Original Article

Inpatient burden of esophageal varices in the United States: analysis of trends in demographics, cost of care, and outcomes

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Background: Esophageal variceal bleeding remains a common reason for hospitalization in the United States. The main objective of this study was to analyze demographic variations and outcomes in hospitalizations related to esophageal varices (EV) in the US.

Methods: We performed a retrospective observational cohort study using National Inpatient Sample (NIS) database for all hospitalizations with discharge diagnoses of EV, with and without hemorrhage from 2001 to 2011.

Results: In 2001, there were 19,167 hospitalizations with discharge diagnoses of EV with and without bleeding compared to 45,578 in 2011 (P<0.001). There was a 138% increase in the number of total EV hospitalizations, a 221% increase in hospitalizations with EV without hemorrhage, and a 7% increase in hospitalizations for patients with EV and hemorrhage. Age group 50–64 was the most affected, accounting for 31.4% of EV hospitalizations in 2001 and 46.7% of EV hospitalizations in 2011 (P<0.001). The overall in-hospital mortality rate was 3.4% for patients with EV without hemorrhage and 8.7% for patients with EV with hemorrhage (P=0.0003).

Conclusions: The number of hospitalizations for patients with asymptomatic EV increased significantly between 2001 to 2011, with only a small concurrent increase in the number of hospitalizations for patients with esophageal variceal bleeding.

Keywords: Esophageal varices (EV); cirrhosis; endoscopic treatment

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Introduction

The prevalence of cirrhosis is increasing at an alarming rate in the U.S., to a great extent being driven by the increased number of cases of nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) (1,2). The prevalence of NAFLD-associated advanced fibrosis and NASH-associated cirrhosis increased 2-fold and 2.5-fold, respectively, between the years 1999–2002 and 2009–2012 (3). In addition, the number of patients presenting with HCV-related cirrhosis is predicted to double over the next twenty years (4).

Cirrhosis is the twelfth leading cause of death in the U.S. (5). Cirrhosis accounted for 37,890 deaths in 2013 (5). One study estimated that the annual incidence of cirrhosis-related deaths would increase to 60,000 deaths if diagnostic codes for viral hepatitis and cirrhosis complications were also considered (6). As a result, cirrhosis poses a large economic burden. One study estimated the annual cost of care of patients with cirrhosis to be about $2 billion (7).

Esophageal variceal bleeding is a common complication of cirrhosis. Nearly 30% of patients with esophageal varices (EV) bleed within the first year after diagnosis (8). Patients hospitalized for esophageal variceal bleeding are at significantly increased risk of in-hospital mortality, compared to patients admitted with non-bleeding varices. Currently, the estimated burden of treating bleeding EV remains unknown. Accordingly, an accurate understanding of trends in EV-related hospitalizations is necessary for appropriate healthcare planning. This study was therefore undertaken to identify vulnerable groups and the impact of variceal bleeding within a nationally representative patient sample (9).

Methods

Source of data

The National Inpatient Sample (NIS), designed by Agency for Healthcare Research and Quality (AHRQ), is the largest all-payer inpatient database in the U.S. This data is compiled yearly and contains discharge data from over 1,200 hospitals located across 45 states in the U.S. The NIS was designed to approximate a 20% stratified sample of community hospitals in the country and provides sampling weights to calculate national estimates (10). The NIS contains information included in a typical discharge summary, with safeguards in place to protect the privacy of individual patients, physicians, and hospitals. Each individual hospitalization is de-identified and is maintained in the NIS as a unique entry with one primary discharge diagnosis and approximately 24 secondary diagnoses during that hospitalization. Each entry also carries information on demographic details, insurance status, comorbidities, primary/secondary procedures, hospitalization outcomes, length of stay, and cost of care. The internal validity of the database is guaranteed by annual data quality assessments of the sample. Moreover, comparisons with data sources like the American Hospital Association (AHA) Annual Survey of Hospitals, the National Hospital Discharge Survey from the National Center for Health Statistics, and the Medicare Provider and Analysis Review (MedPAR) inpatient data from the Centers for Medicare and Medicaid Services strengthen the external validity of the sample (11,12).

Study design

We queried the NIS database from year 2001 to 2011 using a retrospective observational cohort study design to identify all hospitalizations with EV. We extracted data regarding all of the hospitalizations from 2001 to 2011 with primary or secondary diagnosis of EV with hemorrhage and without hemorrhage, which in turn were identified with validated International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes 456.0 and 456.1, respectively. Patients with age less than 18 years were excluded. Also, all hospitalizations with missing information related to age, gender, admission/discharge date, and in-hospital mortality status were excluded to gather and document accurate demographics of EV hospitalizations. To calculate the estimated cost of hospitalizations, the NIS data were merged with cost-to-charge ratio (CCR) files available from the Healthcare Cost and Utilization Project. We estimated the cost of each inpatient stay by multiplying the total hospital charge with the CCR.

Variables and statistical analysis

SAS 9.4 (SAS Institute Inc., Cary, NC, USA) and Joinpoint Trend Analysis Software (version 4.5.0.1) were utilized for complex statistical analyses. Since NIS represents a 20% stratified random sample of U.S. hospitals, analyses were performed using hospital-level discharge weights provided by the NIS, to obtain national estimates of hospitalizations. Community hospitals are oversampled as the NIS only includes data from community hospitals. The NIS is sampled from the State Inpatient Databases (SID), which

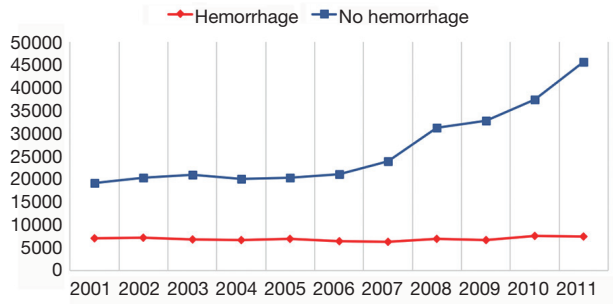

Figure 1 Trend in number of EV hospitalizations with and without hemorrhage. EV, esophageal varices.

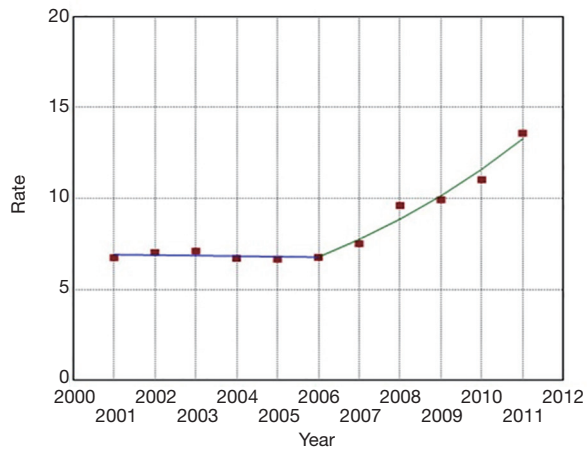

Figure 2 APC in number of hospitalizations. APC, annual percent change.

captures hospital inpatient stays in a given state. The SID encompasses about 97% of all U.S. community hospital discharges. EV-related hospitalizations per million U.S. population were calculated by dividing the number of such hospitalizations in each year by the U.S. census population greater than 18 years age for that year. EV hospitalizations were also calculated in subgroups of age (18–34, 35–49, 50–64, 65–79, and ≥80 years), gender, race (white, black, Hispanic, and other), insurance status (Medicare/Medicaid, private insurance, and self-pay/other), hospital location in different U.S. regions (Northeast, Midwest, South, and West), and teaching status of the hospital. According to AHRQ, a hospital is considered to be a teaching hospital if it is: (I) an AMA-approved residency program, (II) a member of the Council of Teaching Hospitals, or (III) a hospital with a full-time resident-to-bed ratio more than 0.25 (13). The Cochrane-Armitage trend test was used to calculate trends in categorical variables (14). The Wilcoxon rank sum test was used to assess continuous variables (15). To calculate the annual percent change (APC) in the number of hospitalizations, we obtained the age-adjusted crude hospitalization rate for each year and then multiplied it by the age distribution of the standard population for that year. Finally, Joinpoint regression was utilized to obtain APC values (16).

Results

EV hospitalizations and demographics

A total of 292,851 hospitalizations for EV (as a primary or secondary discharge diagnosis) were identified in the U.S. population from 2001 to 2011. (*Figure 1*). EV hospitalizations increased by 138% from 19,167 in 2001 to 45,578 in 2011 (P<0.001). The number of U.S. hospitalizations with an EV diagnosis was relatively stable between 2001 and 2006. However, beginning in 2006, there was a significant increase in the percent of U.S. hospitalizations with a diagnosis of EV. (*Figure 2*). Patient characteristics are described in *Table 1*. EV patients were predominantly white (53%) and between 50 and 64 years of age (40.7%). The second most commonly affected race was Hispanic (14.6%). Similar racial distribution was seen in the EV patients in a study conducted by Jamal *et al.* (17). There were more hospitalizations in males (63.8%) than in females (36.2%). The gender ratio was stable throughout the study period. Medicare/Medicaid was the primary payer for 59.5% of EV hospitalizations. A plurality of EV hospitalizations were reported in the South (37.5%), followed by the Midwest (22.7%), West (22.5%), and Northeast (17.4%) (*Table 1*). However, the incidence of EV hospitalizations was highest in the West, accounting for 84 hospitalizations per 100,000 hospitalizations when compared to 74 per 100,000 hospitalizations in the South.

Trends in EV hospitalizations

The EV hospitalization rate more than doubled between 2001 and 2011, increasing from 515 to 1,181 per million U.S. population per year (P<0.001) (*Table 2*). Over the same period, the rate of hospitalization for EV without hemorrhage increased from 326 to 990 per million U.S. population per year, an increase of 203%. The rate of hospitalization for EV with hemorrhage increased from 189 to 191 per million U.S. population per year, an increase

Table 1 Baseline characteristics of the patients with EV hospitalizations

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Overall	P value
Number of obs. (n)	19,167	20,328	20,929	20,097	20,331	21,040	23,896	31,288	32,831	37,368	45,578	29,2851	<0.0010
Hemorrhage (%)													
Yes	36.7	35.6	32.7	33.4	34.0	30.8	26.5	22.2	20.5	20.2	16.2	26.0	<0.0010
No	63.3	64.4	67.3	66.6	66.0	69.2	73.5	77.8	79.5	79.8	83.8	74.0	–
Age in years (%)													
18–34	3.9	4.5	3.8	3.9	4.3	3.8	3.4	3.0	3.0	3.7	4.1	3.7	<0.0010
35–49	25.5	25.8	23.8	23.2	23.0	22.0	20.6	19.7	19.0	19.9	17.4	21.1	<0.0010
50–64	31.4	32.8	35.3	35.7	36.9	39.6	41.2	43.1	43.8	45.6	46.7	40.7	<0.0010
65–79	26.9	26.0	25.5	25.7	24.6	24.4	24.3	24.0	24.6	21.8	24.0	24.4	<0.0010
≥80	11.4	9.7	10.6	10.2	9.6	9.3	9.4	9.1	9.0	7.7	7.1	9.1	<0.0010
Gender (%)													
Male	64.8	63.9	63.3	63.9	63.5	63.8	63.9	63.1	64.3	65.0	62.5	63.8	0.0247
Female	35.2	36.1	36.6	36.1	36.5	36.2	36.1	36.9	35.7	34.9	37.5	36.2	–
Race (%)													
White	50.6	47.1	49.7	47.4	49.6	47.1	47.5	54.2	55.6	59.3	59.7	53.0	<0.0010
Black	8.2	8.8	8.9	10.5	7.2	8.8	8.3	8.3	8.6	9.9	8.2	8.7	<0.0010
Hispanic	13.3	12.1	14.9	13.3	13.2	17.8	14.2	12.3	14.6	14.9	17.4	14.6	0.4222
Others	4.0	4.3	4.6	4.8	5.2	4.8	5.1	6.1	6.4	4.7	5.6	5.2	0.0112
Region (%)													
Northeast	19.0	17.2	18.1	16.7	16.3	18.4	17.0	17.7	18.3	18.1	15.5	17.4	<0.0010
Midwest	22.1	25.2	21.1	24.8	21.2	20.2	22.2	23.5	23.6	22.5	22.5	22.7	0.2595
South	40.0	36.7	39.1	37.8	40.4	39.0	37.7	36.0	36.7	36.7	36.1	37.5	<0.0010
West	18.9	20.9	21.7	20.7	22.2	22.5	23.0	22.7	21.4	22.7	25.9	22.5	<0.0010
Location (%)													
Rural	15.7	15.6	16.5	14.1	14.5	13.4	13.2	11.1	9.5	11.1	10.1	12.5	<0.0010
Urban nonteaching	42.5	45.1	42.3	45.7	45.1	39.4	40.5	41.1	40.5	37.1	39.1	41.1	<0.0010
Urban teaching	41.8	39.4	41.2	40.2	40.3	47.1	46.2	47.7	47.5	50.9	49.6	45.8	<0.0010
Median household income (%)													
Quartile 1	7.8	6.2	31.8	33.2	31.0	34.1	33.7	30.3	30.9	32.2	30.9	28.5	<0.0010
Quartile 2	26.8	22.2	26.5	27.1	25.8	25.2	25.5	27.8	26.6	25.4	24.9	25.8	0.2449

Table 1 (*continued*)

Table 1 (*continued*)

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Overall	P value
Quartile 3	27.0	27.4	21.9	19.6	23.7	20.6	20.7	21.7	21.8	21.9	24.4	22.7	<0.0010
Quartile 4	36.6	41.2	16.5	17.2	16.7	17.1	16.2	17.6	16.9	17.3	17.3	20.0	<0.0010
Payment (%)													
Medicare	42.8	41.7	42.9	42.4	41.9	41.1	43.4	41.7	42.8	40.3	42.6	42.1	0.0220
Medicaid	14.7	17.2	17.0	17.4	16.7	16.4	16.3	16.4	17.4	19.8	18.7	17.4	<0.0010
Private insurance	28.5	27.6	25.5	25.4	27.6	26.4	25.3	28.5	25.6	25.0	25.6	26.3	<0.0010
Others (includes self-pay)	13.8	13.4	14.4	14.5	13.7	16.0	14.9	13.2	14.1	14.7	12.8	14.0	0.0052
Admission day (%)													
Weekday	78.2	77.6	78.4	77.3	77.3	77.5	77.5	78.1	77.9	76.6	76.7	77.5	<0.0010
Weekend	21.8	22.4	21.6	22.7	22.7	22.5	22.5	21.9	22.1	23.4	23.3	22.5	–
In-hospital mortality (%)	5.0	5.3	4.8	4.6	4.2	4.3	4.6	5.6	5.8	4.8	5.1	5.0	0.0003
Median LOS (days)	5.8	5.7	5.8	5.5	5.7	5.7	5.8	6.3	6.3	6.1	6.2	4.0 (3.0–7.0)	<0.0010
AHRQ comorbidity measures (%)													
Obesity	0	2.8	2.4	3.1	3.1	3.1	4.6	6.0	6.8	7.1	9.9	5.3	<0.0010
Hypertension	0	24.5	28.9	33.3	32.8	36.0	38.4	40.2	42.2	43.4	45.3	35.7	<0.0010
Diabetes mellitus	0	23.9	26.3	26.8	27.8	29.0	30.3	30.7	31.3	30.9	33.5	27.8	<0.0010
Congestive heart failure	0	7.0	7.3	7.8	7.4	8.0	8.7	8.2	8.8	8.3	8.5	7.6	<0.0010
Chronic pulmonary disease	0	11.1	11.2	12.9	12.5	13.2	14.2	13.6	14.2	14.4	16.4	12.9	<0.0010
Peripheral vascular disease	0	1.8	2.0	2.3	2.5	2.4	3.1	3.4	3.5	3.5	5.2	3.0	<0.0010
Renal failure	0	22.8	22.8	26.9	29.0	32.8	34.1	38.9	42.4	43.0	46.4	33.8	<0.0010
Neurological disorders	0	6.3	4.6	5.4	5.5	5.5	7.0	7.1	6.6	7.3	7.7	6.1	<0.0010
Anemia	0	33.3	34.1	38.1	37.7	41.5	44.2	45.0	48.1	51.0	55.1	41.8	<0.0010
Solid tumor without metastasis	0	5.2	1.9	2.6	2.7	3.3	2.8	3.4	3.7	4.1	4.6	3.3	<0.0010
Weight loss	0	3.2	2.9	3.6	3.9	4.4	4.9	7.6	8.5	9.0	11.6	6.4	<0.0010
Rheumatic disorders	0	1.3	1.4	1.5	1.6	1.7	2.0	2.1	2.2	2.2	2.8	1.9	<0.0010
Psychiatric disorders	0	9.3	10.1	11.1	11.9	13.5	14.7	16.9	17.0	19.7	21.4	14.7	<0.0010
Liver disease	0	68.8	70.8	73.4	73.1	72.6	74.9	75.8	75.9	75.1	76.1	69.3	<0.0010

Variables are AHRQ comorbidity measures; neurological disorders include hemiplegia, paralysis, and others; psychiatric disorders include depression, psychosis, and others; rheumatic disorders include rheumatoid arthritis and other collagen vascular disorders. Of note, data related to comorbidity measures were available only from 2002 to 2010. EV, esophageal varices; AHRQ, Agency for Healthcare Research and Quality; LOS, length of stay.

Table 2 EV hospitalization/1 million U.S. population

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Average	Percent change
Overall (n)	515	538	548	520	519	533	604	784	833	958	1,181	685	129.2
Hemorrhage (n)													
Yes	189	191	179	174	177	164	160	174	171	193	191	179	1.2
No	326	346	369	346	343	369	444	611	662	765	990	506	203.4
Age in years (n)													
18–34	20	24	21	20	22	20	21	23	25	36	49	26	142.7
35–49	131	139	130	120	119	117	125	155	158	191	206	145	56.6
50–64	162	176	193	185	192	211	249	338	365	436	552	278	240.8
65–79	139	140	139	134	128	130	147	188	205	208	283	167	104.2
≥80	59	52	58	53	50	50	57	71	75	74	84	62	42.8
Gender (n)													
Male	334	344	347	332	329	340	386	495	535	623	738	437	121.0
Female	181	194	201	188	189	193	218	289	297	335	443	248	144.1
Race (n)													
White	261	253	272	246	258	251	287	425	463	568	705	363	170.0
Black	42	47	48	54	37	47	50	65	72	95	97	60	130.4
Hispanic	68	65	82	69	69	95	86	97	122	143	206	100	200.8
Others	2	2	2	2	2	2	2	2	3	4	5	3	189.8
Region (n)													
Northeast	98	92	99	87	85	98	103	139	153	174	183	119	87.0
Midwest	114	135	116	129	110	107	134	185	197	215	266	155	132.9
South	21	20	21	20	21	21	23	28	31	35	43	26	107.0
West	98	112	119	108	115	120	139	178	178	217	306	154	213.8
Location (n)													
Rural	81	84	90	73	75	71	80	87	79	106	119	86	47.5
Urban nonteaching	219	242	231	238	234	210	245	322	337	355	462	281	110.6
Urban teaching	216	212	225	209	209	251	279	374	395	487	585	313	171.5
Median household income (n)													
Quartile 1	40	33	174	172	161	182	204	238	257	308	365	194	811.1
Quartile 2	138	119	145	141	134	135	154	218	221	244	293	177	112.2
Quartile 3	139	147	120	102	123	110	125	170	181	210	288	156	106.9
Quartile 4	189	222	90	89	87	91	98	138	140	166	204	138	7.9
Payment (n)													
Medicare	220	224	235	220	217	219	262	327	356	386	503	288	128.0
Medicaid	76	92	93	90	87	88	99	129	145	190	221	119	191.9
Private insurance	147	148	140	132	143	141	153	224	213	239	303	180	106.0
Others (includes self-pay)	71	72	79	75	71	85	90	104	117	141	151	96	112.9

EV, esophageal varices.

of 1.2%. The number of hospitalizations for EV with hemorrhage increased only 7% over the decade, from 7,036 hospitalizations in 2001 to 7,451 hospitalizations in 2011.

The hospitalization rate increased across all age groups. The magnitude of rise in EV-related hospitalizations was highest in the 50–64 age group (relative increase 240.8%, P<0.001) and lowest in >80 years age group (relative increase 42.8%, P<0.001) (*Table 2*).

The EV hospitalization rate was higher in white males than other racial groups throughout the study. The EV hospitalization rate for whites was 261 per million U.S. population in 2001, increasing to 705 per million U.S. population in 2011, a 170% increase. Hispanics saw a greater surge in EV hospitalizations, with an EV hospitalization rate of 68 per million U.S. population in 2001, increasing to 206 per million U.S. population in 2011, a 201% increase (P<0.001).

The EV hospitalization rate for men and women were 334 and 181, respectively, per million U.S. population in 2001. The hospitalization rates increased to 738 and 443, respectively, per million U.S. population in 2011. This amounted to a 121% increase for men and a 144% increase for women (P<0.001).

All-cause in-hospital mortality

The mortality rate for patients hospitalized for EV without hemorrhage increased from 2.6% to 4.3% between 2001 and 2011 (P<0.001). Not unexpectedly, the mortality rate for patients hospitalized for EV with hemorrhage was higher. However, magnitude of the rise was not as dramatic, going from a mortality rate of 9.2% in 2001 to 9.6% in 2011 (P<0.001) (*Table 3*).

Across the age groups, the mortality rate was highest in >80 years age group at 5.5%. The mortality rate was slightly higher in males (5.3%), non-whites and other races (5.9%), and patients with Medicaid insurance (5.6%) (*Table 3*).

Length of stay and regional differences in cost of care

The median LOS was 4 days with an interquartile range of 2–7 days (P=0.0002) (*Figure 3*). After adjustment for inflation, the mean cost of hospitalizations with an EV diagnosis increased from $11,274 in 2001 to $15,160 in 2011 (P<0.001) (*Figure 4*). The mean cost of hospitalization was $12,322 for EV without hemorrhage, compared to $15,202 for EV and hemorrhage (P<0.001) (see *Table 4*). We estimate the annual national cost of managing patients with an EV diagnosis to have been $216 million in 2001 and $690 million in 2011. The mean cost of care was lowest if EV-related hospitalization was in the Northeast ($4,628) and rural hospitals ($3,337). It was highest in the South ($9,983) and urban teaching hospitals ($12,179) (*Table 4*).

Comorbidities associated with EV-related hospitalizations

As per AHRQ comorbidity measures, EV-related hospitalizations were most commonly associated with anemia (41.8%), followed by hypertension (35.6%) and renal disease (33.8%). Up to 15% of hospitalizations with EV were associated with psychiatric disorders (*Table 1*). Patients with EV and hemorrhage were found to have more comorbidities compared to patients with EV without hemorrhage (*Table 5*).

Discussion

Our study reports important findings associated with EV-related hospitalizations over an 11-year period in the U.S. There was a significant increase in the total number of EV-related hospitalizations over the study period. However, the increase in the number of cases of EV with hemorrhage was much lower than the increase in the number of cases of EV without hemorrhage. We postulate that this may be due to improved surveillance of patients at risk for having EV. Current guidelines recommend the performance of esophagogastroduodenoscopy every 2–3 years in patients without a prior history of EV and every 1–2 years in patients with small varices (18). It is possible that the implementation of these recommendations in practice is leading to: (I) increased diagnosis of patients with EV; (II) increased use of prophylactic strategies to prevent bleeding, like beta blocker therapy and endoscopic variceal ligation. It is also possible that hospitals are employing more thorough coding techniques as they review charts for billing purposes.

Hospitalizations for patients with EV with hemorrhage were associated with more comorbidities and higher costs that hospitalizations for patients with EV without hemorrhage. Not surprisingly, EV hospitalizations with hemorrhage had a higher mortality rate than those without hemorrhage. Interestingly, the overall mortality rate of 8.7% for the study period was much lower than the approximate 20% mortality rate that is typically quoted in discussions of variceal bleed management (19-21). This potentially reflects inaccuracies in the overall coding system.

Surprisingly, our data showed rising rates of mortality

Table 3 In-hospital mortality for EV hospitalization

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Overall (average)	Percent change	P value for trends
Overall (%)	5.0	5.3	4.8	4.6	4.2	4.3	4.6	5.6	5.8	4.8	5.1	4.9	1.8	<0.0010
Hemorrhage (%)														
Yes	9.2	9.7	7.9	7.9	7.9	8.7	7.9	8.7	10.9	7.8	9.6	8.7	4.7	0.0003
No	2.6	2.9	3.3	3.0	2.3	2.4	3.4	4.7	4.5	4.1	4.3	3.4	62.8	
Age in years (%)														
18–34	2.7	5.1	3.0	2.2	2.5	4.9	1.8	5.3	3.0	3.1	2.9	3.3	10.5	0.0400
35–49	4.9	4.8	3.6	4.6	3.5	3.9	4.1	4.6	5.2	3.0	5.1	4.3	5.2	0.0400
50–64	5.1	5.2	4.8	4.4	5.5	4.8	4.0	5.8	5.6	5.3	5.3	5.1	2.5	0.1800
65–79	5.4	6.0	5.9	4.9	3.8	3.8	6.2	5.8	6.5	5.5	5.3	5.4	–1.1	0.0090
≥80	5.1	4.6	6.0	6.2	3.4	4.7	5.6	7.0	7.5	5.7	5.2	5.5	2.0	0.0600
Gender (%)														
Male	5.3	6.1	5.6	4.9	4.5	4.4	4.7	6.3	5.9	5.2	5.4	5.3	2.3	0.2300
Female	4.5	3.9	3.4	4.1	3.7	4.2	4.5	4.4	5.6	4.2	4.6	4.3	1.8	
Race (%)														
White	5.4	5.4	4.8	4.8	4.2	3.7	3.9	5.4	5.6	4.6	4.9	4.8	–7.9	0.0020
Black	4.5	5.3	4.7	5.4	4.2	5.3	6.7	6.3	5.0	5.6	6.0	5.4	33.1	<0.0010
Hispanic	4.3	5.0	5.2	4.6	3.9	5.0	5.4	4.9	6.5	5.3	5.6	5.1	29.4	0.0200
Others	8.3	5.9	7.4	6.3	5.5	7.2	2.3	6.6	6.1	4.0	5.0	5.9	–40.1	0.0004
Region (%)														
Northeast	5.5	4.9	6.8	7.4	5.5	5.8	5.6	6.0	4.9	3.9	4.4	5.5	–19.2	0.0010
Midwest	3.1	5.3	4.0	4.2	3.8	3.3	5.3	5.2	4.8	3.6	5.9	4.4	87.2	0.4400
South	5.0	5.0	4.5	3.6	3.9	3.9	4.3	5.4	6.5	5.4	4.5	4.7	–9.8	0.1000
West	6.9	6.1	4.5	4.9	4.3	4.8	3.7	6.0	6.6	5.9	5.8	5.4	–16.3	0.0200
Location (%)														
Rural	4.0	4.0	4.3	3.0	3.0	2.9	3.6	2.6	5.5	3.3	3.1	3.6	–23.3	0.2700
Urban nonteaching	4.8	5.2	4.0	4.0	3.8	3.8	4.4	4.9	5.4	4.8	4.8	4.5	–1.2	0.1500
Urban teaching	5.6	5.9	5.8	5.9	5.1	5.2	5.1	6.9	6.1	5.2	5.8	5.7	3.6	0.1800
Median household income (%)														
Quartile 1	4.8	5.7	5.1	5.3	4.2	4.0	5.4	5.2	6.4	5.7	5.3	5.2	11.6	0.2800
Quartile 2	4.9	4.7	4.0	4.0	4.5	4.4	4.4	5.8	5.0	3.5	4.8	4.6	–1.8	0.2900
Quartile 3	4.9	5.1	4.5	4.6	4.3	4.2	4.4	5.1	5.7	4.9	5.4	4.8	9.1	0.3800
Quartile 4	5.0	5.7	5.6	4.9	3.7	4.5	3.9	6.5	6.3	4.8	4.7	5.0	–5.2	0.4000
Payment (%)														
Medicare	5.3	5.5	5.4	5.1	3.9	3.8	5.1	5.8	5.7	5.2	5.3	5.1	–0.8	0.0400
Medicaid	4.9	7.5	4.8	4.3	4.9	6.5	4.9	5.7	7.2	5.7	5.4	5.6	9.6	0.0020
Private insurance	4.7	3.5	4.7	4.4	4.9	4.0	4.3	5.5	5.5	3.9	4.7	4.5	–0.2	0.8700
Others (includes self-pay)	4.8	5.6	3.2	4.0	2.9	3.9	3.6	4.9	4.9	4.3	4.9	4.3	1.9	0.1700

EV, esophageal varices.

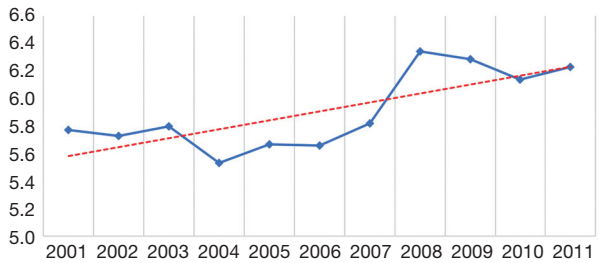

Figure 3 Trends in median LOS and in-hospital mortality. LOS, length of stay.

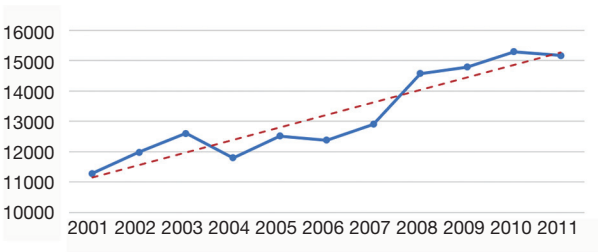

Figure 4 Trends in cost of care for EV hospitalizations. EV, esophageal varices.

for patients with EV without and with hemorrhage between 2001 and 2011. This finding could reflect changes in diagnostic coding. Alternatively, it could reflect the fact that hospitals are caring for older cirrhotic patients with more comorbidities.

Most of the hospitalizations in our study were identified in the 50–64 years age group; the fewest were in the 18–34 years age group. This finding correlates with what is felt to be an aging U.S. population of patients with cirrhosis. It may be attributed to the development of NAFLD in an older population of individuals with obesity and diabetes, and due to the aging of persons who were originally infected with hepatitis C in the 1970s and 1980s.

The number of hospitalizations for cirrhosis is steadily increasing in the U.S. One study recorded 337,956 cirrhosis hospitalizations in 2002, as compared to 570,220 cirrhosis hospitalizations in 2012 (22). However, the data is conflicting regarding trends in hospitalizations for esophageal variceal bleeding (EVB). Jamal *et al.* reported a decline in EVB hospitalizations from 1988 to 2002 (17). This does not correlate with data that we analyzed. This is likely because of better implementation of variceal screening during our study period. Pant *et al.* also reported a decrease in the incidence of EVB, for the period from 2002 until

Table 4 Cost of care for EV hospitalizations

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Average	Percent change	P value
Number of obs. (n)	19,167	20,328	20,929	20,097	20,331	21,040	23,896	31,288	32,831	37,368	45,578	26,623	–	–
Average cost ($)	11,274	11,980	12,599	11,793	12,511	12,373	12,899	14,570	14,781	15,289	15,160	13,203	34.5	<0.0010
Hemorrhage ($)														
Yes	13,260	14,882	14,434	14,247	14,668	15,473	15,654	15,912	15,476	16,510	16,708	15,202	26.0	<0.0010
No	9,982	10,447	11,750	10,588	11,377	10,949	11,876	14,191	14,802	14,873	14,716	12,323	47.4	<0.0010
Total cost per year ($)	216,077,619	243,527,832	263,693,144	237,002,363	254,359,374	260,328,699	308,216,365	455,858,118	485,273,942	571,333,569	690,970,395	362,421,947		
Age in years ($)														
18–34	745	920	789	775	874	806	822	934	969	1,397	1,875	991	151.9	<0.0010
35–49	4,888	5,254	4,970	4,653	4,680	4,618	4,925	6,165	6,247	7,432	7,942	5,616	62.5	<0.0010
50–64	6,024	6,662	7,386	7,166	7,509	8,333	9,837	13,493	14,375	17,026	21,301	10,828	253.6	<0.0010
65–79	5,156	5,290	5,327	5,174	4,999	5,128	5,814	7,496	8,074	8,132	10,927	6,502	111.9	<0.0010
≥80	2,193	1,972	2,219	2,053	1,951	1,961	2,254	2,850	2,946	2,889	3,250	2,413	48.2	<0.0010

Table 4 (*continued*)

Table 4 (*continued*)

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Average	Percent change (%)	P value
Gender ($)														
Male	12,419	12,991	13,255	12,834	12,900	13,418	15,278	19,755	21,096	24,305	28,486	16,976	129.4	0.0247
Female	6,748	7,337	7,668	7,263	7,417	7,622	8,613	11,533	11,725	13,057	17,091	9,643	153.3	Ref
Race ($)														
White	9,704	9,573	10,404	9,522	10,093	9,913	11,351	16,957	18,265	22,145	27,188	14,101	180.2	<0.0010
Black	1,564	1,783	1,852	2,101	1,454	1,845	1,990	2,582	2,836	3,713	3,739	2,314	139.1	<0.0010
Hispanic	2,544	2,463	3,116	2,666	2,683	3,741	3,391	3,860	4,801	5,566	7,941	3,888	212.1	0.4222
Others	774	882	961	963	1062	1,013	1,220	1,899	2,085	1,761	2,546	1,379	228.8	0.0112
Region ($)														
Northeast	3,635	3,495	3,794	3,345	3,314	3,866	4,059	5,547	6,017	6,780	7,054	4,628	94.1	0.0300
Midwest	4,243	5,122	4,417	4,991	4,302	4,239	5,313	7,362	7,757	8,390	10,253	6,035	141.6	0.2595
South	7,660	7,463	8,186	7,593	8,206	8,205	9,019	11,272	12,033	13,721	16,457	9,983	114.8	<0.0010
West	3,628	4,248	4,532	4,167	4,508	4,730	5,505	7,108	7,024	8,477	11,813	5,976	225.6	<0.0010
Location ($)														
Rural	2,999	3,164	3,453	2,828	2,955	2,809	3,148	3,472	3,129	4,153	4,591	3,337	53.1	<0.0010
Urban nonteaching	8,151	9,165	8,842	9,188	9,178	8,278	9,687	12,855	13,298	13,867	17,816	10,939	118.6	<0.0010
Urban teaching	8,016	7,999	8,613	8,081	8,197	9,915	11,032	14,932	15,584	19,011	22,584	12,179	181.7	<0.0010
Median household income ($)														
Quartile 1	1,491	1,254	6,649	6,667	6,310	7,177	8,052	9,493	10,129	12,020	14,096	7,576	845.5	<0.0010
Quartile 2	5,142	4,506	5,551	5,449	5,237	5308	6,092	8,705	8,722	9,501	11,324	6,867	120.2	0.2449
Quartile 3	5,178	5,564	4,581	3,945	4,827	4,332	4,949	6,783	7,152	8,180	11,116	6,055	114.7	<0.0010
Quartile 4	7,022	8,378	3,448	3,447	3,394	3,594	3,881	5,508	5,540	6,462	7,862	5,322	12.0	<0.0010
Payment ($)														
Medicare	8,196	8,476	8,981	8,516	8,508	8,636	10,367	13,054	14,035	15,049	19,397	11,201	136.7	0.0220
Medicaid	2,818	3,497	3,559	3,497	3,396	3,457	3,901	5,126	5,699	7,406	8,538	4,627	203.0	<0.0010
Private insurance	5,462	5,602	5,344	5,104	5,613	5,552	6,033	8,915	8,406	9,325	11,675	7,003	113.7	<0.0010
Others (includes self-pay)	2,638	2,714	3,004	2,907	2,793	3,360	3,553	4,143	4,633	5,481	5,828	3,732	120.9	0.0052

EV, esophageal varices; Ref, referent.

Table 5 Predictors of bleeding for EV hospitalizations

Variables	Odds ratio	95% confidence limits		P value
Age in years (%)				
18–34	*Referent*			
35–49	1.08	0.97	1.21	0.170
50–64	0.94	0.85	1.05	0.290
65–79	0.82	0.73	0.92	<0.001
≥80	0.81	0.71	0.93	<0.001
Race (%)				
White	*Referent*			
Black	1.13	1.05	1.21	<0.001
Hispanic	1.24	1.14	1.36	<0.001
Others	1.21	1.08	1.35	<0.001
Region (%)				
Northeast	*Referent*			
Midwest	1.05	0.98	1.14	0.180
South	1.33	1.25	1.41	<0.001
West	1.23	1.15	1.31	<0.001
AHRQ comorbidity measures (%)				
AIDS	1.44	1.16	1.77	<0.001
Alcohol abuse	1.27	1.21	1.33	<0.001
Deficiency anemias	0.76	0.72	0.81	<0.001
Rheumatic disorders	1.17	1.01	1.35	0.040
Chronic blood loss anemia	2.20	2.07	2.35	<0.001
Coagulopathy	1.13	1.07	1.18	<0.001
Depression	0.66	0.61	0.72	<0.001
Diabetes mellitus	1.16	1.10	1.22	<0.001
Hypertension	0.87	0.83	0.91	<0.001
Lymphoma	1.26	1.01	1.58	0.040
Fluid and electrolyte disorders	0.95	0.90	1.00	0.030
Metastatic cancer	1.73	1.53	1.94	<0.001
Obesity	0.77	0.70	0.85	<0.001
Peripheral vascular disorders	0.76	0.66	0.87	<0.001
Psychiatric disorder	0.77	0.68	0.86	<0.001
Pulmonary circulation disorders	0.64	0.54	0.76	<0.001
Renal failure	0.80	0.74	0.87	<0.001
Weight loss	0.80	0.73	0.88	<0.001

EV, esophageal varices; AHRQ, Agency for Healthcare Research and Quality; AIDS, acquired immune deficiency syndrome.

2012 (22). However, their study included only cirrhotic patients with EVB. They did not include hospitalizations of EVB secondary to other causes like portal vein thrombosis and splenic vein thrombosis. Our study reports a 138% increase in the number of discharges for EV between 2001 and 2011. There was a 221% increase in the diagnosis of EV without hemorrhage and a 7% increase in the diagnosis of EV with hemorrhage.

There was a significant increase in both the length of stay and cost of care over the study period. This finding is likely due to an aging population and the multiple comorbidities experienced by older patients (23).

Analysis of the NIS database permitted us to study a large population. Such an analysis should decrease the inherent bias seen in studies that are confined to a single region or hospital. However, our analysis had a number of significant limitations. Administrative databases are susceptible to errors that arise from coding inaccuracies. The EV diagnosis and the presence of comorbidities were based on the presence of administrative codes. ICD-9-CM codes 456.0 and 456.1 were validated for EV (with and without hemorrhage, respectively) in the administrative database. The database did not permit us to determine which patients assigned a code of "EV with hemorrhage" were hospitalized for the new onset of variceal bleeding, as opposed to patients who had a diagnosis of variceal bleeding in the past.

There is a risk that our analysis could underestimate the number of variceal bleeds each year. If an EV diagnosis accompanied other "serious" conditions—e.g., "cirrhosis" —the latter might be listed as a primary diagnosis, even if a patient's presenting complaint was actually acute variceal bleeding.

Our analysis could also overestimate the number of patients with EV. Indeed, the NIS considers each hospitalization as separate entry. Thus, there is no coding method that can separate index cases from readmissions in the NIS database.

An increase in the readmission rate for patients with decompensated cirrhosis has been reported (24). Such an analysis is beyond the scope of the current study. It is possible that the increase in the incidence of nonbleeding varices that we observed corresponds with an increase in the number of readmissions for patients with decompensated cirrhosis (24).

Unfortunately, the design of the database allowed us to examine in-hospital characteristics only. It did not permit analysis of long-term follow-up of patient outcomes. It did not permit us to study health care utilization in out-patient settings or emergency departments.

In conclusion, our review of hospitalization trends over the last decade found a consistent increase in the number of hospitalizations associated with EV. There was also an increase in the length of stay and cost of care. The most striking finding was the relatively small increase in the number of cases of EV with hemorrhage compared to the number of cases of EV without hemorrhage. We believe that improved out-patient care and implementation of variceal screening and prophylaxis measures will help to reduce the number of hospitalizations for variceal bleeding nation-wide. This will further reduce the economic burden of cirrhosis upon the health care system.

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None.

Footnote

Conflicts of Interest: Presented at Digestive Disease Week. McCormick Place, Chicago, IL, USA. May 2017.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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