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Original Article

Psychiatry/Mental Health Section

Assessment of Treatment Patterns in Patients with Alcohol Withdrawal Syndrome during Hospitalisation and Post-discharge: A Retrospective Cohort Study

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ABSTRACT

Introduction: Alcohol dependence is an increasing and pervasive problem. Alcohol Withdrawal Syndrome (AWS) is a cluster of symptoms that occur in alcohol-dependent individuals after cessation or reduction of alcohol consumption. However, studies on the clinicoepidemiological profile of patients with AWS and treatment patterns in India are scarce.

Aim: To assess the treatment patterns during hospitalisation and after discharge in Indian patients with AWS.

Materials and Methods: A retrospective observational study was conducted using data from 1000 patients with AWS who were admitted to nine addiction centres across India. Data from medical charts from the previous five years were collected over six months, from January to June 2022. The study included patients of either sex, aged ≥18 years at the time of data collection, who had been hospitalised for AWS symptoms and had ≥3 months of documented follow-ups. The primary endpoints of the study were the most commonly used medications and their dose titrations in the treatment of AWS, as well as the duration of treatment in the hospital and post-discharge. Key secondary endpoints included the socio-demographic profile of patients, common co-morbidities, common signs and symptoms, the association between prescription patterns of Benzodiazepines (BZDs) and liver enzyme levels, and the average duration of hospital stay. Continuous variables were summarised as mean and Standard Deviation (SD), while categorical variables were summarised as frequency and percentages. Levels of serum Aspartate Aminotransferase (AST), Alanine Transaminase (ALT), γ-Glutamyl Transferase (GGT), and bilirubin were recorded from the source data, if available, and the association with the use of chlordiazepoxide and lorazepam was analysed using the Chi-square test.

Results: The mean±SD age of the 1000 enrolled patients was 41.4±9.6 years, with the majority (n=997; 99.7%) being males. BZDs were the mainstay pharmacotherapy, with lorazepam (n=686; 68.6%) and chlordiazepoxide (n=482; 48.2%) being the two most commonly prescribed BZDs during hospitalisation. During post-discharge treatment, 57.0% (n/N=74/130) of patients received lorazepam, while 52.0% (n/N=67/130) received chlordiazepoxide. Frequently used drug regimens during hospitalisation included fixed doses of chlordiazepoxide {25 mg twice a day (BID:143/482; 29.7%), 20 mg thrice a day (TID:103/482; 21.4%), or 25mg TID (87/482; 18.0%)}, or lorazepam {2 mg TID (188/686; 27.4%), 2 mg BID (183/686; 26.7%), or 2 mg once a day (OD;175/686; 25.5%)}. Commonly observed signs and symptoms included tremors (n=567; 56.7%), irritability (n=539; 53.9%), and agitation (n=500; 50.0%). Depression (n=182; 18.2%) and anxiety (n=136; 13.6%) were the most commonly reported co-morbidities. Among the patients, only 13.4% (86/641) had an AST/ALT ratio >2, and 12.9% (44/340) had AST and GGT levels >2× Upper Limit of Normal (ULN). There was no significant difference in these patients between those receiving and not receiving chlordiazepoxide (p>0.05). The mean±SD duration of hospitalisation was 23.1±18.97 days, while the mean±SD duration of treatment during hospitalisation and post-discharge was 22.3±16.36 days and 71.6±52.3 days, respectively.

Conclusion: The two most commonly prescribed drugs during hospitalisation and post-discharge were the BZDs, lorazepam and chlordiazepoxide. Fixed-dose regimens of chlordiazepoxide at 25 mg BID or TID, or 20 mg TID, and lorazepam at 2 mg TID, BID, or OD were frequently used during hospitalisation.

Keywords: Alcohol dependence, Benzodiazepines, Chlordiazepoxide, Deaddiction, Pharmacotherapy

INTRODUCTION

Alcohol dependence is a major public health problem in India, with an estimated 34-42% of adult Indians reported to have used alcohol in their lifetime. Approximately 5-7% are estimated to be alcohol abusers, and it is believed that 10-20 million individuals require treatment for alcohol dependence [1]. Worldwide, an estimated 76.3 million people have Alcohol Use Disorders (AUDs), resulting in 1.8 million deaths annually. It is estimated that upto 42% of patients admitted to general hospitals and one-third of patients admitted to hospital Intensive Care Units (ICUs) have AUD [2].

The AWS typically presents as mild to moderate symptoms that resolve within a few days. However, severe cases of AWS can lead to generalised seizures, hallucinations, and Delirium Tremens (DT), which can be fatal [3]. Factors such as increasing age, longer duration of alcohol use, higher Alcohol Use Disorder Identification Test (AUDIT) scores, and specific symptoms related to hallucinations, orientation, and seizures have been found to be associated with severe alcohol withdrawal [4,5]. Socio-demographics, mental health, and family history can also influence the risk of alcoholism [6].

The management of AWS is tailored to the severity of symptoms. Some patients with minor withdrawal signs may only require supportive care, while those with moderate or severe withdrawal may require medication and other interventions [7]. BZDs are considered the "gold-standard" treatment for AWS. They have proven efficacy in preventing the development of complicated forms of AWS, reducing the incidence of seizures, DT, and the associated

risk of mortality [8,9]. Studies suggest that long-acting BZDs like chlordiazepoxide and diazepam provide smoother withdrawal compared to short-acting BZDs like lorazepam, without the risk of rebound symptoms occurring late during withdrawal [9,10]. However, in patients with reduced liver metabolism (such as the elderly or those with advanced liver disease), short-acting agents like oxazepam and lorazepam may be preferred to avoid excessive sedation and respiratory depression [11].

The use of long-acting BZDs is limited in patients with liver disease due to their dependence on demethylation and hydroxylation metabolic pathways, long half-lives, and the presence of active metabolites, which can lead to drug accumulation. Short-acting BZDs may be effective in patients with liver disease but carry a higher risk of rebound symptoms [3]. There are two primary approaches to administering BZDs during alcohol withdrawal treatment: the traditional Fixed-dose (FD) approach and the Symptom-Triggered Dose (STD) approach. The FD approach is beneficial for patients who receive general anaesthesia and beta blockers for cardiovascular disorders. However, the benefit of the STD approach is yet to be established, although it appears to be effective when the correct dose of BZDs is administered based on symptoms [10].

Currently, there is a lack of nationwide studies on the clinical and epidemiological profiles of patients with AWS, as well as the clinical presentation and treatment patterns of AWS in Indian settings for alcohol deaddiction [1,3,4,12-14]. This retrospective study is the first to demonstrate holistic management approaches, from hospitalisation to discharge, for patients with AWS admitted to deaddiction centres across India. The primary objective of this pan-India study was to assess hospitalisation and post-discharge treatment patterns in patients with AWS, while the secondary objective was to evaluate the clinical and demographic profiles of patients with AWS.

MATERIALS AND METHODS

This multicentre, observational, retrospective cohort study aimed to collect data from patients with AWS who met all the eligibility criteria through the review of their medical charts/records at nine study sites in India. Data from medical charts over the past five years were collected over a six-month period, from January 2022 to June 2022. [Table/Fig-1] lists the centres where the study was conducted and the number of patients enrolled at each centre.

Inclusion criteria: Male or female patients aged ≥18 years at the time of data collection who had been hospitalised for AWS symptoms and had atleast three months of documented follow-ups were included in the study.

Exclusion criteria: Patients directly admitted to the ICU when alcohol withdrawal treatment was initiated and patients with a positive urine toxicology screen for BZDs (unless given for the treatment of alcohol withdrawal), barbiturates, opiates, or other illegal substances were excluded from the study.

Study endpoints: The primary endpoints were: 1) medications used in the management of AWS and their dose titration; and 2) average duration of treatment during hospitalisation and after discharge. Secondary endpoints included: 1) socio-demographic characteristics of patients with AWS; 2) common signs and symptoms of AWS; 3) common co-morbid conditions in patients with AWS; 4) association between BZD use and liver enzyme levels; 5) adjunctive treatment used for alcohol deaddiction; 6) average duration of hospital stay; and 7) non pharmacological treatment during the post-discharge period.

Study Procedure

Medical records of 1000 patients diagnosed with AWS were evaluated to obtain adequate data to generate statistically and clinically meaningful results for the planned objectives. Demographic characteristics, including age, Body Mass Index (BMI), gender, relevant AWS-related history (such as family history of alcohol dependence/other psychiatric illness), occupation, details of smoking consumption, other substance use, and history of alcohol withdrawal seizures or DT, were collected. Detailed medical history, such as the time of occurrence of the first related symptom of AWS, medication history, and current medical conditions (including current medications), were recorded. The clinical assessment of AWS diagnosis was performed using available data at each site. Symptoms of AWS, such as nausea/vomiting, auditory disturbances, tactile disturbances, visual disturbances, tremors, paroxysmal sweats, agitation, irritability, anxiety, headache, orientation (clouding of sensorium), hepatomegaly, icterus, and ascites, were captured as available. The time of onset of withdrawal symptoms was recorded from the source data.

Data on the management of AWS, such as the BZDs used and their dosage patterns (once a day [OD], twice a day [BID], or thrice a day [TID]), other medications (including adjunctive treatment) used with their dosage patterns, non pharmacological treatment, duration of treatment for hospitalised patients, duration of hospital stay, post-discharge treatment used for AWS, and medication-related adverse events were recorded if available.

Results of clinical laboratory tests, such as levels of serum AST, ALT, GGT, and bilirubin, were recorded if available and associated with the use of BZDs.

S. No.	Centre name	IEC name	ICE number and approval date	No. of patients enrolled
1	Lokmanya Tilak Municipal Medical College and General Hospital, Mumbai, Maharashtra, India	Institutional Ethics Committee Human Research, Lokmanya Tilak Municipal Medical College and General Hospital	IEC/94/21 22 Dec 2021	100
2	Spandana Hospital Rehabilitation Centre, Bengaluru, Karnataka, India	Royal Pune Independent Ethics Committee	RPIE131121 10 Nov 2021	100
3	Tulasi Health Care, New Delhi, India	Royal Pune Independent Ethics Committee	RPIE261221 21 Dec 2021	50
4	Ashirbad Drug Deaddiction Centre, Bhubaneswar, Odisha, India	Royal Pune Independent Ethics Committee	RPIE131121 10 Nov 2021	100
5	Chetana Hospital, Hyderabad, Telangana, India	Royal Pune Independent Ethics Committee	RPIE131121 10 Nov 2021	100
6	Tekchand Sidana Memorial Psychiatric Hospital and Deaddiction Centre, Sri Ganganagar, Rajasthan, India	Royal Pune Independent Ethics Committee	RPIE261221 21 Dec 2021	150
7	Central Institute of Behavioural Sciences, Nagpur, Maharashtra, India	Royal Pune Independent Ethics Committee	RPIE261221 21 Dec 2021	150
8	Asha Hospital, Hyderabad, Telangana, India	Ethics Committee, Asha Hospital	20 Mar 2022	70
9	Kanoria Hospital and Research Centre, Gandhinagar, Gujarat, India	Royal Pune Independent Ethics Committee	RPIE131121 10 Nov 2021	180

[Table/Fig-1]: Participating centres.

STATISTICAL ANALYSIS

Categorical variables were summarised as frequency and percentages. The median duration of treatment given to hospitalised patients and the median duration of treatment post-discharge were estimated using the Kaplan-Meier method [15]. Gender, occupation, medical history, family history of alcohol dependence/other psychiatric illness, history of daily alcohol intake, common AWS signs and symptoms, and adjunctive treatment used for alcohol deaddiction were summarised using frequency and percentages. Continuous variables were summarised using mean and Standard Deviation (SD). The association between BZD use and liver enzyme levels was determined using the Chi-square test. Missing data were not imputed. Statistical analysis was performed using R software version 4.1.

RESULTS

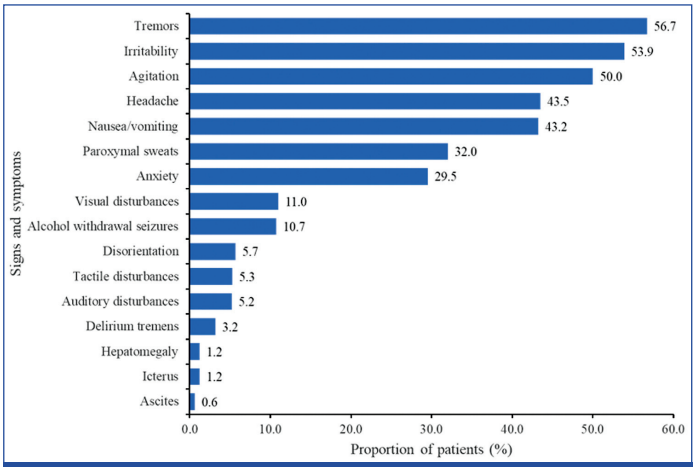
Demographics and baseline characteristics: Patient demographic details and baseline characteristics are summarised in [Table/Fig-2]. The majority of the patients were males 997 (99.7%). The most common occupation was business 440 (44.0%), while 88 (8.%) of patients were unemployed. Family history of alcohol dependence and psychiatric illness was reported by 168 (16.8%) and 54 (5.4%) of patients, respectively. Only 253 (25.3%) of subjects had a personal history of smoking, and 149 (14.9%) had a history of substance abuse. While the majority of patients (n=651; 65.1%) did not have any Co-morbidities, depression and anxiety were reported by 182 (18.2%) and 136 (13.6%) of patients, respectively.

Characteristics	Overall (N=1000)
Age (years), mean±SD	41.4±9.6
BMI (kg/m^2), mean±SD	24.0±3.6
Occupation, n (%)	
Business	440 (44.0)
Unemployed	88 (8.8)
Farming	75 (7.5)
Driving	66 (6.6)
Labour	65 (6.5)
Services	49 (4.9)
Others*	217 (21.7)
Co-morbidities, n (%)	
Depression	182 (18.2)
Anxiety	136 (13.6)
Diabetes	56 (5.6)
Hypertension	56 (5.6)
Family history, n (%)	
Alcohol dependence	168 (16.8)
Psychiatric illness	54 (5.4)
Personal history, n (%)	
Smoking	253 (25.3)
Other substance abuse	149 (14.9)

[Table/Fig-2]: Patient demographics and baseline characteristics.
*Others include security guards, information technology employees, electricians, mechanics, plumbers, students, government employees, non government employees, engineers, teachers, managers, accountants, police and doctors

Clinical signs and symptoms of AWS: [Table/Fig-3] presents the signs and symptoms of AWS observed in the study population. The most common symptoms were tremors (n=567; 56.7%), followed by irritability (n=539; 53.9%) and agitation (n=500; 50.0%). Delirium Tremens (DT) was observed in only 3.2% (n=32) of patients.

Management of AWS: During hospitalisation, the most prescribed medications were lorazepam (n=686; 68.6%) and chlordiazepoxide (n=482; 48.2%). During the post-discharge period, lorazepam and chlordiazepoxide were prescribed to 57.0% (74/130) and 52.0% (67/130) of patients, respectively. The most frequently prescribed drug regimen during hospitalisation was a fixed dose of chlordiazepoxide at 25 mg BID to 29.7% (143/482) of patients, followed by 20 mg TID to 21.4% (103/482) of patients and 25 mg TID to 18.0% (87/482) of patients. For lorazepam, 2 mg TID (27.4% [188/686]), followed by 2 mg BID (26.7% [183/686]) and 2 mg OD (25.5% [175/686]) were the most commonly prescribed fixed doses [Table/Fig-4].



[Table/Fig-3]: Clinical signs and symptoms of Alcohol Withdrawal Syndrome (AWS).

Drugs and dosing regimen, n (%)	During hospitalisation (N=1000)	After discharge (N=130)
Lorazepam	686 (68.6)	74 (57.0)
2 mg TID	188 (27.4)	
2 mg BID	183 (26.7)	
2 mg OD	175 (25.5)	
Chlordiazepoxide	482 (48.2)	67 (52.0)
25 mg BID	143 (29.7)	
20 mg TID	103 (21.4)	
25 mg TID	87 (18.0)	
Clonazepam	48 (4.8)	1 (0.8)
1 mg HS	22 (2.2)	
Oxazepam	1 (0.1)	1 (0.8)
10 mg HS	1 (100)	

[Table/Fig-4]: Prescription patterns of most frequently used Benzodiazepines (BZD) for Alcohol Withdrawal Syndrome (AWS).
*AWS: Alcohol withdrawal syndrome; OD: Once a day; BID: Twice a day; TID: Thrice a day; HS: Bedtime

Thiamine (n=420; 42.0%), disulfiram (n=187; 18.7%), and acamprosate (n=111; 11.1%) were the most commonly prescribed adjunctive treatments, and the frequently prescribed dosage regimens for these drugs were 100 mg BID (55.7% [234/420]), 250 mg OD (85.5% [160/187]), and 333 mg TID (85.5% [95/111]), respectively [Table/Fig-5]. Antipsychotics and antidepressants were prescribed for 18.9% (n=189) and 19.3% (n=193) of patients, respectively.

Drugs, n (%)	During hospitalisation (N=1000)	After discharge (N=130)
Vitamins		
Thiamine	420 (42.0)	54 (41.0)
100 mg OD	138 (32.8)	
100 mg BID	234 (55.7)	
100 mg TID	30 (7.1)	
Benfothiamine	30 (3)	2 (1.5)
150 mg BID	9 (30.0)	
100 mg BID	8 (26.6)	
100 mg OD	7 (23.3)	

Anti-craving medicines		
Disulfiram	187 (18.7)	69 (53.0)
250 mg OD	160 (85.5)	
250 mg BID	22 (11.7)	
500 mg BID	4 (2.2)	
Acamprosate	111 (11.1)	63 (48.0)
333 mg TID	95 (85.5)	
333 mg BID	10 (9.0)	
333 mg OD	6 (5.5)	
Naltrexone	21 (2.1)	5 (3.8)
50 mg OD	16 (76.2)	
50 mg BID	5 (23.8)	

[Table/Fig-5]: Adjunctive treatment for Alcohol Withdrawal Syndrome (AWS).
OD: Once a day; BID: Twice a day; TID: Thrice a day; HS: Bedtime

The mean±SD duration of treatment during hospitalisation was 22.3±16.36 days, and the mean±SD duration of hospitalisation was 23.1 (18.97) days. The mean±SD duration of treatment post-discharge was 71.6±52.3 days. During the follow-up period, 500 (50.0%) patients underwent non pharmacological treatments such as group therapy 230 (23%), cognitive-behavioural therapy 140 (14%), and motivational enhancement therapy 67 (6.7%).

Association between liver enzyme abnormalities and prescription pattern of pharmacotherapy for AWS: Most of the patients (86.6%) in the present study did not had an elevated AST/ALT ratio. Further, the prescription patterns of the two most prescribed BZDs, chlordiazepoxide and lorazepam, in patients with or without abnormal liver enzyme levels were evaluated [Table/Fig-6]. Significant p-values for AST and ALT indicate a statistical association, suggesting that AST or ALT levels greater than 2 times the Upper Limit of Normal (ULN) may be a reason for prescribing chlordiazepoxide less frequently and lorazepam more frequently. However, out of the 641 patients with measurable AST/ALT ratios, 555 patients did not have a ratio greater than 2 times ULN. Among the remaining 86 patients with an elevated AST/ALT ratio, lorazepam was prescribed to 64.0% (55/86) of patients, while chlordiazepoxide was prescribed to 43.0% (37/86) of patients.

Liver enzyme level	Type of BZD, n (%)		p-value*
	Chlordiazepoxide not given	Chlordiazepoxide given	
AST <2×ULN (n=536)	268 (50.0)	268 (50.0)	0.011
AST >2×ULN (n=117)	74 (63.2)	43 (36.8)	
ALT <2×ULN (n=599)	303 (50.6)	296 (49.4)	0.004
ALT >2×ULN (n=48)	35 (72.9)	13 (27.1)	
AST/ALT <2 ULN (n=555)	296 (53.3)	259 (46.7)	0.607
AST/ALT >2 ULN (n=86)	49 (57.0)	37 (43.0)	
GGT <2×ULN (n=208)	107 (51.4)	101 (48.6)	0.742
GGT >2×ULN (n=138)	74 (53.6)	64 (46.4)	
AST and GGT <2×ULN (n=186)	91 (48.9)	95 (51.1)	
AST and GGT >2×ULN (n=44)	16 (36.4)	28 (63.6)	0.182
Bilirubin <2×ULN (n=472)	292 (61.9)	180 (38.1)	0.001
Bilirubin >2×ULN (n=152)	25 (16.4)	127 (83.6)	
AST <2×ULN (n=536)	249 (46.5)	287 (53.5)	0.002
AST >2×ULN (n=117)	36 (30.8)	81 (69.2)	
ALT <2×ULN (n=599)	272 (45.4)	327 (54.6)	0.006
ALT >2×ULN (n=48)	12 (25.0)	36 (75.0)	
AST/ALT <2 ULN (n=555)	250 (45.0)	305 (55.0)	0.147
AST/ALT >2 ULN (n=86)	31 (36.0)	55(64.0)	
GGT <2×ULN (n=208)	96 (46.1)	112 (53.9)	>0.999
GGT >2×ULN (n=138)	63 (45.7)	75 (54.3)	
AST and GGT <2×ULN (n=186)	86 (46.2)	100 (53.8)	0.410
AST and GGT >2×ULN (n=44)	24 (54.5)	20 (45.5)	
Bilirubin <2×ULN (n=472)	181 (38.3)	291 (61.7)	0.001
Bilirubin >2×ULN (n=152)	105 (69.1)	47 (30.9)	

[Table/Fig-6]: Association between liver enzyme levels and prescription pattern of Benzodiazepines (BZD).
*Chi-square test; AST >2×ULN was defined as a value >96 U/L; ALT >2×ULN was defined as a value >110 U/L; GGT >2×ULN was defined as a value >122 U/L; bilirubin >2×ULN was defined as a value >2.4 mg/dL
ALT: Alanine transaminase; AST: Aspartate transaminase; BZD: Benzodiazepine; GGT: Gamma glutamyltransferase; ULN: Upper limit of normal

In the case of 230 patients with measurable AST and GGT values, 186 patients did not have levels greater than 2 times ULN. Among the remaining 44 patients with elevated levels (AST >96 U/L; GGT >122 U/L), chlordiazepoxide was prescribed to 63.6% (28/44) of patients, and lorazepam was prescribed to 45.5% (20/44) of patients. Thus, based on a statistically significant trend for only AST and ALT, and a statistically insignificant trend for the remaining enzymes, it was difficult to draw any conclusive inference regarding the association between liver enzymes and drug prescription patterns.

DISCUSSION

In this multicentre, retrospective analysis conducted on data collected from 1000 patients with AWS across nine sites in India, nearly all patients were males (997), with a family history of alcohol dependence observed in 16.8% of the study cohort. The mean±SD duration of treatment during hospitalisation was 22.3±16.36 days. Chlordiazepoxide and lorazepam were the most prescribed BZDs during hospitalisation and after discharge, and no significant association was found between impaired liver function, as assessed by AST/ALT ratios greater than 2, or AST and GGT levels greater than 2 times ULN, and the prescription pattern of these two drugs.

A male preponderance in this study was consistent with a study conducted on drug utilisation evaluation of lorazepam among AWS patients, where 94.4% of the study population were males [16]. This pattern may indicate the presence of social stigma or restrictions by family members on women seeking help for alcohol affliction in India [17]. According to the World Health Organisation's global status report on alcohol and health (2005), men surpass women in heavy drinking by a ratio of 4:1, which could also explain the predominance of alcohol dependence-related problems in men in this study. Family history of alcohol dependence was observed in only 16.8% of the patients in the study cohort. It is well-established that family history of alcohol dependence is a risk factor for AUD, and patients with a positive family history have a greater predisposition to lifetime alcohol dependence than those with a negative family history [18,19].

Studies conducted in the general population have shown that individuals with depressive disorders have a two-to-three-fold greater risk of alcohol-related disorders [20]. This retrospective observational study found that common co-morbidities were depression and anxiety, which was consistent with the known presence of depressive disorders in patients with AWS. The most frequent symptoms associated with AWS in this study were tremors, irritability, and agitation, which are known to be prevalent in patients experiencing alcohol withdrawal of mild to moderate severity [4,13,21].

Chlordiazepoxide and lorazepam were found to be the most commonly prescribed BZDs for managing AWS during hospitalisation and after discharge. BZDs have been the preferred drugs for treating AWS due to their low abuse potential and fewer withdrawal symptoms [22,23]. Long-acting BZDs such as chlordiazepoxide and clonazepam are preferred for

moderate alcohol detoxification, while medium-acting BZDs like oxazepam and lorazepam are recommended if liver function is compromised [24,25]. In this study, patients mostly received fixed-dose regimens, with common dosing regimens being 25 mg BID, 20 mg TID, or 25 mg TID for chlordiazepoxide, and 2 mg TID, 2 mg BID, or 2 mg OD for lorazepam. Another study employed symptom-triggered treatment, starting lorazepam and chlordiazepoxide at a dose of 8 mg/day and 80 mg/day, respectively, and tapering them to 2 mg/day and 20 mg/day over a 12-day period [4]. Some studies comparing chlordiazepoxide and lorazepam found no significant differences between the two drugs in terms of withdrawal symptoms during hospitalisation with tapered dosing [17,23,26]. However, additional studies are needed to determine the optimal dosing regimens of BZDs for Indian patients with AWS.

The most commonly used adjunctive treatments for alcohol deaddiction during hospitalisation in this study were thiamine and disulfiram. Vitamin B1 (thiamine) supplementation helps prevent Wernicke's encephalopathy and should be administered orally or intramuscularly to all patients [3]. To support abstinence and prevent relapse, patients require concurrent treatment with disulfiram and/or acamprosate [27].

AST/ALT ratio >2 and AST and GGT levels >2 times ULN are considered important markers of liver damage in patients with AUD [28,29]. In this study, the majority of patients did not have an AST/ALT ratio >2 (86.6%) or AST and GGT >2 times ULN (87.1%). Among the remaining patients, no significant difference was observed in the prescription pattern of the two most commonly prescribed BZDs, lorazepam and chlordiazepoxide. These findings were consistent with another study that found no significant differences in the levels of various liver biomarkers between the lorazepam and chlordiazepoxide groups at baseline and end of the study [23]. Additionally, chlordiazepoxide, like other BZDs, has rarely been associated with elevations in ALT levels and clinically apparent liver injury [30]. Therefore, the choice of BZD in this study did not appear to be influenced by markers of liver damage. However, prospective studies are needed to evaluate the impact of specific BZD treatment modalities on liver enzymes in order to establish their effect on liver biomarkers and physicians' prescription preferences.

The strengths of this study include the nationwide assessment of AWS treatment patterns in a large cohort of patients admitted to deaddiction centres for AUD, providing real-world data.

Limitation(s)

A key limitation of this study was its retrospective design, which may have introduced selection bias. Additionally, there may be risks of recall and observer bias due to reliance on memory. Furthermore, the impact of treatment on liver biomarkers could not be assessed due to the observational design.

CONCLUSION(S)

The most commonly prescribed drugs for patients with AWS during hospitalisation and after discharge were the BZDs lorazepam and chlordiazepoxide. Fixed-dose regimens of chlordiazepoxide (25 mg BID, 20 mg TID, or 25 mg TID) or lorazepam (2 mg TID, 2 mg BID, or 2 mg OD) were frequently used during hospitalisation. While the majority of patients did not exhibit abnormalities in liver damage markers, such as an AST/ALT ratio >2 and AST and GGT >2 times ULN, among those with these abnormalities, there were no significant differences in the prescription patterns of lorazepam and chlordiazepoxide. However, prospective studies are needed to assess the impact of treatment on liver function abnormalities.

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