

Clinical characteristics and health outcomes in patients with alcohol withdrawal syndrome: an observational study from Oman

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BACKGROUND: Globally, alcohol withdrawal syndrome (AWS) is considered a serious medical diagnosis associated with increasing morbidity and mortality. Little information has been reported on the scope of the problem in Oman.

OBJECTIVES: Study clinical characteristics, management, quality of care, and health outcomes of patients managed for AWS.

DESIGN: Retrospective medical record review.

SETTINGS: University hospital.

PATIENTS AND METHODS: The study included all patients with AWS admitted from 1 October 2019 to 30 September 2020. We collected demographic and clinical characteristics and did a univariate analysis of factors related to 90-day readmission.

MAIN OUTCOME MEASURES: Length of hospital stay, 90-day readmission, referral rate to alcohol rehabilitation center.

SAMPLE SIZE AND CHARACTERISTICS: 150 male patients with median (IQR) age of 39.5 (32-48) years.

RESULTS: Most patients (70.7%, n=106) were smokers and 44 (29.3%) had a history of drug abuse. The average length of hospital stay was 2.3 (0.9-4.6) days. Approximately 9% of total hospital bed days were used to care for patients with AWS. Chronic liver disease (35.3%), diabetes mellitus (24.7%), and hypertension (24.0%) were common among AWS patients. The 90-day readmission rate (32.7%) was high, and there was low referral to alcohol rehabilitation (16.7%). Diabetes and epilepsy were associated with 90-day readmission.

CONCLUSION: AWS is an important diagnosis that represents an important burden on acute medical services. Establishing a drug and alcohol service in our institution is an essential step to optimise care for patients with alcohol-related disorders.

LIMITATIONS: Retrospective, so unable to collect data on manifestations of AWS such as delirium tremens, which is the most severe form of AWS. Also, the reason for the lack of referral to an outpatient alcohol rehabilitation program was not apparent.

CONFLICT OF INTEREST: None.

Alcohol-related disorders are a growing health concern worldwide; an estimated 3.8% of deaths and 4.6% of health complications are related to alcohol drinking.¹ Alcohol-related social harm and alcohol-associated health care spending cost more than 1% of the gross national product in middle and high-income countries.² Alcohol withdrawal syndrome (AWS) is a life-threatening condition that occurs when alcohol-dependent patients cut down or stop drinking alcohol.^{3,4} Symptoms of AWS range from mild symptoms like nausea and vomiting to severe symptoms such as life-threatening seizures and delirium tremens.⁵ AWS has been reported among the significant risk factors for morbidity and mortality worldwide.⁶ The inpatient mortality rate of AWS is estimated to be 2.4%.⁷ Benzodiazepines have been used to treat AWS over the last three decades.^{8,9} There are two well-known strategies for the treatment of alcohol withdrawal with benzodiazepines: first, a fixed schedule regimen with additional per-need doses depending on symptoms; second, a symptom triggered regimen by which benzodiazepines are administered according to the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar) dosing protocol.⁸ An alcohol rehabilitation program is an essential intervention to improve care for people suffering from alcohol-related disorders.¹⁰

Like other Arabic countries, drug and alcohol abuse is a growing health issue in Oman, especially among young males.^{11,12} According to the World Health Organisation, the prevalence of alcohol-related disorders in Oman is 0.37%.¹² Also, the prevalence of alcohol use was 5% and 10.7% among school and university students, respectively.^{12,13} Overall, there is limited research on alcohol-related disorders, health outcomes, accessibility to services and the quality of care in this part of the World.^{14,15} Given this dearth of information, this study aimed to study clinical characteristics, management, and health outcomes in patients managed for AWS in Oman.

PATIENTS AND METHODS

The study was a retrospective chart review that included all patients with AWS admitted to Sultan Qaboos University Hospital (SQUH) from 1 October 2019 to 30 September 2020. SQUH is a 600-bed multispecialty tertiary care hospital that provides care for parts of Muscat, and is considered a major referral centre for many specialities that provide high-quality care for patients referred from the entire country of Oman. There is no specialised drug and alcohol service at SQUH, and patients with AWS are admitted under the care of the General Medicine Unit for acute management.

Upon discharge, patients were offered referral to the outpatient alcohol rehabilitation program at Al Masarra Hospital, the only public hospital in Oman with a drug and alcohol unit. All patients were treated using a fixed-dosage regimen of benzodiazepines. In addition, the following variables were collected: relevant demographic data, relevant medical history, data on management of AWS, data related to inpatient morbidity and mortality, information on referral to the alcohol rehabilitation program, and information on 90-day readmission to the hospital with AWS.

We defined alcohol withdrawal syndrome according to the criteria proposed by the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).¹⁶⁻¹⁸ Categorical variables are reported as numbers and percentages. Nonuniform continuous variables are reported as the median and interquartile range (IQR). Continuous variables between the two groups were compared using Mann Whitney Wilcoxon Test. The chi-square test or the Fisher exact test were used to assess the association between categorical variables as appropriate. A 2-sided *P* value <.05 was considered statistically significant. Statistical calculations were performed using the Stata v. 16.1 software package (StataCorp). The study was approved by the Medical Ethics Committee of the College of Medicine and Health Sciences at SQUH (REF. NO. SQU-EC/ 326/2021 MREC #2358).

RESULTS

The 150 patients admitted during the study period were all males with a median age of 39.5 (32-48) years (**Table 1**). Fifty-seven patients (38.0%) were admitted with a primary diagnosis of AWS, while 93 patients (62.0%) were admitted with other health issues and developed AWS during admission. Smoking (70.7%) and concurrent abuse of other drugs (29.3%) were common among the patients. Chronic liver disease (35.3%), diabetes mellitus (24.7%), and hypertension (24.0%) were prevalent in our cohort. In addition, 13 patients (8.7%) were diagnosed with epilepsy before hospitalization. The median length of hospital stay was 2.3 (0.9-4.5) days. A total of 730 hospital bed days were used by the patients with AWS, which is approximately 9% of the total hospital bed days available in the male medical ward during the study period. Six patients (4%) were admitted to the intensive care unit (ICU), and 13 patients (8.7%) required care in the high dependency unit (HDU). Twenty-one patients (14%) developed seizures during hospitalization. The median total dose of diazepam was 40 (15-83) mg, administered during hospitalization or prescribed upon discharge. Nineteen

patients (12.7%) left the hospital against medical advice and before completing management. One patient was admitted with decompensated liver disease and died because of alcohol-related liver cirrhosis. Another patient was admitted with infective endocarditis secondary to IV drug abuse and died of refractory septic shock. Twenty-five patients (16.7%) were referred to the alcohol rehabilitation service at Al-Massara Hospital. Forty-nine patients (32.7%) were readmitted with AWS within 90 days. Diabetes mellitus ($P=.047$) and epilepsy ($P=.029$) were significantly prevalent among patients who were readmitted within 90-days (**Table 2**).

DISCUSSION

This study was the first to study clinical characteristics, management, quality of care and health outcomes of patients managed for AWS in Oman. All of our patients were male, with a high rate of 90-day readmission related to AWS. Also, a small percentage of patients were referred to alcohol rehabilitation services, and a relatively high number of patients left the hospital against medical advice. That all were male could be explained by the effect of religious prohibition and shame associated with alcohol drinking, especially among women in the Arabic region.⁵ Overall, alcohol misuse and AWS occur mainly in males.^{6,8}

Patients with AWS occupied 9% of total hospital bed days during the study period in the male medical ward. In addition, 8.7% of patients were managed in HDU, and 4% were managed in the ICU, reflecting the significant burden of this condition in acute health care resources of a major tertiary hospital. Several studies in the US showed that around 20% of hospital admissions and up to 39% of ICU admissions are related to AWS,^{19,20} and patients suffered higher incidence of sepsis (12.9% vs 7.6%, $P<.001$), septic shock (3.6% vs. 2.1%, $P=.001$), and organ damage (67.3% vs. 45.8%, $P<.001$).²⁰ Our cohort of patients was treated traditionally using a fixed dose regimens of benzodiazepines; however, evidence suggests that symptom-triggered treatment using the CIWA-Ar score is safe and an effective modality to shorten the duration of treatment and is associated with a lower incidence of delirium terms.^{4,21,22} Therefore, we recommend implementing symptom-triggered treatment using the CIWA-Ar score to treat AWS in our hospital.

Most of the patients (70.7%) were smokers, which is consistent with previous studies findings.²³ Moreover, smoking cessation was proven to be associated with a decrease in alcohol intake.^{6,24,25} Therefore, we encourage physicians to refer smokers to the smoking cessation clinic at our hospital. Twenty-one patients (14%)

Table 1. Demographic and clinical characteristics of patients admitted with alcohol withdrawal syndrome (n=150).

Age (years)	39.5 (32-48)
Male	150 (100)
Comorbidities	
Smoking	106 (70.7)
Other drug of abuse	44 (29.3)
Diabetes mellitus	37 (24.7)
Chronic liver disease	53 (35.3)
Hypertension	36 (24.0)
Chronic kidney disease	3 (2.0)
Ischemic heart disease	7 (4.7)
Epilepsy	13 (8.7)
Heart failure	0
Primary diagnosis	
Alcohol withdrawal syndrome	57 (38.0)
Acute alcohol induced pancreatitis	24 (16.0)
Opioid overdose	17 (11.3)
Gastrointestinal bleeding	9 (6.0)
Decompensated liver disease	8 (5.3)
Others	35 (23.3)
Hospitalization	
Seizure	21 (14)
Total dose of diazepam (mg)	40 (15-85)
Total dose of thiamine (mg)	600 (300-900)
Need for HDU admission	13 (8.7)
Need for ICU admission	6 (4)
Length of hospital stay (days)	2.3 (0.9-4.6)
Disposition	
Discharged home	129 (86)
Left hospital against medical advice	19 (12.6)
Died during hospitalization	2 (1.3)
Referral to drug and alcohol service	25 (16.7)
Re-admission in 90 days	49 (32.7)

Data are number (%) or median (interquartile range).

developed seizures during hospitalization, which usually occurs in severe alcohol withdrawal,^{26,27} and is associated with heavy alcohol consumption.²⁸ About one-third (n=49, 32.7%) were readmitted within 90 days with AWS. A retrospective study of patients admitted to general medical services with a primary diagnosis of AWS in the Midwestern US reported that 44% of patients had multiple admissions and underlying psychiatric diagnoses ($P=.0303$), a lower educational level ($P=.0071$), concurrent drug misuse ($P=.0002$), a higher Charlson comorbidity index score ($P=.0010$) and a higher CIWA-Ar score ($P<.0001$) were associated with increased risk of readmission.²⁹ Also, a 5-year follow-up study in Germany showed a tremendously high readmission rate for patients with alcohol-induced psychotic disorders.³⁰ On the other hand, a previous study illustrated a reduction in 30-day readmission in symptom-triggered therapy using CIWA-Ar score compared to fixed doses regimen.³¹ Our univariate analysis showed that diabetes mellitus and epilepsy prevalence was significantly higher in the readmitted group than in the non-readmitted with AWS ($P=.047$ and $P=.029$, respectively). This finding is similar to a previous study that concluded that specific comorbidities, including diabetes mellitus, were associated with a higher readmission rate with alcohol withdrawal.²⁹ Also, a large-scale study in primary care settings showed that alcohol drinking patients with diabetes mellitus were more likely to exceed daily alcohol limits than non-diabetic drinkers.¹ This could potentially contribute to the magnitude of alcohol dependence in diabetic patients and the burden of diabetes with its complications; hence, the concurrent presence of AWS and diabetes increases the recurrent admissions with AWS. To our knowledge, there are no previous studies showing that epilepsy is associated with an increased risk of readmission with AWS. We believe that there are several explanations for the high rate of readmission in our cohort, including the absence of drug and alcohol services in our hospital, the high prevalence of diabetes mellitus, the high rate of concurrent smoking and drug abuse, and the use of fixed doses regimen of benzodiazepines in the treatment of AWS instead of symptom-triggered treatment using CIWA-Ar score.

We found that 12.6% of patients left the hospital against medical advice, probably indicating poor patient satisfaction with the care. Furthermore, only 16.7% of the patients were referred to Al-Massara Hospital for alcohol rehabilitation services. A recent study showed that elective detoxification with specialist follow-ups at alcohol and drug centers provides a cost-effective service with successful alcohol abstinence at 12 months,

Table 2. Univariate analysis of potential factors associated with alcohol withdrawal syndrome 90-day readmissions.

	Readmission (n=49)	No readmission (n=101)	P value
Age (years)	40 (32-49)	39 (32-47)	.8852
Comorbidities			
Smoking	13 (73.5)	70 (69.3)	.599
Other drug of abuse	13 (26.5)	31 (30.7)	.599
Diabetes mellitus	17 (34.7)	20 (19.8)	.047
Chronic liver disease	12 (42.9)	32 (31.7)	.179
Hypertension	8 (16.3)	28 (27.7)	.125
Chronic kidney disease	2 (4.1)	1 (1.0)	.249
Ischemic heart disease	3 (6.1)	4 (4.0)	.683
Epilepsy	8 (16.3)	6 (5.9)	.029
Primary diagnosis			
Alcohol withdrawal syndrome	21 (42.8)	36 (35.6)	.393
Acute alcohol induced pancreatitis	9 (18.4)	15 (14.9)	.778
Opioid overdose	5 (10.2)	12 (11.9)	.999
Gastrointestinal bleeding	2 (4.1)	7 (6.9)	.482
Decompensated liver disease	3 (6.1)	5 (5.0)	.717
Others	9 (18.3)	26 (25.7)	.163
Hospitalization			
Seizure	6 (12.2)	0	.666
Total dose of diazepam (mg)	40 (20-95)	30 (10-70)	.0986
Total dose of thiamine (mg)	600 (300-900)	600 (300-900)	.7839
Need for HDU admission	4 (8.2)	9 (8.9)	.999
Need for ICU admission	0 (0)	6 (5.9)	.178
Length of hospital stay (days)	2.2 (1.0-4.4)	2.4 (0.5-4.8)	.5871
Disposition			
Discharged home	45 (91.8)	84 (83.2)	.211
Left hospital against medical advice	4 (8.2)	15 (14.9)	.304
Referral to drug and alcohol service	9 (18.4)	16 (15.8)	.697

Data are number (%) or median (interquartile range).

reducing the overall burden of alcohol dependence in acute care settings.³² We strongly recommend establishing a drug and alcohol unit at SQUH. Meanwhile, health care providers should refer all patients with alcohol misuse upon discharge to the outpatient drug and alcohol unit at Al Masarra Hospital.

The median total dose of diazepam was 40 mg (15-85 mg), and some patients were discharged on a tapering dose of diazepam tablets, which creates concern about potential benzodiazepines abuse. Two patients (1.3%) died during hospitalization. The underlying causes of death were alcohol-related advanced chronic liver cirrhosis and infective endocarditis of a prosthetic valve due to *Pseudomonas aeruginosa* in an IV drug abuser. Overall, our inpatient mortality rate was comparable to the previously reported rates with AWS.⁷

Due to the retrospective design of our study and inadequate documentation, we could not collect data on important manifestations of AWS, including delirium tremens, which is the most severe form of AWS. Also, the reason for the lack of referral to the outpatient alcohol rehabilitation program was not apparent. We understand why patients may decline referral on some occasions, but emphasize that health care providers

should ensure proper counselling of patients to emphasise the importance of alcohol rehabilitation programs in treating alcohol misuse and associated health-related poor outcomes.

This study demonstrated the male predominance of patients treated for AWS. Smoking and concurrent drug-abuse were common. A high proportion of patients were readmitted within 90 days with AWS. Also, drug and alcohol service was poorly engaged in managing patients with AWS due to lack of service in our hospital and underutilisation of the outpatient alcohol rehabilitation program. A relatively high number of patients left the hospital against medical advice before completing the treatment, indicating poor management satisfaction. High occupancy of acute medical beds and the need for treatment in high care settings (ICU, HDU) reflect the added burden of alcohol-related health outcomes in our busy health care system. AWS is a life-threatening condition that might require management in a high-care setting. AWS is an avoidable overburden on the health care system. Therefore, we strongly believe that a drug and alcohol unit is an essential service in a tertiary care setting to improve the care of patients with drug and alcohol withdrawal.

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