








## ORIGINAL ARTICLE

# Factors Associated with Alcohol Withdrawal or Alcohol-Withdrawal Delirium among Inpatients with Alcohol Use in a General Hospital Setting: A Comparison Before and During the COVID-19 Pandemic

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## Main Points

- Alcohol withdrawal and delirium tremens are serious but preventable complications in alcohol-dependent hospitalized patients.
- Clinicians should be concerned about the risk of alcohol withdrawal if there is a rising serum aspartate aminotransferase, an abnormality of serum sodium or potassium, or a previous history of alcohol withdrawal symptoms.
- These factors were strongly related to alcohol withdrawal syndrome without the effect of coronavirus disease 2019 (COVID-19).

## Abstract

The present study aims to identify the risk factors related to alcohol withdrawal syndrome or alcohol-withdrawal delirium (delirium tremens) in patients with alcohol dependence admitted to a general hospital during the coronavirus disease 2019 and non-coronavirus disease 2019 periods. A retrospective chart review of patients diagnosed with alcohol dependence and admitted to a general hospital pre- and post-coronavirus disease 2019 outbreak was conducted. In both datasets, clinical and laboratory information from eligible medical records were reviewed and compared between two groups: an alcohol-dependent group without alcohol withdrawal syndrome or delirium and an alcohol-dependent group with alcohol withdrawal syndrome or delirium. Clinical or laboratory risk factors related to alcohol withdrawal syndrome were analyzed using Pearson's chi-square test, *t*-test, odds ratio, and logistic regression analysis for each dataset. The *p* value for statistical significance was set at .05. The results show a total of 626 alcohol-dependent inpatient charts were reviewed, consisting of 249 cases of alcohol withdrawal syndrome or delirium tremens, which was defined as a positive disease outcome (first dataset: 89/200 total cases; second dataset: 160/426 total cases). Abnormalities in serum aspartate aminotransferase levels greater than 1.5 times the upper normal limit and psychiatric consultation were strongly related to alcohol withdrawal syndrome or delirium tremens, whether coronavirus disease 2019 was in effect or not. Regarding the sub-analysis of related factors, abnormalities in serum sodium and potassium levels and a history of alcohol withdrawal were significantly related to alcohol withdrawal syndrome or delirium tremens in the first set, while abnormalities in serum aspartate

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aminotransferase and psychiatric consultation were significantly related to alcohol withdrawal syndrome or delirium tremens in the second set. In conclusion, alcohol withdrawal and delirium tremens are serious but preventable complications in hospitalized patients with alcohol dependency. Clinicians should be alerted by increased serum aspartate aminotransferase, an abnormality in serum sodium or potassium, or a previous history of alcohol withdrawal symptoms.

**Keywords:** Addictions to alcohol, alcohol dependence, alcohol-use disorder, alcohol withdrawal, alcohol-withdrawal delirium, delirium tremens

## Introduction

Alcohol-use disorder encompasses multiple medical conditions such as liver disease, cardiovascular disease, cancer, accidents, and neuropsychiatric conditions that lead to poor quality of life (Hearne et al., 2002; International Health Policy Program, 2021; Sitdhiraksa et al., 2012; World Health Organization, 2008). Previous studies have reported the under-recognition and delayed treatment of alcohol-use disorders in clinical settings (Rattapha et al., 2014; Wansrisuthon et al., 2017). When patients with a history of alcohol dependence are hospitalized for medical treatment, some develop withdrawal symptoms or alcohol-withdrawal delirium, also known as delirium tremens (DT) (Schuckit, 2014). Therefore, identifying risk factors for the development of withdrawal symptoms and DT is essential for early treatment. If left untreated, the mortality rate is high (Schuckit, 2014).

Previous studies have reported that factors such as a history of DT and seizures during withdrawal symptoms, abnormal laboratory parameters such as low platelet count, abnormal electrolyte levels, and liver enzymes (alanine aminotransferase [ALT], aspartate aminotransferase [AST], gamma-glutamyl transferase [GGT]), mean corpuscular volume (MCV), and decreased platelet volume are risk factors for the development of alcohol withdrawal symptoms and DT (Eastes, 2010; Goodson et al., 2014; Grover & Ghosh, 2018; Rathlev et al., 2006; Sarkar et al., 2017).

At the national level, only a limited number of studies have investigated population-based risk factors for the development of DT. Lokapan et al. (2022) found that a history of DT, the highest average temperature in the first 24 hour, alcohol withdrawal seizures, and reduced blood platelet and potassium levels were related to severe alcohol withdrawal. Ukranun (2019) found that a history of other drug use, respiration rate at admission, lower serum creatinine levels, and higher serum glutamic-oxaloacetic transaminase (SGOT) enzyme levels were related to DT. However, Burapakajornpong et al. (2011) found that age, previous history of DT and epilepsy, history of alcohol use, frequency and quantity of drinking, signs of simple withdrawal at first admission, and benzodiazepine dosage were not risk factors for DT.

Regarding the coronavirus disease 2019 (COVID-19) pandemic that began in January 2020, a range of practices has been suggested at the country level to deal with the challenges of the pandemic (Calvey et al., 2020; Scheibein et al., 2021). Thailand began to prevent the epidemic, as announced in the Government Gazette on March 25, 2020, after the Declaration of a State of Emergency in all localities throughout the kingdom (Government Gazette, 2021), with periodic policy changes in response to the epidemic situation. These included limiting the sale of alcoholic beverages during the epidemic (Government Gazette, 2021). To reduce domestic violence, the

Thai government implemented policies prohibiting the sale of liquor and alcohol during this period. Furthermore, self-isolation (or lockdown) may have limited access to medical services in the alcohol-user population, potentially increasing alcohol withdrawal and delirium.

Based on preliminary data on risk factors collected in the previous period (2012 – 2013), the COVID-19 epidemic situation, and various policies related to alcohol restriction, the present study aimed to identify the characteristics and risk factors that affect alcohol withdrawal symptoms and DT in patients with alcohol dependence admitted to a general hospital for the treatment of their medical conditions during the 2020 – 2021 period (the COVID-19 pandemic) by using a combined dataset.

## Material and Methods

We conducted a retrospective review of hospital charts from January 2020 to December 2021 and January 2012 to December 2013. Initially, the recruited medical records were screened for the right diagnosis using the tenth revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes (F10.1 [mental and behavioral disorders due to alcohol use, harmful use]; F10.2 [alcohol use disorder], F10.3 [alcohol withdrawal], or F10.4 [alcohol withdrawal delirium]) given by medical statisticians. After reviewing the online database, the diagnoses in the recruited medical records were re-evaluated. Records that did not meet the diagnostic criteria were excluded. Information in the eligible medical records on sex, age, educational level, employment status, changing employment status during the COVID-19 period, marital status, previous history of alcohol withdrawal delirium, alcohol withdrawal seizures, and alcohol-related diseases were then reviewed and recorded as the outcome risk factors. Information on the length of stay; amount, frequency, and duration of alcohol consumption calculated for the standard drink; duration prior to psychiatric consultation; and abnormalities of sodium, potassium, liver enzymes (AST and ALT), mean red blood cell corpuscular volume (MCV), and platelets were also analyzed as risk factors to identify statistically significant risks that contributed to the disease outcome. During the COVID-19 period, the sequelae of the government's policy and the Gazette might result in an alteration of the characteristics of some factors, such as the decreased amount of standard drinks, employment status, changing employment status during the COVID-19 period, and length of stay were hypothesized. All analyses were performed using Predictive Analytics Software (PASW) Statistics for Windows (IBM SPSS Corp.; Armonk, NY, USA). Comparisons of categorical variables between the two groups were made using Pearson's chi-square test; however, for continuous variables, the independent samples *t*-test was applied. The odds ratios (OR) were calculated. Statistical significance was set at  $p < .05$ . Figure 1 presents the conceptual framework of this study.

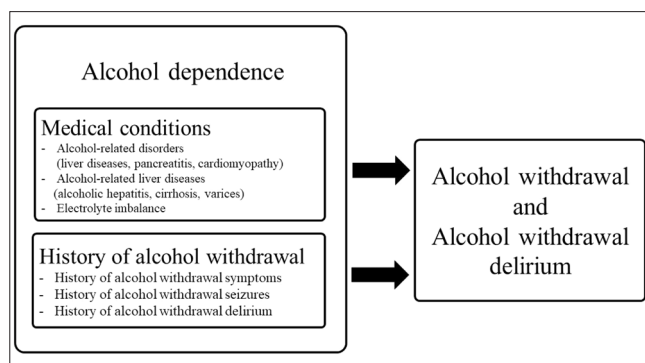


Figure 1. The Conceptual Framework of Risk Factors That Affect Alcohol Withdrawal Symptoms, Alcohol-Withdrawal Delirium, Medical Conditions, and History of Alcohol Withdrawal.

### Ethics Committee Approval

Before starting this research, its protocol was approved by the Mahidol University Siriraj Institutional Review Board (SIRB); CoA: 988/2021, Approval date: December 14, 2021 – December 13, 2022.

### Informed Consent

Data retrieved from the medical records was permitted to be used in this retrospective research with the permission of the hospital director after the research protocol had been approved by the institutional review board without requesting individual informed consent.

### Results

A total of 626 alcohol-dependent inpatient charts from January 2012 to December 2013 (first dataset) and January 2020 to December 2021 (second dataset) were reviewed. There were 200 alcohol-dependent inpatients during the COVID-19 pandemic from January 2020 to December 2021; 44.5% (89 of 200 cases) were diagnosed with alcohol withdrawal syndrome or alcohol withdrawal delirium, whereas in the previous dataset, 37.6% (160 of 426 inpatient cases) were diagnosed. Of the 626 patients, 249 were included in this study.

The majority of patients were male in both datasets as well as in the combined dataset. Most patients were married, discharged from the hospital in an improved condition, employed, and had no prior history of alcohol withdrawal or alcohol withdrawal seizures in any of the datasets, as shown in Table 1.

The first data set revealed that the male sex ( $p = .039$ ), mean age at admission ( $p = .023$ ), length of hospital stay ( $p = .001$ ), being employed ( $p = .001$ ), having a prior history of alcohol withdrawal or an alcohol withdrawal seizure (both  $p = .001$ ), number of standard drinks ( $p = .004$ ), psychiatric consultation ( $p = .001$ ), abnormal serum sodium (normal range 135 – 145) ( $p = .004$ ), and abnormal serum potassium, AST, and platelet counts ( $p = .027$ ,  $.001$ ,  $.001$ , respectively) are significantly related to alcohol withdrawal syndrome or alcohol-withdrawal delirium.

The second data set showed statistically significant correlations between alcohol withdrawal or alcohol-withdrawal delirium and factors such as younger admission age ( $p = .028$ ), higher standard

drink consumption ( $p = .036$ ), psychiatric consultation ( $p < .001$ ), abnormalities of serum potassium (normal range 3.5 – 5) ( $p = .001$ ), AST liver enzyme abnormalities (more than 1.5 times the normal upper limit or above 53 based on the laboratory reference of the hospital) ( $p < .001$ ), and abnormal platelet level (normal range 160 – 365  $\times$  103).

The combined data set still showed that male sex ( $p = .015$ ), age of admission ( $p = .004$ ), length of hospital stay ( $p = .001$ ), being employed ( $p = .001$ ), previous alcohol withdrawal or alcohol withdrawal seizure history (both  $p < .001$ ), number of standard drinks per day ( $p < .001$ ), psychiatric consultation ( $p < .001$ ), and laboratory abnormalities of serum sodium ( $p = .001$ ), potassium ( $p < .001$ ), AST ( $p < .0001$ ), and platelets ( $p < .001$ ) were significantly correlated with alcohol withdrawal syndrome or alcohol-withdrawal delirium.

The authors found a significant abnormal increase in AST levels in patients with alcohol withdrawal or DT, but not in ALT levels. The AST-to-ALT ratio, which usually increases in chronic liver disease or cirrhosis and is often  $> 1$  were further analyzed; however, this ratio is not specific to cirrhosis and can increase above 1 in other circumstances such as biliary obstruction and drug-induced esophageal varices. The AST-to-ALT ratio in the three datasets was significantly related to positive disease outcome, outcomes, with  $p < .001$  in all datasets. Only AST abnormalities (greater than 1.5 times the normal upper limit) were selected for logistic regression analysis to prevent multicollinearity of the analyzed factors.

Noticeably, the standard drinks in the first and second data set had nearly equal values (approximately 24 and 12 drinks per day in patients with and without alcohol-withdrawal delirium, respectively). While the duration (days) from admission to psychiatric consultation was not significantly different, early consultation (median, 1 day; IQR, 0 – 5) was still related to better outcomes compared with the alcohol withdrawal or delirium group (median 2 days, IQR 1 – 3.75).

Using logistic regression analysis, the factors in the first dataset that were significantly related to DT were psychiatric consultation ( $p < .001$ , OR = 3.517, 95% CI: 1.824 – 6.782), history of alcohol withdrawal ( $p = .002$ , OR = 3.939, 95% CI: 1.675 – 9.260), abnormal AST level ( $p < .001$ , OR = 3.517, 95% CI: 1.824 – 6.782), and abnormal sodium level ( $p = .048$ , OR = 1.888, 95% CI: 1.007 – 3.540). In the second dataset, psychiatric consultation ( $p = .002$ , OR = 3.371, 95% CI: 1.544 – 7.358) and abnormal AST levels ( $p = .002$ , OR = 3.894, 95% CI: 1.624 – 9.335) contributed to alcohol-withdrawal delirium, as shown in Table 2. In the combined dataset, the significantly correlated factors were psychiatric consultation ( $p < .001$ , OR = 3.634, 95% CI: 2.194 – 6.021), abnormal potassium levels ( $p = .035$ , OR = 1.639, 95% CI: 1.036 – 2.593), and abnormal AST levels ( $p < .001$ , OR = 3.624, 95% CI: 1.989 – 6.603).

### Discussion

This study aimed to identify the characteristics and risk factors affecting alcohol withdrawal symptoms and DT in patients with alcohol dependence admitted to a general hospital. Three main factors were reviewed: demographic data, clinical data, and laboratory results. This may raise awareness among clinicians with regard

**Table 1.** Distribution and Comparison of the Demographic, Clinical, and Laboratory Characteristics Between Patients with Alcohol Dependence Versus Those Without Alcohol Withdrawal/Alcohol-Withdrawal Delirium from 2012 to 2013 (N = 426), 2020 – 2021 (N = 200), and Combined Data

Characteristics	2020 – 2021 (N = 200)		2012 – 2013 (N = 426)		All data (N = 626)		p
	Alcohol Withdrawal Symptoms (n = 89)	No Withdrawal Symptoms (n = 111)	Alcohol Withdrawal Symptoms (n = 160)	No Withdrawal Symptoms (n = 266)	Alcohol Withdrawal Symptoms (n = 249)	No Withdrawal Symptoms (n = 377)	
Sex							.039*
Male (%)	84 (94.4)	102 (91.9)	143 (89.4)	218 (82.0)	227 (91.2)	320 (84.9)	
Female (%)	5 (5.6)	9 (8.1)	17 (10.6)	48 (18.0)	22 (8.8)	57 (15.1)	
Age: median [IQR]	49.00 [39.00 – 57.00]	53.00 [43.00 – 60.00]	46.00 [40.25 – 52.00]	48.00 [39.00 – 57.00]	47.00 [40.00 – 54.00]	49.00 [40.00 – 58.00]	.010*
Length of stay: median [IQR]	8.00 [5.00 – 15.00]	6.00 [3.00 – 15.00]	9.00 [6.00 – 14.00]	6.00 [3.00 – 12.00]	9.00 [6.00 – 14.00]	6.00 [3.00 – 13.00]	<.001*
Marital status							.254
Single (%)	24 (33.3)	32 (31.7)	51 (34.7)	73 (28.7)	75 (34.2)	105 (29.6)	
Married (%)	42 (58.3)	67 (66.3)	83 (56.5)	147 (57.9)	125 (57.1)	214 (60.3)	
Divorce (%)	6 (8.3)	2 (2.0)	13 (8.8)	34 (13.4)	19 (8.7)	36 (10.1)	
Discharge status							N/A
Improved (%)	82 (92.1)	100 (90.1)	N/A	N/A	82 (92.1)	100 (90.1)	.775
Not improved (%)	2 (2.2)	2 (1.8)	N/A	N/A	2 (2.2)	2 (1.8)	
Dead (%)	5 (5.6)	9 (8.1)	N/A	N/A	5 (5.6)	9 (8.1)	
Employment status							.001*
Employed (%)	63 (71.6)	82 (74.5)	129 (84.3)	182 (69.7)	192 (79.7)	264 (71.2)	
Unemployed (%)	25 (28.4)	28 (25.5)	24 (15.7)	79 (30.3)	49 (20.3)	107 (28.8)	
Employment changing during COVID-19							.753t
Change (%)	5 (5.8)	5 (4.6)	N/A	N/A	5 (5.8)	5 (4.6)	
No change (%)	81 (94.2)	103 (95.4)	N/A	N/A	81 (94.2)	103 (95.4)	
History of alcohol WD							<.001*
Yes (%)	18 (20.2)	11 (9.9)	84 (52.5)	39 (14.8)	102 (41.0)	50 (13.4)	

**Table 1.** Distribution and Comparison of the Demographic, Clinical, and Laboratory Characteristics Between Patients with Alcohol Dependence Versus Those Without Alcohol Withdrawal/ Alcohol-Withdrawal Delirium from 2012 to 2013 (N = 426), 2020 – 2021 (N = 200), and Combined Data (Continued)

Characteristics	2020 – 2021 (N = 200)		2012 – 2013 (N = 426)		All data (N = 626)		p
	Alcohol Withdrawal Symptoms (n = 89)	No Withdrawal Symptoms (n = 111)	Alcohol Withdrawal Symptoms (n = 160)	No Withdrawal Symptoms (n = 266)	Alcohol Withdrawal Symptoms (n = 249)	No Withdrawal Symptoms (n = 377)	
No (%)	71 (79.8)	100 (90.1)	76 (47.5)	224 (85.2)	147 (59.0)	324 (86.6)	<.001*
History of alcohol WD seizure	1.000						<.001*
Yes (%)	1 (1.1)	2 (1.8)	34 (21.3)	10 (3.8)	35 (14.1)	12 (3.2)	
No (%)	88 (98.9)	109 (98.2)	126 (78.8)	253 (96.2)	214 (85.9)	362 (96.8)	
Age at first drink: median [IQR]	24.50 [19.00 – 36.00]	25.00 [19.00 – 35.00]	N/A	N/A	24.50 [19.00 – 36.00]	25.00 [19.00 – 35.00]	.912
Standard drink: median [IQR]	24.00 [12.00 – 24.00]	14.75 [6.00 – 24.00]	24.00 [12.00 – 24.00]	12.00 [7.50 – 24.00]	24.00 [12.00 – 24.00]	12.50 [6.63 – 24.00]	.004* .001*
Psychiatric consultation	<.001*						<.001*
Yes (%)	55 (61.8)	35 (31.5)	114 (71.3)	95 (36.0)	169 (67.9)	130 (34.7)	
No (%)	34 (38.2)	76 (68.5)	46 (28.8)	169 (64.0)	80 (32.1)	245 (65.3)	
Duration prior to consultation: median [IQR]	2.00 [1.00 – 3.00]	1.00 [0.00 – 5.00]	N/A	N/A	2.00 [1.00 – 3.00]	1.00 [0.00 – 5.00]	.756
Alcohol-related disease	.836						N/A
Alc-related liver (%)	14 (15.7)	21 (18.9)	N/A	N/A	14 (15.7)	21 (18.9)	
Alc-related non liver (%)	18 (20.2)	21 (18.9)	N/A	N/A	18 (20.2)	21 (18.9)	
No (%)	57 (64)	69 (62.2)	N/A	N/A	57 (64)	69 (62.2)	
Sodium abnormalities	.062						.004*
Yes (%)	36 (40.4)	31 (27.9)	66 (42.0)	65 (28.0)	102 (41.5)	96 (28.0)	
No (%)	53 (59.6)	80 (72.1)	91 (58.0)	167 (72.0)	144 (58.5)	247 (72.0)	

(Continued)

**Table 1.** Distribution and Comparison of the Demographic, Clinical, and Laboratory Characteristics Between Patients with Alcohol Dependence Versus Those Without Alcohol Withdrawal/Alcohol-Withdrawal Delirium from 2012 to 2013 (N = 426), 2020 – 2021 (N = 200), and Combined Data (Continued)

Characteristics	2020 – 2021 (N = 200)		2012 – 2013 (N = 426)		All data (N = 626)		P
	Alcohol Withdrawal Symptoms (n = 89)	No Withdrawal Symptoms (n = 111)	Alcohol Withdrawal Symptoms (n = 160)	No Withdrawal Symptoms (n = 266)	Alcohol Withdrawal Symptoms (n = 249)	No Withdrawal Symptoms (n = 377)	
Potassium abnormalities							.027*
Yes (%)	42 (47.2)	29 (26.1)	88 (56.1)	103 (44.6)	130 (52.8)	132 (38.6)	
No (%)	47 (52.8)	82 (73.9)	69 (43.9)	128 (55.4)	116 (47.2)	210 (61.4)	
AST abnormalities							<.001*
Yes (%)	66 (79.5)	46 (47.9)	133 (88.7)	120 (58.8)	199 (85.4)	166 (55.3)	
No (%)	17 (20.5)	50 (52.1)	17 (11.3)	84 (41.2)	34 (14.6)	134 (44.7)	
ALT abnormalities							.015*
Yes (%)	29 (34.9)	22 (22.9)	51 (34.0)	52 (25.5)	80 (34.3)	74 (24.7)	
No (%)	54 (65.1)	74 (77.1)	99 (66.0)	152 (74.5)	153 (65.7)	226 (75.3)	
MCV abnormalities							.967
Yes (%)	27 (30.3)	33 (29.7)	39 (36.4)	63 (36.2)	66 (33.7)	96 (33.7)	
No (%)	62 (69.7)	78 (70.3)	68 (63.6)	111 (63.8)	130 (66.3)	189 (66.3)	
Platelet abnormalities							<.001*
Yes (%)	58 (65.2)	52 (46.8)	105 (67.3)	111 (46.8)	163 (66.5)	163 (46.8)	
No (%)	31 (34.8)	59 (53.2)	51 (32.7)	126 (53.2)	82 (33.5)	185 (53.2)	
The AST-to-ALT ratio: median [IQR]	2.78 [2.03 – 3.80]	1.59 [1.10 – 2.42]	<.001* 2.74 [1.73 – 3.79]	1.87 [1.32 – 2.77]	<.001* 2.77 [1.84 – 3.79]	1.80 [1.26 – 2.63]	<.001*

Note: Alc = alcohol; ALT = alanine aminotransferase; AST = aspartate aminotransferase; COVID-19 = Coronavirus disease 2019; IQR = interquartile range; MCV = mean corpuscular volume; WD = withdrawal. \*P-value < .05.

**Table 2.**  
Selected Statistically Significant Characteristics Analyzed by Logistic Regression

Characteristics	<i>p</i>	Odds Ratio (95 % CI)
The 2012 – 2013 dataset ( <i>n</i> = 426)		
History of alcohol withdrawal	.005	2.375 (1.298, 4.343)
Psychiatric consultation	<.001	3.679 (2.038, 6.641)
Abnormal AST	<.001	4.288 (2.050, 8.967)
The 2020 – 2021 dataset ( <i>n</i> = 200)		
Psychiatric consultation	.001	3.515 (1.715, 7.207)
Abnormal AST	<.001	5.508 (2.556, 11.872)
Combined dataset ( <i>n</i> = 626)		
History of alcohol WD seizure	.014	3.359 (1.273, 8.865)
Psychiatric consultation	<.001	4.102 (2.616, 6.430)
Abnormal potassium (K)	.029	1.647 (1.053, 2.575)
Abnormal AST	<.001	4.332 (2.544, 7.377)

Note: AST = aspartate aminotransferase; WD = withdrawal.

to the complications of alcohol cessation in patients with alcohol dependency during hospitalization. Delirium tremens increases the length of hospital stay, resource usage, morbidity, and mortality.

It is found that abnormal AST levels were correlated with alcohol withdrawal and DT (more than 1.5 times the normal upper limit

or above 53 based on the laboratory reference of the hospital). If the AST levels are abnormally high, visiting a clinician as soon as possible to detect alcohol withdrawal symptoms was recommended. This may be an early sign of alcohol withdrawal or DT. However, further studies are required to confirm our hypotheses. Early psychiatric consultation may aid in the early detection of withdrawal and result in better outcomes in hospitalized patients with alcohol use disorder.

Clinicians should be aware that psychiatric consultations in patients with alcohol dependency are more likely to result in alcohol withdrawal or alcohol-withdrawal delirium. The factors identified in this study are consistent with those reported in previous population-based studies. Lokapan et al. (2022) conducted a study in psychiatric and illicit drug treatment units. The risk factor identified in that study were similar to those identified factors by the present study, including a previous history of DT and seizures. Lokapan et al. also identified a history of alcohol use and frequency and quantity of drinking as predictors. A previous prospective study considered the frequency and quantity of drinking and found these factors to be unreliable. In addition to the different associated medical conditions and history of alcohol withdrawal, Ukranun (2019) reported that some factors such as serum creatinine and SGOT enzyme levels were related to DT. In contrast, Burapakajornpong et al. (2011) found no related factors predicting severe alcohol withdrawal. The factors considered in that study included age, previous history of DT and epilepsy, history of alcohol use, frequency and quantity of drinking, signs of simple withdrawal at first admission,

**Table 3.**  
Comparing the Risk Factors for the Development of Alcohol-Withdrawal Delirium in the Context of a Country

Study	Burapakajornpong et al. (2011)	Ukranun (2019)	Lokapan et al. (2022)	Present Study
Study design	Prospective study	Retrospective study	Retrospective study	Retrospective study
Setting	Psychiatric ward and drug treatment center	Drug treatment center	Psychiatric ward	General medical ward
Diagnosis	Alcohol dependence	Alcohol dependence	Alcohol dependence	Alcohol dependence
Number of participants	10 with DT 9 without DT (total 19)	50 with DT 50 without DT (total 100)	104 with DT 105 with non-severe withdrawal symptoms (total 209)	Two datasets 250 with DT 396 without DT (total 646)
Identified risk factors				
History-related risk factors	Not significant	History of other drug use	<ul style="list-style-type: none"> <li>Reason for stopping consumption (unintentional and unforced)</li> <li>Alcohol withdrawal seizure</li> <li>History of DT</li> </ul>	<ul style="list-style-type: none"> <li>History of alcohol withdrawal symptoms</li> <li>Psychiatric consultation</li> </ul>
Physical examination-related risk factors	Not significant	Respiratory rate >20/min	Highest average temperature in the first 24 hours	–
Investigation-related risk factors	Not significant	Creatinine <0.67 mg/dL AST ≥150 UL		Abnormal AST level Abnormal potassium level
Factors that prevent severe alcohol withdrawal	–	–	<ul style="list-style-type: none"> <li>Blood level of platelets</li> <li>Blood potassium level</li> </ul>	

Note: AST = aspartate aminotransferase; DT = delirium tremens; SGOT = serum glutamic-oxaloacetic transaminase.

and dosage of benzodiazepines. A comparison of the available population-based studies is shown in Table 3. However, the risk factors of severe withdrawal or DT remain unclear. The results differ from study to study, depending on the context of the hospital/service, patient characteristics, and investigated factors. A recent meta-analysis identified a history of DT, low platelet count, and low potassium levels as predictors. Another recent meta-analysis by Wood et al. (2018) found that a history of DT and baseline systolic blood pressure  $\geq 140$  mm Hg were associated with an increased likelihood of severe alcohol withdrawal symptoms. History-related or laboratory parameters that predict severe withdrawal symptoms or DT may be critical in the management of patients with alcohol-use disorder.

The abnormality in AST and psychiatric consultation indicates their relationship with alcohol withdrawal or alcohol-withdrawal delirium, regardless of the COVID-19 period or prior to COVID-19. The only factor that differed in the years before COVID-19 related to alcohol cessation complications was a history of previous alcohol withdrawal. Clinicians should review documented history or ask patients or family members to prevent complications. An abnormal serum sodium level ( $<135$  or  $>145$ ) is another laboratory finding that was significantly related to alcohol withdrawal or alcohol-withdrawal delirium during the non-COVID-19 period. Potassium abnormalities may also predict disease outcomes in patients admitted due to alcohol consumption.

The medical records reviewed in this study were collected approximately 10 years ago. Thus, the data reflected past practices in a general hospital. The COVID-19 pandemic has disrupted global healthcare systems, including services for patients with alcohol use disorders. Therefore, studies on the risk factors associated with alcohol withdrawal and DT were conducted during the COVID-19 pandemic.

Noticeably, the number of hospitalized patients with alcohol-use disorder from January 2020 to December 2021 was approximately half that from January 2012 to December 2013, but the number of alcohol withdrawals or DT during the COVID-19 period was slightly higher than that in the non-COVID-19 period (43% vs. 37%). This may reflect the social distancing policy of decreasing the number of inpatients during the COVID-19 pandemic and the limited number of general inpatients due to the increasing number of COVID-19-infected patients. However, demographic and clinical history that may alert healthcare personnel about alcohol withdrawal or DT during admission include admission age  $<50$  years, male sex, employment, history of alcohol withdrawal seizures, and abnormalities in laboratory results, such as electrolytes and platelet count. It is discovered that daily alcohol consumption of more than 24 standard drinks/day might predict withdrawal symptoms, regardless of whether a COVID-19 pandemic has occurred when compared to the non-withdrawal or DT group, whose average alcohol consumption is less than 12 standard drinks/day. In addition, the length of stay and employment status were not significantly different during the COVID-19 and non-COVID-19 periods. The change in employment status during the COVID-19 period shows that only a small number of patients changed their occupation or status (e.g., unemployed become employed, employed become unemployed, or changing occupations). There were 11 inpatient cases from a total of 200

cases, and none had a statistically significant relationship with the outcome of interest.

However, this study was quite large compared to previous population-based studies in the national context. It would have been beneficial to include more samples in the analysis. This study has several limitations. First, it was a retrospective study, so confounders could not be controlled. Information based on patient reports could minimize bias in the results. Secondly, this was a single-site study. Therefore, it may not adequately represent patients who consume alcohol in different settings and contexts. Third, only potential factors that may be associated with DT development were reviewed in this study. Other factors, including demographic data, clinical symptoms, and investigations of alcohol dependence, were excluded. Further studies with a well-controlled design or systematic reviews are required to better understand the population-based risk factors associated with alcohol use disorder.

Serum aspartate transaminase abnormalities greater than 1.5 times the upper normal limit on the day of admission were correlated with alcohol withdrawal or alcohol-withdrawal delirium in alcohol-dependent hospitalized patients, highlighting the importance of caution regarding alcohol withdrawal symptoms. Furthermore, patients with chronic alcohol use who were consulted were more likely to have alcohol withdrawal symptoms or delirium. Being younger than 50 years of age; male sex; employment; having a prior history of alcohol withdrawal or seizures; and having laboratory aberrations in sodium, potassium, or platelets may alert healthcare providers about alcohol withdrawal or DT.

**Data Availability Statement:** The data that support the findings of this study are available on request from the corresponding author.

**Ethics Committee Approval:** This study was approved by the Ethics Committee of Mahidol University Faculty of Medicine Siriraj Hospital, (Approval no.: CoA: 988/2021, Date: December 14, 2021 – December 13, 2022).

**Informed Consent:** N/A.

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