

# Various Symptoms and Complications Seen in Critically Ill Adult Substance Use Disorders Patients in Intensive Care Unit of a Tertiary Care Hospital: An Observational Study

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## ABSTRACT

**Introduction:** Substance use disorders are a common problem all over the world. Substance dependence may be associated with one or more substances at the same time and may include the use of illicit or illegal substances or misuse of legal substances like alcohol, tobacco, and prescription drugs. Common substance use disorders include tobacco products, alcohol, benzodiazepines, opioids, and derivatives. This leads to increased mortality, morbidity, medical interventions, along with hospital stays.

**Aim:** To find the challenges like delirium, withdrawal, and its complications in adult patients with substance use disorders who are critically ill, posed to the treating staff in the critical care unit.

**Materials and methods:** A cross-sectional observational study included 110 adult patients of both sexes, aged between 18 and 60 years, who were dependent on substances like tobacco, alcohol, opioids, and benzodiazepines and needed admission to the intensive care unit (ICU); from 15<sup>th</sup> February to 15<sup>th</sup> August 2022. Relevant data on adverse events that occurred due to substance withdrawal, any complications from substance use like local or general infection, and any comorbidity were noted. The Confusion Assessment Method for the ICU (CAM-ICU) scale was used to diagnose delirium. A urine toxicology screen was done. The data were collected, tabulated, and statistically analyzed by descriptive-analytical method.

**Results:** A total of 429 adverse events were noted. The most common adverse event due to substance withdrawal was agitation and delirium (46.39%), followed by inconvenience to other patients in the unit 17.02%, increased requirement of sedation and analgesia (15.11%), increased hospital stay (8.39%), arrhythmias including atrial fibrillation and cardiac myopathy in (4.43%). The younger population was addicted to more than one substance intravenously than the older individuals.

**Conclusion:** The symptoms and complications seen in substance dependents in the ICU increase the morbidity, mortality, hospital stay, number of interventions, and financial burden on a family. These patients not only harm themselves but also harm the treating staff and damage hospital equipment and also disturb other fellow patients.

**Keywords:** Critical care unit, Delirium, Substance withdrawal, Withdrawal complications.

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## INTRODUCTION

Common substance use disorders include alcohol, tobacco products, opioids, derivatives, and benzodiazepines. The routes by which these are consumed include oral, intravenous, intramuscular, and sniffing or inhalation. These patients are prone to infectious diseases like human immunodeficiency virus, hepatitis B, C, and D, sepsis, malignancies, pneumonia, immunosuppression, and other critical illnesses depending upon the route of administration.<sup>1</sup> There can be substance withdrawal or overdose symptoms. These symptoms can mimic serious illnesses like sepsis.

Tobacco product use has a dose-related influence on hospital stay, morbidity, and mortality in the ICU. The clinical care of these patients may be complicated by nicotine withdrawal<sup>2</sup> and this may lead to a higher risk of agitation and delirium in these patients.<sup>2,3</sup> Risk of withdrawal symptoms is highest during the 1st week of quitting smoking and may last for 2–4 weeks.<sup>3</sup> Agitation can occur alone or may be associated with delirium in 64% of tobacco users in ICU.<sup>3</sup>

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Consumption of alcohol is common worldwide. The incidence of delirium due to withdrawal varies from 10 to 60% in patients who consume alcohol.<sup>4</sup> Alcohol withdrawal can lead to delirium tremens. Development of delirium with every passing day is associated with an increased mortality rate of 10% in critically ill.<sup>4</sup>

Opioids and derivatives are other common substances taken orally, by inhalation, or intravenously. The patients who use the intravenous route present with conditions like infection at the injection site, generalized sepsis, deep vein thrombosis, infective endocarditis, septic pulmonary emboli, etc. There is a case series that reported delirium due to opioid withdrawal.<sup>5</sup>

Delirium in benzodiazepine withdrawal is less common, but the administration of benzodiazepines in the ICU commonly leads to delirium and agitation. The management of delirium in the ICU includes treating the underlying disease and environmental factors and avoiding benzodiazepines and other psychoactive medications.<sup>6-8</sup> Occurrences of delirium cause an increase in mechanical ventilation days, hospital-acquired infections, and a higher need for psychotropic agents.<sup>8-10</sup>

Intensive care unit (ICU) delirium is seen in 11–80% of patients.<sup>11</sup> Previous studies have shown that prolonged delirium in ICU itself leads to higher mortality risk.<sup>12</sup> The medical interventions, length of stay in ICU, and mortality are higher in substance use disorders patients.<sup>2,4</sup> ICU delirium can contribute to cognitive dysfunction.<sup>13</sup> These patients frequently get agitated and can harm themselves or their caregivers.

Comorbidities like diabetes and hypertension are commonly seen in critically ill patients; many interventions are needed to treat these.<sup>14</sup> Major challenge is to manage psychiatric complications that are seen due to pharmacological measures.<sup>15</sup>

There are few studies on single substance use and its withdrawal effects in the critically ill.<sup>2,5</sup> The present study is done to find out the withdrawal effects and complications with multiple substance withdrawal in adult patients with substance use disorder and who are critically ill.

The present study was done to find the challenges like delirium, withdrawal, and its complications in adult patients with substance use disorders who are in ICU posed to the treating staff in the critical care unit.

## MATERIALS AND METHODS

This is a cross-sectional observational study that is planned in the critical care unit of a tertiary care center from 15<sup>th</sup> February to 15<sup>th</sup> August 2022 and was approved by the institutional ethics board (AU/EC/PH/2K22/136) dated 15.2.2022.

The study included adult critically ill patients, 18–60 years of age, who were admitted to the ICU with various illnesses and had substance use disorder. Patients with a head injury, low Glasgow Coma Scale score, electrolyte disturbances, and a history of psychiatric illness were excluded from the study.

The demographic data and comorbid conditions were recorded. Adverse events related to substance withdrawal and complications and all other relevant data were collected by the attending physician and nursing staff. Delirium was diagnosed by the CAM-ICU scale.<sup>16</sup>

## STATISTICAL ANALYSIS

Data were collected, tabulated and statistically analyzed using the descriptive-analytical method.

## RESULTS

This study included 110 adult patients (male-109, female-1) who had substance dependence on one or more substances. Demographic data are shown in (Table 1).

The substance use is shown in Table 2. Tobacco was the most commonly abused substance, followed by alcohol. Among females, tobacco consumption was noted.

The younger population consumed more than one substance intravenously than the older individuals. The rural population was more addicted to multiple substances than the urban population. Tobacco was more common in urban, alcohol in rural while tobacco plus alcohol consumption was more common in the rural population. Opioid consumption in all forms was more among the less educated. Intravenous substance administration was more common in the rural population. The length of ICU stay was greater in intravenous substance use disorders. Urine screen for substances was positive in 14.54% of patients (Table 3).

A total of 429 adverse events were noted, as shown in Table 4. The most common adverse event due to substance withdrawal was agitation and delirium (46.39%), followed by inconvenience to other patients, as was complained by the patients in the unit (17.02%).

## DISCUSSION

Due to hospitalization substance use disorder, patients are prone to withdrawal symptoms, and this can complicate their management. As many of these patients are positive for serology during agitation,

**Table 1:** Demographic data

Parameter	N (%)	Total n (%)
Age (years) mean ± standard deviation	52.54 ± 8.34	
Sex		
Male	109 (99.09)	110
Female	1 (0.91)	
Locality		
Rural	70 (63.64)	110
Urban	40 (36.36)	
Education		
Below senior secondary	66 (60)	110
Undergraduate	24 (21.8)	
Postgraduate	20 (18.2)	
Comorbidity		
Diabetes	9 (8.18)	14 (12.72)
Hypertension	5 (4.54)	

**Table 2:** Types of substance use

Substance	N (%)		Total (out of 110) N (%)
	Male	Female	
Tobacco (T)	33 (30)	1 (0.90)	34 (30.90)
Alcohol (A)	20 (100)		20
Benzodiazepine (B)	16 (100)		16
Opioids (O)			
Oral	26 (100)		26
Parenteral	14 (100)		14

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**Table 3:** Distribution of combination of agents (substance use) in relation to demographics

	Tobacco (T)	Opioids (O)			Benzodiazepine (B)	T + A	A + O	T + A + O + B	Total (n) (%)	
	(N)	Alcohol (A)	Oral	Parenteral	Both					
Age (years)	49 ± 9.12	40.62 ± 7.56	42 ± 9.4	34.1 ± 5.4	36.2 ± 6.12	45.22 ± 11.58	37.16 ± 15.2	44.76 ± 12.2	28.94 ± 9.68	
Mean ± standard deviation										
Locality										
Rural (n)	16 (14.54)	10 (9.09)	17 (15.45)	10 (9.09)	5 (4.55)	1 (0.90)	4 (3.63)	3 (2.73)	4 (3.64)	70 (63.64)
Urban (n)	13 (11.81)	10 (9.09)	2 (1.82)	4 (3.63)	1 (0.90)	4 (3.63)	6 (5.45)	1 (0.90)	1 (0.90)	40 (36.36)
Education										
Senior secondary or below	28 (25.45)	8 (7.27)	10 (9.09)	4 (3.63)	1 (0.90)	3 (2.73)	5 (4.54)	4 (3.63)	3 (2.73)	66 (60)
Undergraduate	2 (1.81)	4 (3.63)	1 (0.90)	3 (2.73)	2 (1.82)	4 (3.63)	5 (4.54)	1 (0.90)	2 (1.81)	24 (22)
Postgraduate	3 (2.73)	5 (4.54)	1 (0.90)	1 (0.90)	–	2 (1.81)	6 (6.0)	1 (0.90)	1 (0.90)	20 (17)
Duration of stay in ICU (days) mean ± standard deviation	2.1 ± 1.1	4.1 ± 1.8	3 ± 1.1	11 ± 5.2	7 ± 3.2	1.8 ± 0.9	2.8 ± 2.1	2.1 ± 1.4	3.8 ± 2.6	
Urine toxicology screen	–	–	8 (7.27)	2 (1.82)	2 (1.82)	1 (0.90)	–	2 (1.82)	1 (0.90)	16 (14.54)

**Table 4:** Adverse events due to substance withdrawal, complications of its use seen

Incidence of adverse events	Total (n) (%)
Agitation/delirium	199 (46.39)
Requirement of sedation and analgesia	68 (15.85)
Disturbance to other patients in the unit, as complained by patients	73 (17.02)
Increased length of hospital stay due to interventions done	36 (8.39)
Arrhythmias and cardiomyopathy	19 (4.43)
Mortality	4 (0.93)
Sepsis and septic shock due to local or generalized infection due to parenteral substance use	4 (0.93)
Hypotension due to sedatives	4 (0.93)
Invasive mechanical ventilation (due to delirium and pulmonary complications)	3 (0.70)
Accidental fall from bed due to agitation	1 (0.24)
Damage to the monitoring system by pulling the cables	1 (0.24)
Soft tissue infection at the injection site	3 (0.70)
Additional surgical or nonsurgical intervention (debridement)	2 (0.47)
Difficulty in weaning from the ventilator	2 (0.47)
Agitation-induced acute left ventricular failure	3 (0.70)
Deep vein thrombus	2 (0.47)
Upper limb	1 (50)
Lower limb	1 (50)
Infective endocarditis in intravenous substance users	3 (0.70)
Total	429 (100)

staff can get needle stick injuries. Many of the hemodynamic changes like tachycardia, tachypnea, and blood pressure changes may be seen in drug withdrawal or another disease process like sepsis and thus may pose difficulties in resuscitation depending

upon the vital signs. There should be high suspicion of substance use disorders in these patients. The sudden abstinence from smoking upon admission to the hospital is a big risk for agitation and delirium.<sup>17</sup> The nicotine patch and chewing gum had been used with varying results to prevent withdrawal symptoms from tobacco.<sup>18</sup>

Mehta et al. found a significantly higher incidence of delirium in mechanically ventilated critical patients with the consumption of alcohol. Mechanical ventilation and hospital stay were longer in these patients.<sup>19</sup> Diagnosis of alcohol consumption in critically ill patients is important because the risk of alcohol withdrawal is higher in patients who consume alcohol chronically. Alcohol use is a risk factor for developing a critical illness, along with longer ICU stays due to complications associated with substance consumption.<sup>20</sup> These patients should be supplemented with thiamine and chlorthalidone to prevent withdrawal symptoms from alcohol.

The opioid withdrawal has been managed with oral supplementation of buprenorphine in the hospital and posthospitalization period with varying success. It reduces the withdrawal symptoms in dependent patients.

Around 30% of older individuals develop delirium during hospitalization. This is precipitated by substance withdrawal in the critically ill. Substance use disorder may be missed in the absence of proper history because either the family is unaware or the patient is not in a condition to give a history. Patients with delirium during hospitalization have higher morbidity and mortality.<sup>21,22</sup> In ICU, delirium is the most commonly diagnosed condition with a prevalence of 70–90%.<sup>23,24</sup> The incidence is further increased by substance withdrawal. Frequent meetings with relatives are helpful for the prevention of delirium, but that may not be feasible all the time in ICU. The patient should be shifted to the ward from ICU as soon as possible; exposure to sunlight in conscious patients daily reduces the incidence of delirium.

The application of restraints (mechanical or physical) is a controversial issue in ICU physical, psychological, legal, and ethical issues.<sup>25</sup> Management challenges are due to intoxication and



substance withdrawal in critically ill.<sup>26</sup> Utilization of resources in ICU is higher due to acute and chronic sequelae of substance use disorders.<sup>27</sup> Admissions due to substance use disorders utilize almost 25% of resources in ICU.<sup>28</sup> Patients with substance disorders need a more extended hospital stay and a higher economic burden than hospitalization due to other reasons (4.2 vs 2.8 days).<sup>29</sup> As we found in our study, the duration of hospital stay was higher in intravenous substance use disorders. The most crucial risk for substance use disorders is poor socioeconomic status.<sup>30</sup>

Dexmedetomidine is a recent agent that has selective  $\alpha_2$  receptor agonist activity along with anxiolytic, sympatholytic, anaesthetic drug sparing, sedative, and opioid-sparing analgesic effects. It is a common drug used for conscious sedation in ICU because it does not lead to respiratory depression.<sup>31–33</sup> A meta-analysis showed that dexmedetomidine significantly decreases delirium, agitation and confusion, reducing ICU stays and mechanical ventilation days as compared to other sedatives.<sup>34</sup> Maximizing efficacy of targeted sedation and reducing neurological dysfunction trial showed that it lowers the incidence and duration of delirium compared to lorazepam.<sup>35</sup> Riker et al. showed a significantly lower risk of delirium in the dexmedetomidine group as compared to the midazolam group.<sup>36</sup> The benzodiazepines use in ICU should be reduced. The use of haloperidol instead of benzodiazepines reduces the risk of delirium.

## LIMITATIONS

The limitation of this study is that it is difficult to identify patients with hypoactive delirium using this method, so the incidence of delirium may be underestimated. Hyperactive delirium is easily diagnosed. Comorbidity and the primary disease for which the patients were in ICU were not analyzed.

## CONCLUSION

The symptoms and complications seen in substance dependents in ICU increase the morbidity, mortality, hospital stay, number of interventions, and financial burden on a family. These patients not only harm themselves but also harm the treating staff and damage hospital equipment, and also disturb other fellow patients.

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