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Predictors of leaving against medical advice in patients with alcohol-related hepatitis

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Abstract

Background Alcohol-related hepatitis is one of the most severe manifestations of alcohol-related liver disease and has been associated with significant morbidity, mortality and financial burden. Patients with alcohol use disorders are at risk of leaving against medical advice (LAMA); however, there is currently a lack of data in the literature to show which patients are at higher risk. In this study, we investigated the specific demographic factors and comorbidities associated with LAMA.

Methods Patients with a primary or secondary discharge diagnosis of alcohol-related hepatitis (ICD10-CM codes K70.4 and K70.1) between January 2016 and December 2019 were included in this study. Demographics, comorbidities, complications and interventions were studied in for patients who LAMA. Multivariate analysis was conducted to elucidate factors contributing to the increased risk of alcohol-related hepatitis.

Results A total of 538,750 patients were admitted with a diagnosis of alcohol-related hepatitis. Of these, 31,500 (5.84%) patients LAMA. Older age, Hispanic race, private insurance, and higher income status were associated with a lower risk of LAMA, while younger age, African American race, lack of insurance and being in the lowest income quartile were associated with the highest risk.

Conclusions Our findings demonstrated that significant differences exist between patients with alcohol-related hepatitis who LAMA and those who remain hospitalized until discharge. We believe that this study will help healthcare providers identify patients at risk of LAMA, and help promote the targeted education of specific subgroups to improve their understanding of their disease state and decrease adverse events.

Keywords Alcohol-related liver disease, alcoholic hepatitis, National Inpatient Sample, leaving against medical advice, hepatitis

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Introduction

Alcohol-related hepatitis is a major cause of morbidity and mortality for patients, as well as a burden on the healthcare system. Previous studies have suggested that alcohol-related liver disease is associated with high morbidity and mortality [1]. Among patients with alcohol-related hepatitis, leaving against medical advice (LAMA) poses a potentially significant barrier to in-hospital care. These patients are also at higher risk of being lost to outpatient follow up, which results in poor outcomes.

The objectives of this study were to determine the prevalence of LAMA in patients with alcohol-related hepatitis, and to determine hospital and patient characteristics are associated with LAMA. The complications, comorbidities and interventions associated with a higher risk of LAMA were also studied.

Materials and methods

Data source

We obtained data from the Nationwide Inpatient Sample (NIS) database, the largest openly accessible all-payer inpatient healthcare database in the United States (US). The NIS database was created by the Healthcare Cost and Utilization Project (HCUP) to frame health policies at the federal, state and county levels. The HCUP is a program developed by the Agency for Healthcare Research and Quality. It contains de-identified hospitalization records for more than 7 million unweighted annual hospital stays and 35 million weighted annual hospitalizations in the US. We included data for hospitalizations from 2016-2019.

Study population

Patients from the dataset were selected based on the codes of the International Classification of Diseases, Clinical Modification-10th Revision (ICD-10-CM), which can be found in Supplementary Table 1. Patients hospitalized with a primary or secondary discharge diagnosis of alcohol-related hepatitis were included in the study (ICD-10-CM codes K70.4 and K70.1). We excluded patients for whom data on age, race, sex, primary insurance status or income were missing. We also excluded pregnant patients, patients aged less than 18 years, patients transferred out to another facility, and those who died during the hospitalization.

Study outcomes and variables

The primary outcome of the study was to assess the percentage of patients who LAMA. We collected data on patient demographics such as age, race, insurance status and income quartile. Data were collected on hospital characteristics such as region, hospital size, the location of the hospital, as well as whether the institution is academic or not. The Charlson Comorbidity Index was used to identify the comorbidity burden between the 2 groups [2]. Data were also collected on the common conditions associated with alcoholic hepatitis, such as HIV, substance abuse, hepatitis C and tobacco use. We also collected information on complications and common infections in these patients, such as pneumonia, urinary tract infection (UTI), ascites and variceal bleeding. Data were also collected on the interventions done on these patients, such as blood transfusion, endoscopy, colonoscopy, need for mechanical ventilation and intensive care unit (ICU) admission.

Statistical analysis

Descriptive statistics are presented in tables as totals with percentages for categorical variables. Mean and 95% confidence intervals are reported for continuous measures. Baseline characteristics, comorbidities, complications of the disease, and interventions were compared using the Pearson chi-squared test for categorical variables. Univariate logistic regression was performed to identify the patient demographics, hospital characteristics, complications, comorbidities and interventions that were associated with a higher risk of LAMA. A P-value of 0.1 was considered as a cutoff for inclusion in the multivariate logistic regression model. Multivariate logistic regression was carried out to determine significant predictors for LAMA and is presented in a tabular format with an odds ratio and 95% confidence interval. A type I error of <0.05 was considered statistically significant. All statistical analyses were performed using STATA, version 17.0 (Stata Corp., College Station, Texas, USA).

Results

Demographics

A total of 538,750 patients were admitted with a diagnosis of alcohol-related hepatitis. Of these, 31,500 (5.84%) patients LAMA. Patients who LAMA were younger (44.6 vs. 49.8) and more likely to be male (72.5% vs. 66.7%), uninsured (15.9% vs. 11.2%), and in the lowest income quartile (31.6% vs. 27.9%) compared to those routinely discharged. Patients who LAMA had a higher prevalence of HIV/AIDS, hepatitis C, drug use, and smoking. A complete list of demographic differences between the 2 groups is presented in Table 1.

Complications

Patient who LAMA had a lower incidence of varices, sepsis, acute kidney injury (AKI), pneumonia, UTI and sepsis compared to those routinely discharged (Table 2).

Interventions

Patients who LAMA had a lower incidence of esophagogastroduodenoscopy (EGD), colonoscopy, blood transfusion, mechanical ventilation, and ICU admission compared to those routinely discharged. Differences in the interventions during hospital stay between the LAMA group and those routinely discharged are presented in Table 3.

Results of multivariate analysis to predict factors associated with LAMA

On multivariate analysis, patients aged 18-44 years had a 339% higher risk of LAMA compared to patients over 65 years of age. Women had a 23% lower risk of LAMA. Hispanic patients had the lowest risk of LAMA. Caucasian and African

Table 1 Patient demographics, hospital characteristics and comorbidities of patients with alcohol-related hepatitis who were recently discharged compared to those leaving against medical advice (LAMA)

Characteristics	Routine discharge N (%)	LAMA N (%)	P-value
Total number	507,250	31,500	
Age, years (SD)	49.6 (49.5-49.7)	44.6 (44.3-44.9)	<0.001
Age, categorized			<0.001
18-45	173,880 (34.2)	15,730 (50.0)	
45-65	285,600 (56.3)	15,065 (47.8)	
>65	47,770 (9.4)	705 (2.2)	
Sex			<0.001
Male	338,540 (66.7)	22,845 (72.5)	
Female	168,710 (33.3)	8,655 (27.5)	
Race			0.003
White	356,935 (70.4)	21,910 (69.6)	
Black	51,275 (10.1)	3,660 (11.6)	
Hispanic	66,580 (13.1)	3,860 (12.3)	
Asian/Pacific Islander	6,145 (1.21)	350 (1.1)	
Native American	11,825 (2.3)	745 (2.4)	
Other	14,490 (2.9)	975 (3.1)	
Insurance			<0.001
Medicare	103,815 (20.5)	4,125 (13.1)	
Medicaid	191,160 (37.7)	15,470 (49.1)	
Private	131,675 (26)	5,405 (17.2)	
Self-pay/uninsured	56,815 (11.2)	4,990 (15.9)	
Income			<0.001
Lowest quartile	141,480 (27.9)	9,940(31.6)	
Second quartile	130,500 (25.7)	7,870 (25)	
Third quartile	129,805 (25.6)	7,700 (24.4)	
Highest quartile	105,465 (20.9)	5,995 (19.0)	
Region			<0.001
Northeast	98,900 (19.5)	8,805 (27.9)	
Midwest	118,895 (23.4)	6,690 (21.2)	
South	160,230 (31.6)	8,740 (27.8)	
West	129,225 (25.5)	7,265 (23)	
Elective admission			<0.001
Yes	489,090 (96.4)	30,780 (97.7)	
No (urgent or emergent)	17,385 (3.43)	695 (2.2)	
Other	775 (0.2)	25 (0.11)	
Hospital location			0.1846
Rural	34,155 (6.73)	2,275 (7.2)	
Urban	473,095 (93.3)	29,225 (92.8)	
Hospital size			<0.001
Small	107,075 (21.1)	7,365 (23.44)	
Medium	152,580 (30.1)	9,870 (31.3)	
Large	247,595 (48.8)	14,265 (45.3)	
Hospital teaching status			0.0917
Non-teaching	149,070 (29.4)	9,615 (30.5)	
Teaching	358,180 (70.6)	21,885 (69.55)	
Charlson Comorbidity Index			<0.001
0-1	188,205 (37.1)	16290 (51.7)	
2	69165 (13.6)	5130 (16.3)	
3 or more	249,880 (49.3)	10080 (32)	
Comorbidities			
HIV/AIDS	1,715 (0.3)	155 (0.50)	0.0412
Hepatitis B	3,790 (0.75)	215 (0.7)	0.567
Hepatitis C	45,120 (8.90)	3,650 (11.6)	<0.001
Opioid use disorder	1,525 (30.1)	225 (71.4)	<0.001
Drug use	71,780 (14.2)	7,340 (23.3)	<0.001
Smoking	11,500 (2.3)	915 (2.9)	0.009

Table 2 Complications in patients with alcohol-related hepatitis stratified by discharge status

Complications	Routine discharge N (%)	LAMA N (%)	P-value
Varices	16,840 (3.3)	735 (2.3)	<0.001
Ascites	15,1720 (30)	5,040 (16)	<0.001
AKI	10,8480 (21.4)	3,925 (12.5)	<0.001
Pneumonia	27,130 (5.3)	1,035 (3.3)	<0.001
UTI	49,100 (9.7)	2,005 (6.4)	<0.001
Sepsis	19,345 (3.8)	925 (2.9)	<0.001

LAMA, leaving against medical advice; AKI, acute kidney injury; UTI, urinary tract infection

Table 3 Interventions in patients with alcohol-related hepatitis stratified by discharge status

Interventions	Routine discharge N (%)	LAMA N (%)	P-value
EGD	12,990 (2.6)	485 (1.5)	<0.001
Colonoscopy	13,160 (2.6)	250 (0.8)	<0.001
Blood transfusion	39,425 (7.8)	1,400 (4.4)	<0.001
Mechanical ventilation	27,180 (5.4)	940 (3.0)	<0.001
ICU admission	29,080 (5.7)	990 (3.1)	<0.001

LAMA, leaving against medical advice; EGD, esophagogastroduodenoscopy; ICU, intensive care unit

American patients were at 30% and 35% higher risk of LAMA, respectively. Patients in the highest income quartile were at a lower risk of LAMA, as were patients with private insurance. No significant difference was noted between patients admitted to teaching vs. non-teaching hospitals. The presence of hepatitis C, substance use, opioid use disorder or tobacco use was associated with a greater risk of LAMA. Patients with ascites, AKI, pneumonia or UTI were at lower risk of LAMA. The presence of bleeding esophageal varices or sepsis had no association with the risk of LAMA. Patients who underwent colonoscopy or blood transfusion were at lower risk of LAMA. Undergoing an EGD, mechanical ventilation or admission to the ICU had no association with the risk of LAMA. The results of the multivariate logistic regression analysis are depicted in Table 4.

Discussion

The incidence of alcohol-related hepatitis has continued to increase in the US over the last decade and is associated not only with a high mortality rate, but also with a significant burden on the healthcare system [1]. LAMA has consistently been shown to be a common phenomenon in patients with substance use disorders, but can also be seen in patients with

Table 4 Results of multivariate logistic regression to identify predictors of LAMA after adjusting for demographics, comorbidities, complications and interventions

Demographics	Odds ratio	Confidence interval	P-value
Age category			
18-44 years	4.39	3.64- 5.29	<0.001
45-64	3.02	2.52-3.61	<0.001
>65	Reference		
Gender			
Male	Reference		
Female	0.77	0.72-0.81	<0.001
Race			
Hispanic	Reference		
White	1.3	1.19-1.41	<0.001
African American	1.35	1.18-1.52	<0.001
Asian/Pacific Islander	1.1	0.86-1.42	0.447
Native American	1.28	1.06-1.55	0.01
Other	1.16	0.99-1.37	0.074
Insurance status			
Private	Reference		
Medicare	1.43	1.3-1.59	<0.001
Medicaid	1.68	1.56-1.81	<0.001
Self-pay/uninsured	1.85	1.68-2.03	<0.001
Median income			
Lowest quartile	1.25	1.15-1.36	<0.001
Second quartile	1.08	0.99-1.17	0.069
Third quartile	1.05	0.97-1.14	0.223
Highest quartile	Reference		
Elective admission	0.76	0.63-0.91	0.003
Hospital size			
Small	Reference	0.89-1.04	0.327
Medium	0.96	0.85-0.99	0.019
Large	0.92		
Hospital region			
Northeast	1.52	1.39-1.66	<0.001
Midwest	0.98	0.90-1.07	0.649
West	0.93	0.85-1.01	0.097
South	Reference		
Hospital teaching status			
Teaching hospitals	0.94	0.89-1	0.067
Non-Teaching hospitals	Reference		
Charleson Comorbidity Index			
0-1	1.36	1.27-1.46	<0.001
2	1.33	1.22-1.44	<0.001
3 or more	Reference		
Comorbidities			
HIV/AIDS	0.87	0.82-0.92	<0.001
Drug use	1.37	1.27-1.46	<0.001
Smoking	1.13	0.97-1.31	0.116
Opioid use disorder	1.39	1-1.94	0.053
Hepatitis C	1.38	1.27-1.5	<0.001
Complications			
Varices	1.14	0.94-1.38	0.179
Ascites	0.63	0.59-0.68	<0.001
AKI	0.78	0.72-0.84	<0.001
Pneumonia	0.83	0.71-0.96	0.012
UTI	0.85	0.77-0.95	0.004
Sepsis	0.91	0.78-1.06	0.243

(Contd...)

Table 4 *(Continued)*

Demographics	Odds ratio	Confidence interval	P-value
Interventions			
Endoscopy	0.89	0.71-1.11	0.292
Colonoscopy	0.41	0.31-0.54	<0.001
Blood transfusion	0.86	0.76-0.98	0.024
Mechanical ventilation	0.82	0.42-1.57	0.543
ICU admission	0.86	0.46-1.63	0.649

LAMA, leaving against medical advice; AKI, acute kidney injury; UTI, urinary tract infection; ICU, intensive care unit

alcohol-related hepatitis [3]. However, the underlying factors associated with the risk of LAMA have not been delineated. To the best of our knowledge, this is the first nationwide study attempting to investigate the demographics, comorbidities, complications and interventions associated with risk of LAMA in patients with alcohol-related hepatitis. Our study found significant differences in the risk of LAMA based on age, sex, race, insurance status and household income.

Our study found that women had a 24% lower rate of LAMA compared to men admitted with alcohol-related hepatitis. In the literature, the available data regarding sex-related differences with respect to healthcare compliance remains mixed. Manuel *et al* studied discharge dispositions in emergency department visits and suggested that the incidence of women LAMA was higher compared to men [4]. A study by Ibrahim *et al* of US hospitalizations in 2002 suggested that women were less likely to be LAMA in the acute care hospital setting compared to men [5]. Regarding individual factors, it has been well documented in the literature that occupational, financial and family obligations are all factors that play a role in patients' decision to LAMA [6]. The influence of these underlying factors on the sex disparities remains a complex issue and further research is required [7].

Younger patients (18-44 years) had a 375% higher risk of LAMA compared to the older patients (>65 years) in on multivariate analysis. Our results are similar to those of several previous studies, which have consistently shown that younger patients are much more likely to LAMA [8-11]. It has been suggested that younger patients are generally healthier, with fewer comorbidities compared to older patients, which may provide a sense of reassurance and comfort when deciding on LAMA. Our data confirm that, even after adjustment for the Charlson Comorbidity Index, common diseases associated with alcohol-related hepatitis, interventions, complications and other patient demographics, younger patients remain at a significantly higher risk of LAMA compared to older patients. This finding highlights the likely possibility that there are additional factors contributing to the decision to LAMA. Studying these additional factors will be of clinical importance as targeted approaches to the younger age group may help decrease the rates of LAMA in these patients.

When studying racial differences, we found that Hispanic patients were at a significantly lower risk of LAMA compared to White and African American patients. A study by Franks *et al* evaluated race as a predictor of LAMA. They found that Hispanic patients were at lower risk, which suggested that unmeasured factors, such as cultural norms and beliefs, may play a role in these differences [12]. Recent data have shown that a patient's trust in the healthcare system may play a role in hospital outcomes [13]. Previous studies have demonstrated that African American patients have a lower level of trust in the healthcare system compared to other races, which in part can be attributed to the historical treatment of minorities within the US medical system [13-17]. In our study, African American patients were at the highest risk of LAMA as compared to other races, in line with previous findings, further supporting the need for focused interventions in this vulnerable patient population. Additionally, in our study, White patients were noted to be at a 33% higher risk of LAMA compared to Hispanic patients. Excluding our data on alcohol-related hepatitis, current literature demonstrating higher rates of LAMA in White patients is sparse, and more information is required to evaluate the factors that may be contributing to these differences.

Socioeconomic and insurance status had a significant effect on LAMA rates in our study. Patients in the lowest income quartile were 25% more likely to LAMA compared to the patients in the higher income group, highlighting the role of healthcare disparities. Similarly, the type of insurance also influenced rates of LAMA. Patients with no insurance had the highest risk of LAMA, while patients with private insurance were least likely to be LAMA. A higher risk of LAMA was also seen in patients with Medicare and Medicaid. These results are similar to those in the study by Yuan *et al* [18].

Comorbidities such as hepatitis C, opioid and drug use were associated with a greater risk of LAMA, consistent with the results published in the literature [19,20]. Ascites, pneumonia, UTI and AKI were associated with a lower risk of LAMA. ICU admission and mechanical ventilation had no association with LAMA, while transfusion of blood products was associated with a lower risk. The association between disease severity and the risk of LAMA is complex. Patients with severe disease may not feel well enough to consider LAMA. However, similar patients may have extended hospitalizations, leading to frustration and distress, which may contribute to the their decision to LAMA.

Our study demonstrated that less than 1% of LAMA patients completed a colonoscopy. There is a possibility that patients who completed the preparation were more compliant and likely to stay, as procedure preparation requires time and effort. Another possibility is that colonoscopies were only offered to patients who the providers considered more likely to be compliant. Since multiple factors are involved in determining which patients undergo colonoscopy, we should not draw inferences from this finding.

The major limitation of our study was the inability to track patients over a period of time, as NIS data are per patient hospitalization. There is a possibility that some patients were readmitted and re-included in the data analysis. To prevent this, we excluded patients who were transferred out of the hospital. We were not able to calculate the disease-specific severity scores (Maddrey or model for end-stage liver disease-Na) scores because the necessary variables were not available in the database. Organ dysfunction, such as AKI, shock, sepsis

and mechanical ventilation, were used as surrogate markers of the severity of alcohol-related hepatitis. The strength of the study comes from the large population size and the diversity of the study sample.

In conclusion, we found significant differences in rates of LAMA in patients with alcohol-related hepatitis. The greatest risk of LAMA was seen in younger patients, African American patients, those of lower socioeconomic status, and those without insurance. Patients who were older, of Hispanic ethnicity and had private insurance were less likely to be LAMA. It is important for healthcare professionals to be aware of the risk factors and potentially design targeted interventions for patients at high risk of LAMA.

Summary Box

What is already known:

- Not much is known about the characteristics of patients leaving against medical advice (LAMA)

What the new findings are:

- The greatest risk of LAMA was seen in younger patients, African American patients, those of lower socioeconomic status, and those without insurance
- Women had a lower risk of LAMA compared to men
- Patients who were older, of Hispanic ethnicity and with private insurance were less likely to be LAMA

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Supplementary material

Supplementary Table 1 ICD-10-CM Codes

Alcoholic Hepatitis	K70.4, K70.1
Hepatitis B	B18.1, B19.1, B16
Hepatitis C	B18.2, B19.2
HIV	B20.x-B22.x, B24.x
Substance Use	F11.x-F16.x, F18.x, F19.x, Z71.5. Z72.2
Opioid use disorder	F11.9
Tobacco Use	Z72.0
Bleeding Esophageal Varices	185.01,185.11
Ascites	K70.31, R18, K71.51, K70.11
AKI	N17.0, N17.1, N17.2, N17.8, N17.9
Pneumonia	A01.03, A02.22, A3.701, A3.711, A3.781, A3.791, A5.484, B.012, B.052, B0681, B7781, J09, J1000, J1001, J1008, J1100, J1108, J1281, J1289, J129, J13, J14, J150, J151, J1520, J15211, J15212, J1529, J153, J154, J155, J156, J157, J158, J159, J160, J168, J17, J180, J181, J182, J188, J189, J851, J95851, J120, J121, J122, J123
UTI	N39.0, N10, N30.0
Sepsis	R65.10, R65.11, R65.20
EGD	06L38DZ, 06L37ZZ, 06L38ZZ, 06L37DZ, 06L37CZ, 06L34ZZ, 06L34DZ, 06L34CZ, 06L33ZZ, 0D518ZZ, 0D528ZZ, 0D538ZZ, 0D548ZZ, 0D568ZZ, 0D578ZZ, 0D598ZZ, 0DQ68ZZ, 0DQ78ZZ, 0DQ98ZZ, 0W3P8ZZ
Colonoscopy	0DJD8ZZ, 0DBE8ZX, 0DBE8ZZ, 0DBF8ZX, 0DBF8ZZ, 0DBG8ZX, 0DBG8ZZ, 0DBH8ZX, 0DBH8ZZ, 0DBJ8ZX, 0DBJ8ZZ, 0DBK8ZX, 0DBK8ZZ, 0DBL8ZX, 0DBL8ZZ, 0DBM8ZX, 0DBM8ZZ, 0DBN8ZX, 0DBN8ZZ, 0DBP8ZX, 0DBP8ZZ, 0DBQ8ZX, 0DBQ8ZZ, 0D5E8ZZ, 0D5F8ZZ, 0D5G8ZZ, 0D5H8ZZ, 0D5J8ZZ, 0D5K8ZZ, 0D5L8ZZ, 0D5M8ZZ, 0D5N8ZZ, 0D5P8ZZ, 0D5Q8ZZ
Blood Transfusion	30243N0, 30243N1, 30243P0, 30243P1, 30243H0, 30243H1, 30240N0, 30240N1, 30240P0, 30240P1, 30240H0, 30240H1, 30230H0, 30230H1, 30230N0, 30230N1, 30230P0, 30230P1, 30233N0, 30233N1, 30233P0, 30233P1
Mechanical ventilation	5A1935Z, 5A1945Z, 5A1955Z
Pressor Use	3E030XZ, 3E033XZ, 3E040XZ, 3E043XZ, 3E050XZ, 3E053XZ. 3E060XZ, 3E063XZ
ICU admission	Mechanical Ventilation + Pressor Use