Trends of Alcohol Withdrawal Delirium in the Last Decade: Analysis of the Nationwide Inpatient Sample

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Abstract

Background: Alcohol use disorder, high-risk drinking, and emergency visits for acute and chronic complications of alcohol use have been increasing in the USA recently. Approximately half of patients with alcohol use disorder experience alcohol withdrawal when they reduce or stop drinking. Though alcohol withdrawal is usually mild, 20% of patients experience more severe manifestations such as hallucinations, seizures, and delirium. In this study, we utilized the Nationwide Inpatient Sample to examine the trends of alcohol withdrawal delirium (AWD) in the period 2010 - 2019.

Methods: This was a retrospective longitudinal trends study involving hospitalizations with AWD in the USA from 2010 to 2019. We searched the databases for hospitalizations using the International Classification of Diseases (ICD) codes (291.0 and F10231). We involved all hospitalizations complicated by AWD and hospitalizations with AWD as the principal diagnosis for admission. We excluded hospitalizations involving patients under the age of 18. We calculated the crude admission rate and the incidence of AWD per million adult hospitalizations during each calendar year. In addition, we analyzed trends of inpatient mortality, length of stay (LOS), and total hospital charges (THC).

Results: The incidence of AWD per million hospitalizations increased from 2,671.8 in 2010 to 3,405.6 in 2019, with an annual percentage change (APC) of 3.1% (P < 0.001). Similarly, AWD admission rate per million hospitalizations increased from 1,030.3 in 2010 to 1,556.0 in 2019, with an average APC of 5.0% (P < 0.001). There were statistically significant trends of increasing inpatient mortality, THC, and LOS over the studied period. In general, female gender, younger age, and Black race were associated with better clinical outcomes.

Conclusions: Our study showed an increase in the incidence and admission rates of AWD. Mortality, LOS, and THC increased over the studied period. Younger age, female gender, and Black race were associated with better clinical outcomes.

Keywords: Alcohol withdrawal delirium; Alcohol; Withdrawal; Trends; Nationwide Inpatient Sample

Introduction

The lifetime prevalence of alcohol use disorder is estimated to be 29.1% in community-based samples in the USA [1]. In the period 2001 to 2013, there was a noticeable increase in alcohol use disorder and high-risk drinking in the USA [2]. The total per capita consumption of alcohol is expected to increase in the regions of the Americas until 2025 [3].

Alcohol is the third most common modifiable cause of death in the USA after tobacco and poor diet/physical inactivity [4]. It causes approximately 3.8% of all deaths worldwide and accounts for 4.6% of the global burden of disease [5]. The effects of alcohol consumption on mortality are greater than those of diabetes, hypertension, human immunodeficiency virus (HIV), tuberculosis, and violence [3]. Alcohol use results in a significant financial burden on the healthcare system. In 2014, the aggregate costs for all hospitalizations with alcohol-related diagnosis were $30 billion [6].

This study aimed to describe the epidemiologic trends of alcohol withdrawal delirium (AWD) over the last decade using the Nationwide Inpatient Sample (NIS). In addition, we analyzed the demographics and outcomes of these hospitalizations including inpatient mortality, length of stay (LOS), and total hospital charges (THC).

Materials and Methods

Design and data source

This was a retrospective longitudinal trends study involving hospitalizations with AWD in the USA from 2010 to 2019. We sourced data from the NIS databases from 2010 to 2019. The NIS is developed by the Healthcare Cost and Utilization Project (HCUP), a Federal-State-Industry partnership sponsored by the Agency for Healthcare Research and Quality (AHRQ). The NIS

is a database of inpatient stays derived from billing data submitted by hospitals to statewide data organizations across the USA, covering more than 97% of the US population [7]. The provided dataset for a given calendar year approximates a 20% stratified sample of discharges from US community hospitals, excluding rehabilitation and long-term acute care hospitals. This dataset is weighted to obtain US national estimates [8]. Databases before 2016 were coded using the International Classification of Diseases, Ninth Revision, Clinical Modification/Procedure Coding System (ICD-9-CM/PCS). Databases from 2016 were coded using the International Classification of Diseases, 10th Revision, Clinical Modification/Procedure Coding System (ICD-10-CM/PCS). The 2015 NIS has both ICD-9 and 10 codes; hence, requiring a combination of both versions of ICD codes to obtain the studied cohort in accordance with HCUP regulations and methods [9]. In this study, we weighted the 9 months of ICD-9 data in 2015 for the entire year. In the NIS, diagnoses are divided into two separate categories: principal diagnosis and secondary diagnoses. A principal diagnosis was the ICD code that coded for the primary reason for admission. Secondary diagnoses were any ICD code other than the principal diagnosis.

Study population and variables

We searched NIS databases from 2010 to 2019 for this study. The study involved two cohorts of hospitalizations: 1) all hospitalizations complicated by AWD; 2) all hospitalization with AWD as the principal diagnosis for admission. We searched the databases for hospitalizations using ICD codes (291.0 and F10231). We excluded hospitalizations involving patients under the age of 18. The NIS includes variables on patient demographics, including age, sex, race, median household income (MHOI) for patient's zip code (income quartiles referred to patients as 1: low income; 2: middle income; 3: upper middle income; and 4: high income), and primary payer. We assessed the comorbidity burden using Sundararajan's adaptation of the modified Deyo's Charlson comorbidity index (CCI). This modification maps the 17 Charlson comorbidities into ICD-10 codes. The CCI was grouped into four groups in increasing risk for mortality. It has been adapted to population-based research. A score of > 3 has about a 25% 10-year mortality, while a score of 2 or 1 has a 10% and 4% 10-year mortality, respectively. These cut-off points were chosen to assess the risk of mortality [10].

Outcome measures

We highlighted the biodemographic trends over time for AWD hospitalizations. Specifically, we calculated the crude admission rate and the incidence of AWD per million adult hospitalizations during each calendar year. We analyzed trends of mortality, mean LOS, and mean THC over the studied period.

Statistical analysis

We used Stata® Version 16 software (StataCorp, TX, USA) and Joinpoint Regression Program, Version 4.9.1.0 for data analy-

sis. We analyzed and reported the weighted sample following HCUP regulations for using the NIS database. We grouped age in three categories: 18 - 39 years representing young adults, 40 - 64 years representing middle-aged adults, and ≥ 65 years representing elderly. The incidence of AWD among hospitalizations was calculated following the HCUP methodology for disease incidence and prevalence [11]. The crude admission rate was calculated by dividing total hospitalizations with AWD as the principal diagnosis by the total adult hospitalizations for each calendar year and expressed per million hospitalizations. The incidence of AWD per million adult hospitalizations was obtained by dividing the total hospitalizations complicated by AWD by the total number of adult hospitalizations. This was also expressed per million adult hospitalizations. We used multivariable regression analysis to calculate the incidence and admission rates adjusted for age categories, sex, and race using predictive margins. We subsequently used Joinpoint regression analysis to obtain the trends in rates over the study duration, using the adjusted rates and standard errors. Joinpoint regression analysis has been widely used and validated by the National Institute of Health (NIH) National Cancer Institute to model non-linear trends in cancer rates over a given period [12]. This has been adopted in prior HCUP database research [13, 14]. We used multivariable regression trend analysis to obtain trends in mortality, LOS, and THC adjusted for age categories, sex, and race. The study had a threshold of P < 0.05 for statistical significance.

Ethical considerations

The NIS database lacks patient and hospital level identifiers. Therefore, this study did not require Cook County Health Institutional Review Board approval or informed consents. The study was conducted in compliance with the ethical standards of the responsible institution on human subjects as well as with the Helsinki Declaration.

Results

A total of 944,162 hospitalizations complicated by AWD were included in our study. The incidence of AWD per million hospitalizations increased from 2,671.8 in 2010 to 3,405.6 in 2019 (Table 1, Fig. 1), with an annual percentage change (APC) of 3.1% (P < 0.001).

Analysis of the outcomes of all hospitalizations complicated by AWD showed a statistically significant trend of increasing inpatient mortality (odds ratio (OR): 1.01, P trend = 0.044) (Table 2). Multivariate analysis showed that hospitalizations for middle aged and elderly patients were associated with higher mortality rates compared to young adults (OR: 2.54 and 5.44, respectively, P < 0.001). Females had lower odds of mortality when compared to males (OR: 0.87, P = 0.001). Hospitalizations for Blacks were associated with lower odds of mortality compared to Whites (OR: 0.81, P < 0.001).

There was a statistically significant trend of increas-

Table 1. Demographics of All Hospitalizations Complicated by Alcohol Withdrawal Delirium (AWD)

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	P value
Total hospitalizations (million)	31.4	31.5	30.7	30	29.8	30.2	30.2	30.4	30.3	30.2	
Hospitalizations complicated by AWD	83,893	84,819	87,330	87,265	91,055	100,160	101,365	102,570	102,855	102,850	
Incidence of AWD per million hospitalizations	2,671.8	2,692.7	2,844.6	2,908.8	3,055.5	3,316.6	3,356.5	3,374	3,394.6	3,405.6	
Mean age (years) ± SD	52.4 ± 12.5	52.5 ± 12.8	52.4 ± 12.5	52.5 ± 12.5	52.5 ± 12.6	52.5 ± 12.5	52.5 ± 12.8	52.6 ± 12.9	52.4 ± 13.0	52.1 ± 13.1	0.183
Age categories (%)											< 0.001
Young adult	24.6	24.1	24.8	24.8	25.3	25.6	26.3	26.7	27.7	29.5	
Middle aged	59.0	59.5	58.4	58.6	58.0	58.0	56.9	55.7	54.9	53.1	
Elderly	16.5	16.4	16.7	16.7	16.6	16.3	16.8	17.7	17.4	17.4	
Female (%)	18.7	20.2	19.7	19.7	20.1	20.2	19.9	19.8	20.5	20.7	0.014
Race (%)											< 0.001
White	66.6	69.2	72.3	72.9	72.9	72.0	72.9	73.2	73.6	73.8	
Black	10.6	9.2	10.1	9.5	9.4	10.2	9.9	10.0	9.5	9.4	
Hispanic	8.3	7.9	8.3	8.5	8.2	8.6	8.6	9.3	9.8	9.7	
Other	14.5	13.7	9.4	9.1	9.5	9.2	8.6	7.5	7.0	7.1	
Median household income for zip code (%)											0.093
Low income	31.2	30.1	32.2	30.0	31.5	33.4	32.4	31.7	29.9	31.1	
Middle income	25.9	25.1	24.7	26.5	27.4	23.9	24.8	26.1	26.1	25.5	
Upper middle income	22.6	24.1	23.9	24.3	22.9	23.6	23.4	23.9	25.1	24.8	
High income	20.3	20.7	19.3	19.3	18.3	19.2	19.4	18.4	18.9	18.7	
CCI (%)											< 0.001
0	49.8	47.7	47.6	48.2	47.6	47.0	33.2	32.6	32.1	31.7	
1	24.0	24.2	24.8	23.9	24.3	24.3	31.3	31.4	31.7	32.1	
2	9.6	9.8	10.0	10.1	10.0	10.4	14.1	13.9	13.9	14.0	
≥ 3	16.6	18.3	17.6	17.8	18.1	18.3	21.4	22.1	22.3	22.3	
Primary payer (%)											< 0.001
Medicare	28.2	29.0	29.7	29.7	28.5	28.0	27.8	27.4	26.5		
Medicaid	21.2	22.0	22.4	23.2	32.0	34.2	36.0	36.9	37.8		
Private insurance	26.7	26.0	24.6	25.1	24.1	24.6	24.0	22.9	22.8		
Self-pay	23.8	23.0	23.3	22.0	15.4	13.1	12.3	12.8	12.9		

CCI: Charlson comorbidity index; SD: standard deviation.
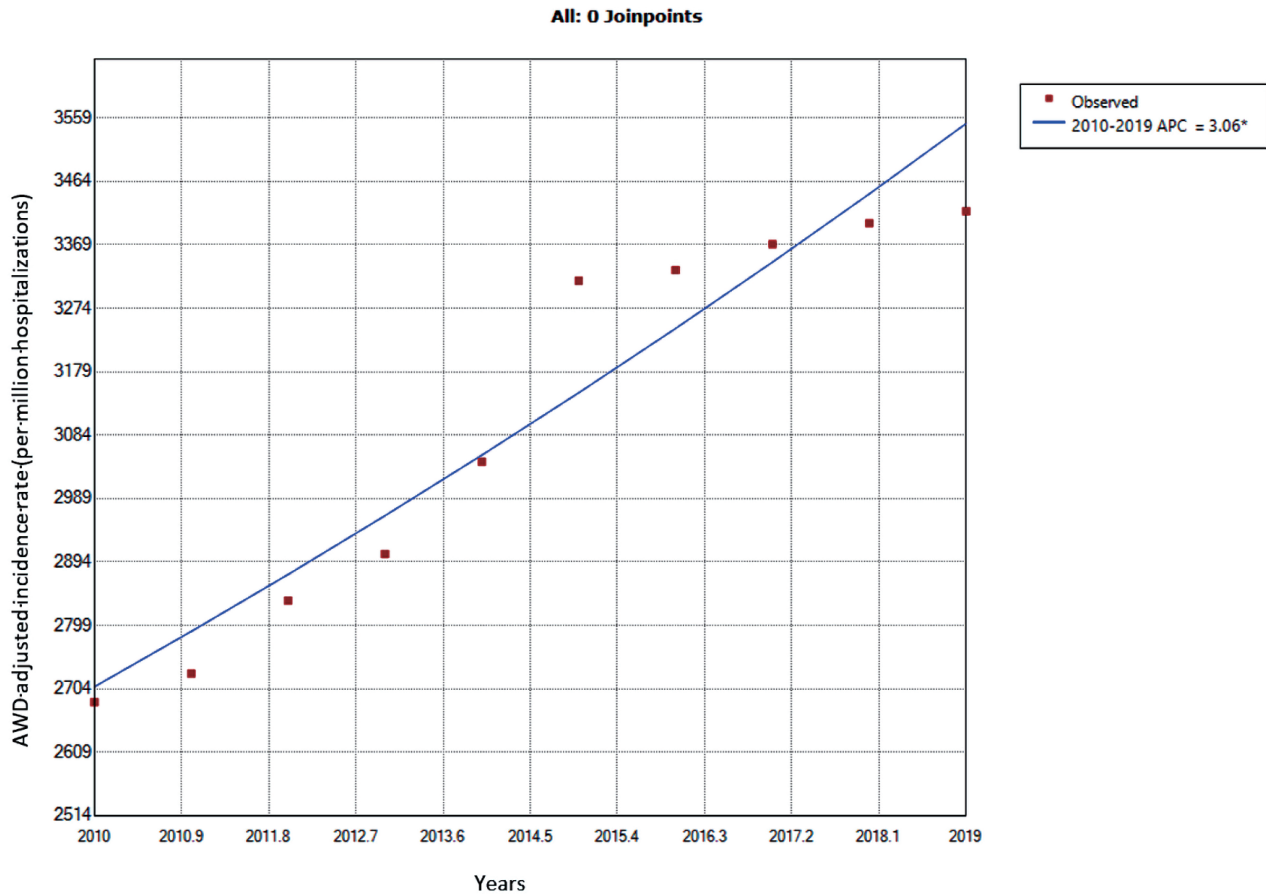
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Figure 1. Trends in the adjusted incidence of alcohol withdrawal delirium among all hospitalizations from 2010 to 2019. *Statistically significant. APC = 3.1%, CI: 2.2 - 4.0, P < 0.001. APC: annual percentage change; AWD: alcohol withdrawal delirium.

ing THC over the studied years (P trend < 0.001) (Table 2). Multivariate analysis showed that hospitalizations for middle aged and elderly patients were associated with higher THC compared to young adults (P < 0.001). Females had lower THC compared to males (P < 0.001). Hospitalizations for Blacks were associated with lower THC compared to Whites; however, this finding did not reach statistical significance (P = 0.114).

LOS increased over the studied period; this trend was statistically significant (P trend = 0.006) (Table 2). Hospitalizations for middle aged adults and elderly patients were associated with longer LOS compared to young adults (P < 0.001). Female gender was associated with shorter LOS (P < 0.001). Hospitalizations for Blacks were associated with longer LOS compared to Whites (P < 0.001).

We included 398,838 hospitalizations with primary diagnosis of AWD (Table 3, Fig. 2). AWD admission rate per million hospitalizations increased from 1,030.3 in 2010 to 1,556.0 in 2019. The APC was 3.3% in the period 2010 - 2012 (P = 0.271), 9.8% in the period 2012 - 2015 (P = 0.016), and 2.2% in the period 2015 - 2019 (P = 0.041). The average APC (AAPC) for the period 2010 - 2019 was 5.0% (P < 0.001).

As shown in Table 4, there was no statistically significant trend for inpatient mortality over the studied period (P trend = 0.797). Multivariate analysis showed that hospitalizations for middle aged and elderly patients were associated with higher mortality rates when compared to young adults (OR: 3.26 and 11.27, respectively, P < 0.001). Females had lower odds of morality when compared to males (OR: 0.60, P = 0.001). Hospitalizations for Blacks were associated with lower odds of

Table 2. Outcomes of All Hospitalizations Complicated by Alcohol Withdrawal Delirium

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	P trend
Mortality (%)	2.4	2.4	2.4	2.6	2.3	2.5	2.6	2.8	2.5	2.4	0.044
THC ($)	71,101	74,031	74,547	77,006	80,545	83,273	88,224	89,806	89,892	91,642	< 0.001
LOS (days)	8.5	8.4	8.5	8.4	8.6	8.6	8.8	8.7	8.6	8.5	0.006

THC: total hospital charges; LOS: length of stay.

Table 3. Demographics of Hospitalizations With Alcohol Withdrawal Delirium (AWD) as the Principal Diagnosis

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	P value
Hospitalization with AWD as principal diagnosis	32,352	31,691	34,130	35,250	38,460	43,970	44,950	44,945	46,100	46,990	
AWD admission rate per million hospitalizations	1,030.3	1,006.1	1,111.7	1,175	1,290.6	1,456	1,488.4	1,478.5	1,521.5	1,556	
Mean age (years) ± SD	48.9 ± 11.3	49.1 ± 11.7	49.0 ± 11.6	49.1 ± 11.7	49.1 ± 11.7	49.4 ± 11.9	49.1 ± 12.1	49.3 ± 12.2	49.2 ± 12.4	48.9 ± 12.4	0.439
Age categories (%)											< 0.001
Young adult	32.8	32.2	33.2	33.2	33.6	33.6	34.7	35.2	35.6	37.5	
Middle aged	58.6	59.1	57.7	58.0	57.4	56.8	55.8	54.2	53.7	52.2	
Elderly	8.6	8.7	9.1	8.8	9.0	9.6	9.6	10.6	10.7	10.3	
Female (%)	18.4	20.4	19.3	19.3	20.2	19.8	19.0	19.2	19.4	20.0	0.231
Race (%)											< 0.001
White	66.3	69.0	71.9	73.3	72.3	71.4	71.9	72.5	72.6	72.7	
Black	9.6	8.3	8.9	8.0	8.2	8.9	9.2	8.8	8.6	8.6	
Hispanic	10.3	9.4	9.8	9.5	9.4	9.9	10.2	11.1	11.4	11.4	
Other	13.8	13.3	9.5	9.2	10.1	9.8	8.7	7.6	7.3	7.4	
Median household income for zip code (%)											0.031
Low income	30.1	27.0	30.3	27.8	29.3	31.2	30.0	29.1	26.6	29.1	
Middle income	24.4	23.6	23.4	26.1	26.3	23.0	24.5	25.1	26.1	24.6	
Upper middle income	23.4	25.6	24.6	24.9	24.0	24.1	24.6	24.8	26.4	26.0	
High income	22.1	23.8	21.7	21.3	20.4	21.8	21.0	21.0	20.9	20.3	
CCI (%)											< 0.001
0	66.9	66.4	64.0	64.7	64.8	59.4	44.1	43.8	42.2	41.7	
1	20.8	21.0	23.1	21.0	21.0	24.8	35.0	35.3	35.3	36.1	
2	5.5	5.3	5.6	6.3	6.0	7.1	10.5	10.2	11.4	11.2	
≥ 3	6.7	7.3	7.3	8.1	8.3	8.7	10.4	10.8	11.1	11.1	
Primary payer (%)											< 0.001
Medicare	19.0	20.6	20.4	20.8	20.9	20.7	20.1	20.0	19.7	18.7	
Medicaid	21.9	22.2	23.3	24.5	35.3	38.1	40.3	41.3	41.5	42.2	
Private insurance	27.3	27.4	25.9	26.9	24.6	25.4	24.4	24.4	23.2	23.8	
Self-pay	31.8	39.9	30.4	27.8	19.2	15.8	15.2	14.3	15.6	15.3	

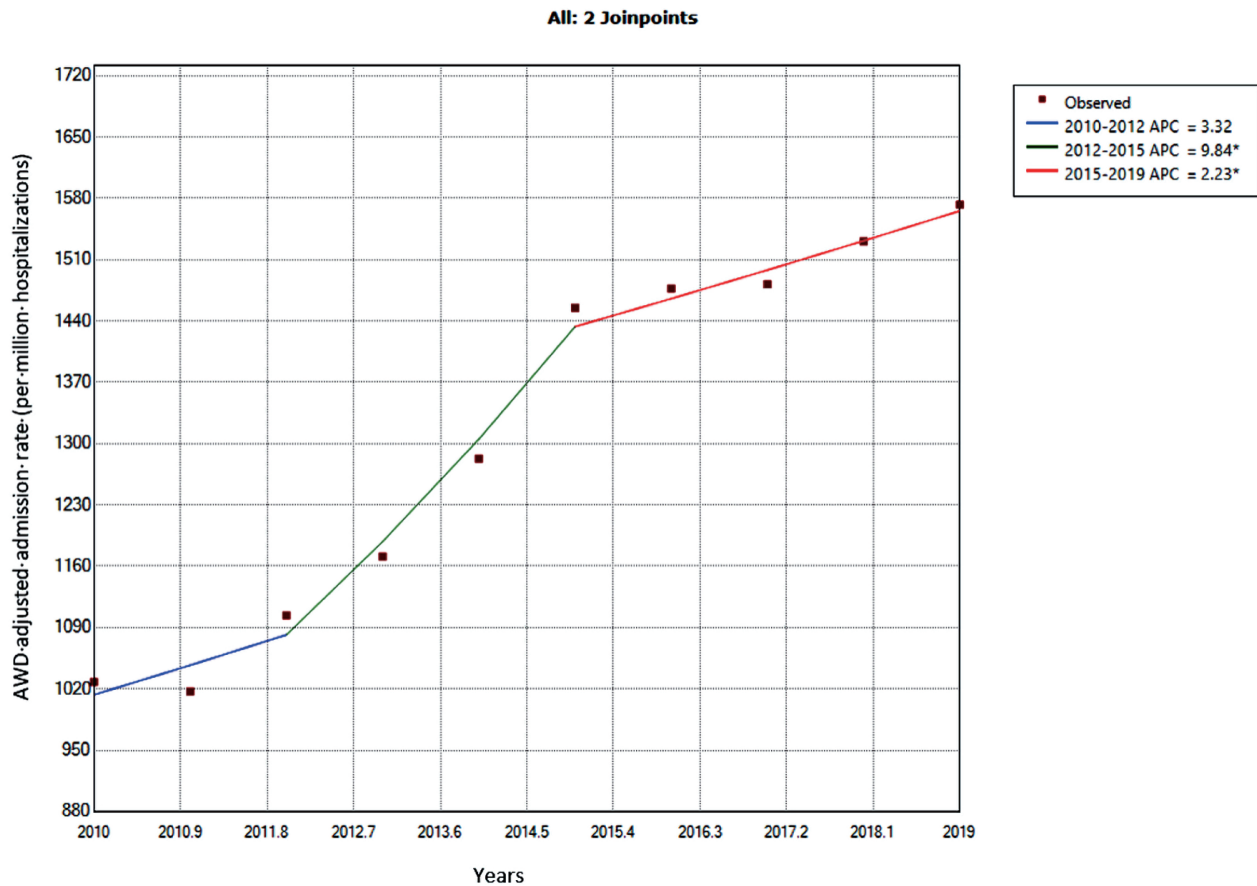CCI: Charlson comorbidity index; SD: standard deviation.

Figure 2. Trends in adjusted alcohol withdrawal delirium admission rate from 2010 to 2019. *Statistically significant. (2010 - 2012) APC = 3.3%, CI: 5.9 - 13.4, P = 0.271; (2012 - 2015) APC = 9.8%, CI: 4.3 - 15.7, P = 0.016; (2015 - 2019) APC = 2.2%, CI: 0.2 - 4.3, P = 0.041; (2010 - 2019) average APC = 5.0%, CI: 3.6 - 6.3, P < 0.001. APC: annual percentage change; AWD: alcohol withdrawal delirium; CI: CI: confidence interval.

mortality compared to Whites; however, this finding was not statistically significant (P = 0.683).

There was a statistically significant trend of increasing THC over the studied years (P trend < 0.001) (Table 4). Multivariate analysis showed that hospitalizations for middle aged and elderly patients were associated with higher THC compared to young adults (P < 0.001). Hospitalizations for Blacks were associated with lower THC compared to Whites; however, this finding did not reach statistical significance (P = 0.473).

LOS of stay increased over the studied period; this trend was statistically significant (P < 0.001) (Table 4). Hospitalizations for middle aged adults and elderly patients were associated with longer LOS compared to young adults (P < 0.001). Female gender was associated with shorter LOS compared

to males (P < 0.001). Hospitalizations for Black patients had longer LOS compared to Whites (P = 0.034).

Discussion

In the period 2000 to 2016, the percentage of drinkers in the world has decreased by almost 5%. However, since the world's population has increased, the decrease in the prevalence of drinking did not translate into fewer current drinkers [3]. In the period 2006 to 2014, the number of acute and chronic alcohol-related emergency department (ED) visits increased significantly [15]. Furthermore, between 2001 - 2002 and 2012 - 2013, 12-month alcohol use, high-risk drinking, and alcohol

Table 4. Outcomes of Hospitalizations With Alcohol Withdrawal Delirium as the Principal Diagnosis

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	P trend
Mortality (%)	0.5	0.5	0.4	0.5	0.4	0.5	0.5	0.4	0.4	0.5	0.797
THC ($)	37,093	38,306	39,497	41,185	44,005	46,293	48,059	49,546	51,075	51,543	< 0.001
LOS (days)	5.8	5.8	5.8	5.9	6.1	6.1	6.2	6.2	6.2	6.0	< 0.001

THC: total hospital charges; LOS: length of stay.

use disorder increased significantly. The increase in these outcomes were greatest among women, older adults, and racial/ethnic minorities [2].

The incidence and the admission rates of AWD increased significantly over the studied period. There was also a trend of worsening clinical outcomes (inpatient mortality, LOS, and THC) in our analysis. Dose-response relationships could be quantified for all alcohol-related disease categories, with the relative risk increasing with increased level of alcohol consumption for most diseases [16]. It has been found that the likelihood of experiencing withdrawal symptoms increased with increasing alcohol consumption [17]. These trends likely reflect the changes in alcohol consumption observed in the last two decades.

Our analysis showed that middle aged adults and elderly patients had higher mortality rates, LOS, and THC when compared to young adults. Alcohol consumption has been increasing in the elderly population particularly in women [18]. In addition, there has been a recent increase in binge drinking in this population [19]. Evidence suggests that elderly have higher mortality from alcoholic liver disease compared to younger patients [20-23]. Liskow et al found that elderly patients had more severe withdrawal and required higher doses of benzodiazepines [24]. Wonjar et al found the elderly patients had longer hospital stays for AWD and more electrolytes abnormalities compared to younger patients [25]. Similarly, Brower et al found that elderly patients had more withdrawal symptoms for longer duration [26]. The etiology of the worse outcomes in this population is multifactorial. Elderly patients with alcohol use disorder have higher rates of respiratory, endocrine, cardiovascular and central nervous system (CNS) diseases, and dementia compared to young patients [27]. In addition, older patients are at higher risk for cognitive and functional impairment during withdrawal [28]. Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents. Benzodiazepines are associated with increased risk of delirium and cognitive impairment in older adults [29]. Furthermore, many older adults drink alcohol and take medications that may interact with alcohol. Some of these interactions are due to age-related changes in the absorption, distribution, and metabolism of alcohol and medications [30]. Exacerbation of therapeutic and adverse effects of medications when combined with alcohol likely contributes to the observed outcomes in our study. Admissions for substance use including cocaine/crack, marijuana/hashish, heroin, non-prescription methadone, and other opiates have increased in the elderly population in the last decade [31, 32].

Our study showed that females had better clinical outcomes in terms of inpatient mortality, LOS, and THC when compared to males, a finding that is consistent with the available evidence [33, 34]. It has been found that withdrawal seizures were significantly more frequent among men than among women [35]. Canales et al found that men with AWD had higher rates of sepsis and longer LOS compared to women [36]. Benedict et al found that male gender was associated with 2.6-fold increase in the risk of benzodiazepine resistant withdrawal [37]. Drinking patterns differ between males and females. According to the global status report on alcohol and health, females are less often current drinkers than males and they drink less

on average and engage less often in heavy episodic drinking [3]. Women prefer mild types of alcoholic beverages such as wine and beer [38-40]. They become intoxicated less frequently and are less likely to abandon personal control while drinking [41]. On the other hand, women tend to present with more severe liver disease, particularly alcoholic hepatitis, and do so after a shorter period of excessive drinking and at a lower daily alcohol intake [42, 43]. They also have higher mortality from alcoholic liver cirrhosis compared to men [44]. Interestingly, Goodson et al found that the presence of liver disease was not predictive of alcohol withdrawal [45].

Glutamate-N-methyl-D-aspartic acid (NMDA), γ-aminobutyric acid (GABA), and many other receptors are involved in the adaptive changes in the brain during chronic ethanol exposure [46]. Evidence from animal studies suggests the alcohol induces gender-selective adaptations at the molecular level. It has been found that alcohol-dependent females did not show the same alterations in gene expression for GABA or NMDA receptors as did alcohol-dependent males [47]. Female rats recover more quickly from withdrawal than male rats, even with a greater volume per weight alcohol intake [48, 49]. Differences at the hormonal level also play a role; Devaud et al suggested that the differences between men and women in AWD may be mediated by allopregnanolone [50], an endogenous GABA receptor ligand with anxiolytic and anticonvulsant properties [51].

Our analysis showed that hospitalizations for Blacks were associated with lower mortality and THC, however, they had longer LOS. Caetano et al found that the prevalence of withdrawal symptoms was generally lower among Blacks than among Whites and Hispanics [17]. It has been found that Caucasian race was 3.6 times more likely to be develop benzodiazepine resistant withdrawal [37]. Chan et al found that White patients have twice the odds of having severe alcohol withdrawal when compared to non-White patients, and Black patients have smaller odds of having severe alcohol withdrawal when compared to non-Black patients [52].

The prevalence of alcohol abuse is greater among Whites than among Blacks [53]. In addition, Naimi et al and Herd et al found that Blacks consistently had the lowest rates of binge drinking episodes compared to other ethnicities [54, 55]. Evidence suggests a racial variation in the toxic effects of alcohol. Stewart et al found that Black non-Hispanic and Mexican Americans were more likely to have a 2-fold elevation in aspartate aminotransferase levels when compared with White non-Hispanic Americans [56].

The reason for the longer LOS observed in Blacks is unclear. It has been found that Black patients were more likely to be cocaine dependent than alcohol dependent and were more likely to experience cocaine withdrawal symptoms rather than alcohol withdrawal symptoms [17]. Whether withdrawal from other drugs have led to the observed higher LOS in this population needs further investigations. The lower mortality rate in this population might also contribute to the observed longer LOS.

Our study showed an increase in the incidence and the admission rates for AWD in the period 2010 to 2019. Mortality, LOS, and THC increased over the studied period. Younger age, female gender, and Black race were associated with bet-

ter clinical outcomes. Our study has some important limitations. The NIS reports information on hospitalizations rather than individual patients, as a result, one patient can be included more than once in the analysis. The severity of AWD could not be determined from the NIS. We could not determine what proportion of patients were managed in the intensive care setting (which may impact outcomes). Therapeutic interventions, medications given, laboratory results, and imaging are not provided in NIS. Finally, the study used ICD codes; therefore, the database may contain errors related to miscoding.

Acknowledgments

Financial Disclosure

None to declare.

Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Author Contributions

Dr. Attar supervised the entire project including the design and the analysis. Dr. Laswi and Dr. Shaka designed the study, performed data analysis, and reviewed the final manuscript. Dr. Kwei, Dr. Ojemolon, and Dr. Ebhohon wrote the manuscript in consultation with Dr. Laswi.

Data Availability

The NIS is a large publicly available inpatient database in the United States, containing data on more than 7 million hospital stays per year. Its large sample size is ideal for developing national and regional estimates and enables analyses of rare conditions, uncommon treatments, and special populations. The authors declare that data supporting the findings of this study are available within the article.

Abbreviations

AAPC: average annual percentage change; AHRQ: Agency for Healthcare Research and Quality; APC: Annual percentage change; AWD: alcohol withdrawal delirium; CCI: Charlson comorbidity index; CI: confidence interval; CNS: central nervous system; GABA: γ-aminobutyric acid; HCUP: Healthcare Cost and Utilization Project; HIV: human immunodeficiency virus; ICD: International Classification of Diseases; ICD-10-CM/PCS: International Classification of Diseases10th Revision, Clinical Modification/Procedure Coding System; ICD-9-CM/PCS: International Classification of DiseasesNinth Revision, Clinical Modification/Procedure Coding System; LOS: length of stay; MHOI: median household income; NIS: Nationwide Inpatient Sample; NMDA: N-methyl-D-aspartic acid; OR: odds ratio; SD: standard deviation; THC: total hospital charges

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