.5 ± 5.6, p=0.027), indicating greater withdrawal severity (Table 1).

Table 1: Baseline Characteristics of Patients with Alcohol Withdrawal Syndrome by Treatment Group

Variable	Total (n=136)	Benzodiazepine Group (n=98)	Non-Benzodiazepine Group (n=38)	p-value
	Frequency (%)/Mean ± SD			
Age (years)	42.6 ± 8.4	43.1 ± 7.8	41.2 ± 9.1	0.281
Gender				
Female	8 (5.9)	5 (5.1)	3 (7.9)	0.621
Male	128 (94.1)	93 (94.9)	35 (92.1)	
Marital Status				
Married	101 (74.3)	72 (73.5)	29 (76.3)	0.742
Unmarried	25 (18.4)	19 (19.4)	6 (15.8)	0.723
Divorced/Widowed	10 (7.3)	7 (7.1)	3 (7.9)	0.867
Employment Status				
Employed	79 (58.1)	59 (60.2)	20 (52.6)	0.432
Unemployed	57 (41.9)	39 (39.8)	18 (47.4)	0.367
Educational Status				
Illiterate	19 (14.0)	13 (13.3)	6 (15.8)	0.739
Primary Education	42 (30.9)	32 (32.7)	10 (26.3)	0.520
Secondary Education	46 (33.8)	34 (34.7)	12 (31.6)	0.741
Higher Education	29 (21.3)	19 (19.3)	10 (26.3)	0.372
Duration of alcohol use (years)	12.6 ± 10.7	13.4 ± 12.3	10.9 ± 9.7	0.172
Daily alcohol consumption (units)	9.2 ± 3.1	9.7 ± 3.4	8.2 ± 2.8	0.048
Previous withdrawal episodes	47 (34.6)	38 (38.8)	9 (23.7)	0.091
Family History of Alcohol Use	53 (39.0)	41 (41.8)	12 (31.6)	0.289
Comorbidities	59 (43.4)	45 (45.9)	14 (36.8)	0.332
Hypertension	26 (19.1)	19 (19.4)	7 (18.4)	0.874
Diabetes	14 (10.3)	12 (12.2)	2 (5.3)	0.213
Alcoholic Hepatitis	9 (6.6)	7 (7.1)	2 (5.3)	0.721
Liver Cirrhosis	7 (5.1)	5 (5.1)	2 (5.3)	0.962
Peripheral Neuropathy	11 (8.1)	8 (8.2)	3 (7.9)	0.943
Seizure Disorder	5 (3.7)	4 (4.1)	1 (2.6)	0.713
Severity of AWS (CIWA-Ar Score)	15.4 ± 5.2	16.1 ± 5.0	13.5 ± 5.6	0.027

Among 136 AWS patients, 72.1% received benzodiazepines, primarily diazepam (57.1%), lorazepam (28.6%), and chlordiazepoxide (14.3%), while 27.9% received non-benzodiazepines, mainly clonidine (57.9%), gabapentin (26.3%), and antipsychotics (15.8%). All patients received thiamine, and 98.5% received multivitamins. Antidepressant use was similar between groups (18.4%). The benzodiazepine group had a longer hospitalization duration (8.3 ± 3.1 vs. 6.9 ± 3.3 days, p=0.037), while discharge against medical advice rates were comparable (7.1% vs. 7.9%, p=0.892) (Table 2).

Table 2: Treatment Patterns and Hospitalization Outcomes in Patients with Alcohol Withdrawal Syndrome

Treatment	Total (n=136)	Benzodiazepine Group (n=98)	Non-Benzodiazepine Group (n=38)	p-value
	Frequency (%)/Mean ± SD			
Benzodiazepines	98 (72.1)	98 (100.0)	0 (0.0)	—
Diazepam	56 (41.2)	56 (57.1)	0 (0.0)	<0.001
Lorazepam	28 (20.6)	28 (28.6)	0 (0.0)	<0.001
Chlordiazepoxide	14 (10.3)	14 (14.3)	0 (0.0)	<0.001
Non-Benzodiazepines	38 (27.9)	0 (0.0)	38 (100)	—
Clonidine	22 (16.2)	0 (0.0)	22 (57.9)	<0.001
Gabapentin	10 (7.4)	0 (0.0)	10 (26.3)	<0.001
Antipsychotics	6 (4.4)	0 (0.0)	6 (15.8)	0.005
Adjunctive medications				
Thiamine	136 (100.0)	98 (100.0)	38 (100.0)	—
Multivitamins	134 (98.5)	97 (99.0)	37 (97.4)	0.612
Antidepressants	25 (18.4)	18 (18.4)	7 (18.4)	1.000
Duration of hospitalization (days)	7.8 ± 3.2	8.3 ± 3.1	6.9 ± 3.3	0.037
Discharge against medical advice	10 (7.4)	7 (7.1)	3 (7.9)	0.892

The mean CIWA-Ar score at admission was higher in the benzodiazepine group (16.1 ± 5.0) than in the non-benzodiazepine group (13.5 ± 5.6, p=0.027), with both groups showing significant reduction by discharge (4.5 ± 2.2 vs. 3.7 ± 2.4, p=0.043). ICU admission rates were comparable (15.3% vs. 10.5%, p=0.477). Common complications included electrolyte imbalance (23.5%), liver dysfunction (19.9%), delirium tremens (15.4%), and seizures (11.8%), with no significant between-group differences. Supportive therapies, such as intravenous fluids (80.1%) and electrolyte replacement (45.6%), were frequently used, with similar distribution across groups (Table 3).

Table 3: Clinical Outcomes and Complications in Patients with Alcohol Withdrawal Syndrome

Outcome	Total (n=136)	Benzodiazepine Group (n=98)	Non-Benzodiazepine Group (n=38)	p-value
	Frequency (%)/Mean ± SD			
Mean CIWA-Ar score at admission	15.4 ± 5.2	16.1 ± 5.0	13.5 ± 5.6	0.027
Mean CIWA-Ar score at 24 hours	10.6 ± 4.1	11.0 ± 4.0	9.7 ± 4.4	0.081
Mean CIWA-Ar score at discharge	4.2 ± 2.3	4.5 ± 2.2	3.7 ± 2.4	0.043
ICU Admission Required	19 (14.0)	15 (15.3)	4 (10.5)	0.477
Complications During Hospital Stay				
Seizures	16 (11.8)	13 (13.3)	3 (7.9)	0.387
Delirium Tremens	21 (15.4)	16 (16.3)	5 (13.2)	0.657
Respiratory Distress	9 (6.6)	7 (7.1)	2 (5.3)	0.713
Electrolyte Imbalance	32 (23.5)	24 (24.5)	8 (21.1)	0.673
Liver Dysfunction	27 (19.9)	21 (21.4)	6 (15.8)	0.473
Use of Supportive Therapy				
Intravenous Fluids	109 (80.1)	82 (83.7)	27 (71.1)	0.084
Electrolyte Replacement	62 (45.6)	47 (48.0)	15 (39.5)	0.358
Oxygen Therapy	14 (10.3)	11 (11.2)	3 (7.9)	0.571

Relapse was significantly associated with poor medication adherence, with 57.7% of relapsed patients showing no adherence compared to 17.9% in the non-relapse group (p<0.001). Higher CIWA-Ar scores at admission (17.2 ± 4.9 vs. 14.1 ± 4.7, p=0.002), previous withdrawal episodes (53.8% vs. 22.6%, p<0.001), ICU admission (13.5% vs. 2.4%, p=0.007), and lack of rehabilitation participation (19.2% vs. 57.1%, p<0.001) were also associated with relapse. Strong family support and employment were protective factors (p<0.001 and p=0.002, respectively). Stress, cravings, and social pressure were major relapse triggers (p<0.05) (Table 4).

Table 4: Multiple Linear Regression Analysis for Factors Associated with Global DNA Methylation

Variable	Relapsed (n=52)	No Relapse (n=84)	p-value
	Frequency (%)/Mean ± SD		
Medication Adherence at 1 Month			
Complete Adherence	12 (23.1)	55 (65.5)	<0.001
Partial Adherence	10 (19.2)	14 (16.7)	0.711
No Adherence	30 (57.7)	15 (17.9)	<0.001
CIWA-Ar Score at Admission	17.2 ± 4.9	14.1 ± 4.7	0.002
Previous Withdrawal Episodes	28 (53.8)	19 (22.6)	<0.001

Participation in Rehabilitation	10 (19.2)	48 (57.1)	<0.001
ICU Admission During Hospitalization	7 (13.5)	2 (2.4)	0.007
Alcohol Abstinence at 3 Months	15 (28.8)	70 (83.3)	<0.001
Readmission for AWS within 6 Months	18 (34.6)	6 (7.1)	<0.001
Psychiatric Disorders at Baseline			
Depression	19 (36.5)	15 (17.9)	0.019
Anxiety	14 (26.9)	12 (14.3)	0.072
Psychosis	4 (7.7)	2 (2.4)	0.218
Suicidal Ideation During AWS	8 (15.4)	5 (6.0)	0.088
Support System			
Strong Family Support	16 (30.8)	62 (73.8)	<0.001
Weak/No Family Support	36 (69.2)	22 (26.2)	<0.001
Employment Status			
Employed	21 (40.4)	58 (69.0)	0.002
Unemployed	31 (59.6)	26 (31.0)	0.002
Trigger for Relapse			
Social Pressure	13 (25.0)	9 (10.7)	0.032
Stress/Depression	21 (40.4)	8 (9.5)	<0.001
Cravings	26 (50.0)	10 (11.9)	<0.001
Family Conflicts	9 (17.3)	5 (6.0)	0.042

DISCUSSION

This study assessed treatment patterns in patients with Alcohol Withdrawal Syndrome (AWS) during hospitalization and post-discharge, examining differences in outcomes based on benzodiazepine and non-benzodiazepine treatment approaches.

The demographic profile of the study population revealed a mean age of 42.6 years, predominantly male (94.1%), and with a significant history of alcohol use. The duration of alcohol consumption was notably high (mean 12.6 years), similar to prior studies that identified prolonged alcohol use as a major risk factor for severe withdrawal symptoms.[13,14] While no significant differences were observed in gender, marital status, or employment status between treatment groups, daily alcohol consumption was significantly higher in the benzodiazepine group (p=0.048), suggesting a greater severity of dependence, which aligns with the findings of Nagappa et al., and Kaur et al.[15,16]

The presence of comorbidities was observed in 43.4% of the cohort, with hypertension (19.1%) and diabetes (10.3%) being the most prevalent, comparable to epidemiological studies that report an increased risk of cardiovascular and metabolic conditions among chronic alcohol users.[17,18] Interestingly, there was no significant difference in comorbidity distribution between benzodiazepine and non-benzodiazepine groups, indicating that baseline health status did not influence treatment selection.

Regarding treatment, benzodiazepines were the predominant choice (72.1%), with diazepam (41.2%) being the most frequently prescribed, consistent with guidelines recommending long-acting benzodiazepines for AWS management [19,20]. Non-benzodiazepine alternatives such as clonidine (16.2%) and gabapentin (7.4%) were prescribed in select cases, aligning with emerging evidence supporting their role in milder cases or contraindications to benzodiazepines.[21] Adjunctive treatments, including thiamine (100%) and multivitamins (98.5%), were widely administered, reinforcing the established practice of nutritional support in AWS to prevent Wernicke's encephalopathy.[22]

The severity of withdrawal symptoms, measured by CIWA-Ar scores, was significantly higher in the benzodiazepine group at admission (16.1 ± 5.0 vs. 13.5 ± 5.6, p=0.027). However, both groups demonstrated significant symptom reduction, with lower CIWA-Ar scores at discharge (4.5 ± 2.2 vs. 3.7 ± 2.4, p=0.043), indicating effective symptom management. ICU admission was required in 14.0% of cases, primarily in those with severe AWS, comparable to previous studies reporting ICU admission rates of 10–20% in severe withdrawal.[23] Complications such as delirium tremens (15.4%) and seizures (11.8%) were consistent with prior reports, underscoring the importance of early intervention.[24]

Post-discharge, medication adherence significantly influenced relapse rates, with complete adherence observed in only 23.1% of relapsed patients compared to 65.5% in those who maintained abstinence (p<0.001). Non-adherence was strongly associated with relapse (57.7% vs. 17.9%, p<0.001), corroborating findings by Bharadwaj et al., and Sliedrecht et al., that poor adherence is a key predictor of alcohol relapse.[25,26] Rehabilitation participation was also markedly lower among relapsed individuals (19.2% vs. 57.1%, p<0.001), further supporting the role of structured therapy in preventing relapse.[27]

Psychiatric comorbidities were significantly associated with relapse, particularly depression (36.5% vs. 17.9%, p=0.019), consistent with studies highlighting coexisting mental health disorders as relapse risk factors.[28] Family and social factors also played a critical role, with weak or absent family support observed in 69.2% of relapsed patients (p<0.001), emphasizing the protective effect of strong social networks.[29] Employment status significantly differed, with higher unemployment rates among relapsed individuals (59.6% vs. 31.0%,

p=0.002), in line with research linking economic instability to increased relapse risk.[30]

Triggers for relapse varied, with stress/depression (40.4%, p<0.001) and alcohol cravings (50.0%, p<0.001) being the most common, mirroring findings from Lohit et al.[31] These results highlight the need for targeted psychological interventions and craving management strategies post-discharge.

Limitations

This study has several limitations, including its single-center design, which limits generalizability, and its retrospective nature, which may introduce information bias. The short follow-up duration may not fully capture long-term relapse patterns, and reliance on self-reported adherence and relapse data introduces recall and social desirability biases. Variability in treatment regimens may affect outcome comparisons, and the lack of standardized psychiatric assessments limits insights into comorbidities. Additionally, the absence of objective biomarkers for alcohol use monitoring and limited socioeconomic data prevent a comprehensive analysis of factors influencing adherence and relapse. These limitations should be considered when interpreting findings.

CONCLUSION

This study highlights the varied treatment patterns for Alcohol Withdrawal Syndrome, emphasizing the role of benzodiazepines and non-benzodiazepine alternatives. Medication adherence, participation in rehabilitation, and strong social support were key factors in reducing relapse rates. Higher CIWA-Ar scores, previous withdrawal episodes, and psychiatric comorbidities increased relapse risk. Despite treatment, complications such as delirium tremens and seizures were observed. The findings underscore the need for individualized treatment strategies, enhanced post-discharge support, and adherence monitoring to improve long-term outcomes. Future research should explore standardized protocols and long-term relapse prevention strategies.

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