

Trends of Readmissions for Gastrointestinal Bleeding After Alcoholic Hepatitis: Analysis of the Nationwide Readmission Database

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Abstract

Background: Alcohol consumption is associated with numerous hepatic manifestations, including alcoholic fatty liver disease, alcoholic hepatitis (AH), and liver cirrhosis. AH is a common and serious complication of alcohol use. Gastrointestinal bleeding (GIB) remains one of the most common causes of death in these patients. In this article, we studied the trends of GIB after AH.

Methods: This was a retrospective interrupted trend study. We analyzed the 2010, 2012, 2014, 2016, and 2018 Nationwide Readmission Databases. The first AH hospitalization in the year was marked as index hospitalization. We identified subsequent hospitalizations with GIB within 30 days and marked them as readmissions. A multivariate regression analysis was used to calculate the risk-adjusted odds of trends for GIB readmissions, including esophageal varices bleeding (EVB), upper GIB, lower GIB, and all GIB.

Results: The volume of index hospitalizations increased from 10,248 in 2010 to 16,479 in 2018. Similarly, all readmissions increased from 1,838 in 2010 to 3,908 in 2018. Of all readmissions, EVB increased from 3.9% in 2010 to 5.9% in 2018 (odds ratio (OR) trend 1.10; $P < 0.001$). Readmissions for upper GIB increased from 2.4% in 2010 to 7.8% in 2018 (OR trend 1.22; $P < 0.001$). On the other hand, lower GIB readmissions decreased from 7.2% in 2010 to 4.7% in 2018 (OR trend 0.95; $P = 0.015$). There was no statistically significant trend for all GIB readmissions (OR trend 1; $P = 0.915$).

Conclusion: Further studies are needed to evaluate the patterns of lower GIB in patients with liver disease and the recent trends of corticosteroids use in AH patients.

Keywords: Trends; Alcoholic hepatitis; Gastrointestinal bleeding; Readmission

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Introduction

Alcohol is the third most common modifiable cause of death in the United States after tobacco and poor diet/physical inactivity [1]. Alcoholic hepatitis (AH) is a common and serious complication of alcohol use. In 2007, more than 50,000 patients were hospitalized with AH in the USA [2]. These patients are at increased risk for complications including infections [3], renal failure [4, 5], progression to liver cirrhosis [6], and death [7]. Studies have shown that the overall mortality rate exceeds 30% [7, 8], with gastrointestinal bleeding (GIB) being the second most common cause of death [7]. In this study, we examined the trends of readmissions for GIB after AH hospitalizations.

Materials and Methods

This was a retrospective interrupted trend study. We analyzed the Nationwide Readmission Database (NRD) using the International Classification of Diseases, Ninth Revision, Clinical Modification/Procedure Coding System (ICD-9-CM/PCS) and the ICD-10-CM/PCS. The NRD is the largest publicly available readmission database drawn from the Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP) State Inpatient Databases (SID). The NRD allows a weighted analysis to obtain 100% of the United States admissions within a given year [9]. We included 2010, 2012, 2014, 2016, and 2018 NRD databases. The codes K70.10, K70.11, and 571.1 were used to identify patients with AH. The first hospitalization in the year was marked as index hospitalization. We identified subsequent hospitalizations within 30 days and marked them as readmissions. Individuals < 18 years, elective, and traumatic hospitalizations were excluded. December hospitalizations were also excluded as they did not contain complete data to assess 30-day readmissions. A multivariate regression analysis was used to calculate the risk-adjusted odds of trends for GIB readmissions, including esophageal varices bleeding (EVB), upper GIB (excluding EVB), lower GIB, and all GIB. P -values ≤ 0.05 were considered statistically significant. Data analysis was performed using Stata[®] Version 16 software (StataCorp, College Station, TX, USA). As the NRD does not include patient-specific or hospital-specific identifiers [9], this study was exempt from the approval of institutional review board (IRB) and ethics committee and did not require subjects' consent.

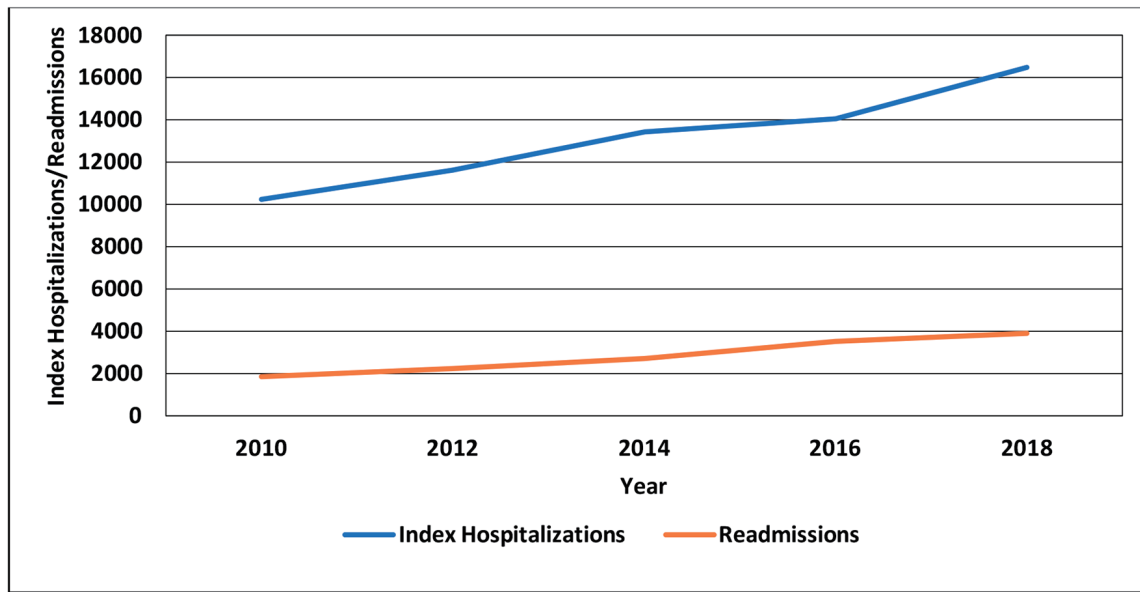


Figure 1. Index hospitalizations for alcoholic hepatitis and all readmissions during 2010 - 2018.

Results

We observed an increase in the number of index hospitalizations and all readmissions over the studied period. The volume of index hospitalizations increased from 10,248 in 2010 to 16,479 in 2018 (Fig. 1 and Table 1). Similarly, all readmissions increased from 1,838 in 2010 to 3,908 in 2018 (Fig. 1 and Table 1). There were statistically significant trends of increasing readmissions for EVB and upper GIB (Fig. 2 and Table 2). Of all readmissions, EVB increased from 3.9% in 2010 to 5.9% in 2018 (odds ratio (OR) trend 1.10; $P < 0.001$). Readmissions for upper GIB increased from 2.4% in 2010 to 7.8% in 2018 (OR trend 1.22; $P < 0.001$). On the other hand, there was a statistically significant trend of decreasing readmissions for lower GIB (Fig. 2 and Table 2). Lower GIB readmissions decreased from 7.2% in 2010 to 4.7% in 2018 (OR trend 0.95; $P = 0.015$). There was no statistically significant trend for all GIB readmissions (OR trend 1; $P = 0.915$). Compared to young adults (18 - 44 years), middle aged adults (45 - 64 years) and older adults (65 years and older) had higher mortality when readmitted after AH (OR 2.1; $P < 0.001$ and OR 2.7; $P < 0.001$, respectively).

Discussion

Alcohol consumption per capita has increased globally and

Table 1. Index Hospitalizations for Alcoholic Hepatitis and All Readmissions During 2010 - 2018

	2010	2012	2014	2016	2018
Index hospitalizations	10,248	11,645	13,444	14,048	16,479
All readmissions	1,838	2,227	2,715	3,502	3,908

nationally [10, 11]. Between 2001 - 2002 and 2012 - 2013, high-risk alcohol drinking and alcohol use disorder increased by 29.9% and 49.4%, respectively [12]. Moreover, in the period 2006 - 2014, both acute and chronic alcohol-related emergency visits increased by 51.5% and 75.7%, respectively [13]. These changes might in part account for the increase in the number of index hospitalizations and readmissions over the studied period. Our findings are consistent with the available data from the last two decades [14-16]. We used ICD codes to identify index hospitalizations and readmissions; therefore, coding errors can affect the results. Pang et al found that the positive predictive value of the ICD-10 code used for AH is 67% [17]. This might have resulted in a modest over- or underestimation of the incidence of AH; however, we do not believe that such inaccuracy has produced the observed trends.

Consistent with the available data from AH and cirrhosis patients [18, 19], we observed an increase in the proportion of patients readmitted for EVB over the studied period. Recently, the severity, comorbidities, and complications associated with AH have worsened [6]. Nguyen et al found a recent trend of increasing model for end-stage liver disease (MELD) score in AH patients [6]. The same study also found an increase in the Charlson comorbidity index over the past decade. Higher MELD score has been associated with increased upper GIB [20]. Similarly, Crooks et al found that non-gastrointestinal comorbidities defined using the Charlson comorbidity index was associated with upper GIB [21].

It has been found that in patients with AH, the diagnosis of cirrhosis increased significantly between 2000 (28%) and 2011 (32%) [6]. Recently, hospitalizations and readmissions for liver cirrhosis have been increasing in the USA [22, 23]. Moreover, Fan et al found that during year 2000 - 2014, portal vein thrombosis (PVT) prevalence among alcoholic cirrhosis patients was increasing with an annual percent change of 8.9% [24]. The increases in the prevalence of liver cirrhosis

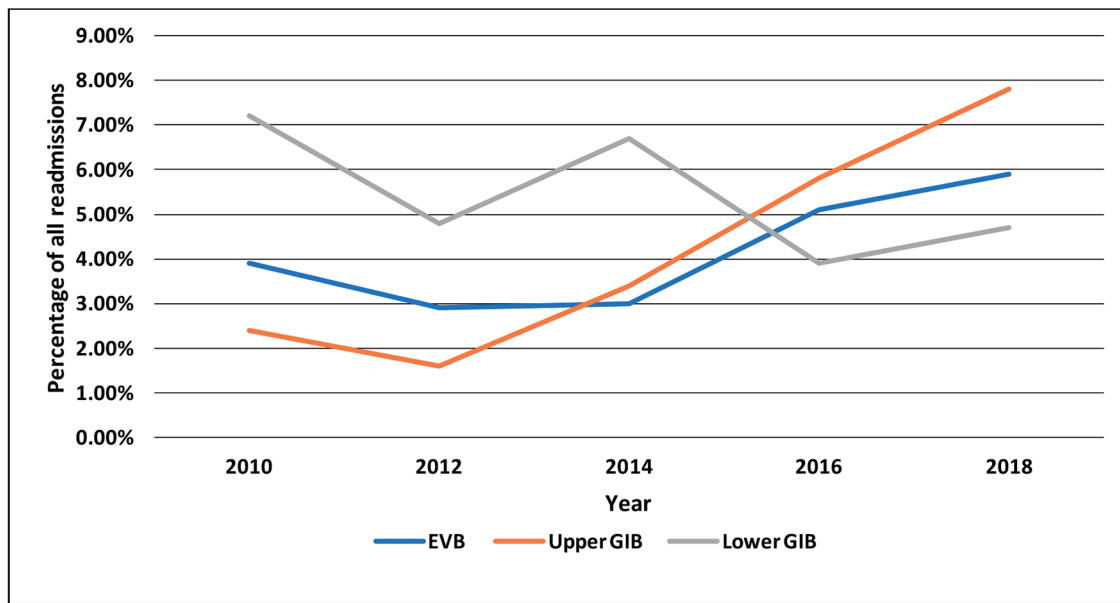


Figure 2. Trends of EVB ($P < 0.001$) and upper GIB ($P < 0.001$) and lower GIB ($P = 0.015$) during 2010 - 2018. GIB: gastrointestinal bleeding; EVB: esophageal varices bleeding.

and PVT likely have contributed to the observed increase in EVB. In addition, evidence suggests that patients with cirrhosis and PVT who receive anticoagulant therapy have increased recanalization and reduced progression of thrombosis [25]. The increase in the use of anticoagulants for PVT would also increase the risk of EVB [26]. Obesity is common in AH and associated with a greater than two-fold increase in short-term mortality [27, 28]. Berzigotti et al found that body mass index (BMI) was an independent predictor of decompensation (including EVB) in cirrhotic patients [29]. From 1999 - 2000 through 2017 - 2018, obesity prevalence in the USA increased from 30.5% to 42.4% [30]. It is unclear if this increase has affected the observed EVB trends.

We found a statistically significant trend of increasing readmissions for upper GIB. The etiology of this trend is likely multifactorial and overlapping with EVB. As discussed above, the increase in the prevalence of cirrhosis and PVT likely have resulted in higher rates of portal gastropathy. In addition, we speculate that the recent increase in alcohol consumption has resulted in more alcohol-induced gastritis. Many studies showed improved short-term mortality with steroids use in patients with severe disease [31-33]. The American Association

Table 2. Trends of EVB, Upper GIB, Lower GIB, and All GIB During 2010 - 2018

	2010	2012	2014	2016	2018	P value
EVB*	3.9%	2.9%	3.0%	5.1%	5.9%	< 0.001
Upper GIB*	2.4%	1.6%	3.4%	5.8%	7.8%	< 0.001
Lower GIB*	7.2%	4.8%	6.7%	3.9%	4.7%	0.015
All GIB	13.1%	9.0%	12.3%	9.5%	12.1%	0.915

*Statistically significant. GIB: gastrointestinal bleeding; EVB: esophageal varices bleeding.

for the Study of Liver Diseases (AASLD) [34], the American Gastroenterological Association (AGA) [35], and the American College of Gastroenterology (ACG) [36] recommend the use of corticosteroids in the treatment of severe AH. The use of steroids is associated with increased risk of GIB [37, 38], with the highest rates occurring within the first month after initiation [38]. Data on the trends of steroids use in AH patients are lacking.

We observed a trend of decreasing lower GIB over the studied period. Studies showed variable results for the trends of lower GIB in the last decade [39-41]. Data on lower GIB in patients with liver disease are very scarce. Khalifa et al found that the most common causes of lower GIB in cirrhotic patients were hemorrhoids followed by portal hypertensive enteropathy or colopathy [42], with 72% of patients with hemorrhoids having either a clinical or radiological evidence of portal hypertension. Similarly, Rabinovitz et al found that esophageal varices were present in most patients with hemorrhoids and that the degree of portal hypertension was associated with the presence of hemorrhoids [43]. On the other hand, a smaller study found no significant difference in the hepatic venous pressure gradient between cirrhotic patients with and without hemorrhoids [44]. The etiology of observed trend is unclear, especially its divergence from EVB trend. Khalifa et al found that 33% of lower GIB patients with cirrhosis had severe bleeding requiring packed red blood cell (PRBC) transfusion and 17% died during hospitalization [42]. In addition, two studies found a trend of increasing lower GIB in elderly patients [40, 45]. Devani et al found that age was an independent predictor of mortality in patients with lower GIB [46]. It is unclear if higher mortality played a role in the observed trend. Further studies are needed to clarify the etiologies of lower GIB in patients with liver disease and their association with portal hypertension.

Conclusion

We noticed trends of increasing readmissions for EVB and upper GIB and a trend of decreasing readmissions for lower GIB. However, there was no statistically significant trend for all GIB over the studied period. The etiology of these trends is likely multifactorial as discussed above. Further studies are needed to evaluate the recent trends of corticosteroids use in AH patients and the patterns of lower GIB in patients with liver disease. Our study has some limitations. Given the use of ICD codes, the database may contain errors related to miscoding. The criteria used to establish the diagnosis of AH cannot be obtained from NRD. In addition, the NRD reports information on hospitalizations rather than individual patients; therefore, patients with many readmissions would be included more than once in the dataset. The NRD does not include any information on laboratory values, medications, nutritional support, or therapeutic interventions. Lastly, we were unable to calculate the MELD, Maddrey's, or Child-Pugh score from the data available in NRD.

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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, analysis, and writing the manuscript. Dr. Laswi and Dr. Shaka designed the study, performed data analysis, and reviewed the final manuscript. Dr. Abusalim and Dr. Khoshbin wrote the manuscript in consultation with Dr. Laswi.

Data Availability

The Nationwide Readmission Database is publicly available as stated in the methods. Any inquiries regarding supporting data of this study should be directed to the corresponding author.

Abbreviations

AASLD: American Association for the Study of Liver Diseases; ACG: American College of Gastroenterology; AGA: American Gastroenterological Association; AH: alcoholic hepatitis; AHRQ: Agency for Healthcare Research and Quality; EVB: esophageal varices bleeding; GIB: gastrointestinal bleeding; HCUP: Healthcare Cost and Utilization Project; ICD-10-CM/PCS: International Classification of Diseases, Tenth Revision, Clinical Modification/Procedure Coding System; ICD-9-CM/PCS: International Classification of Diseases, Ninth Revision, Clinical Modification/Procedure Coding System; IRB: institutional review board; MELD: model for end-stage liver disease; NRD: Nationwide Readmissions Database; OR: odds ratio; PRBC: packed red blood cell; PVT: portal vein thrombosis; SID: State Inpatient Databases

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