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Contents

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Contents

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ORIGINAL ARTICLE

Retrospective Cohort Study

Mortality and health care burden of Budd Chiari syndrome in the United States: A nationwide analysis (1998-2017)

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Institutional review board statement: Since the data used for this this study were de-identified, IRB approval was not required as per local hospital IRB requirements.

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Abstract

BACKGROUND

The Budd Chiari syndrome (BCS) is a rare and potentially fatal disease, but there is a paucity of data on the in- hospital mortality as well its economic burden on the health care system.

AIM

To evaluate trends in mortality, length of hospital stays and resource utilization among inpatients with BCS.

METHODS

Data on all adult patients with a diagnosis of BCS were extracted from the National Inpatient Sample (NIS) from 1998 to 2017. To make inferences regarding the national estimates for the total number of BCS discharges across the study period, sample weights were applied to each admission per recommendations from the NIS.

RESULTS

During the study period, there were 3591 (8.73%) in-patient deaths. The overall in-hospital mortality rates among BCS patients decreased from 18% in 1998 to 8% in 2017; the mortality decreased by 4.41% ($P < 0.0001$) every year. On multivariate analysis, older age, higher comorbidity score, acute liver failure, acute kidney injury, acute respiratory failure, hepatic encephalopathy, hepatorenal syndrome, inferior vena cava thrombosis, intestinal infarct, sepsis/septic shock and cancer were associated increased risk of mortality. The average of length of stay was 8.8 d and it consistently decreased by 2.04% (95%CI: -2.67%, -1.41%, $P < 0.001$) from 12.7 d in 1998 to 7.6 d in 2017.The average total charges after adjusted for Medical Care Consumers Price Index to 2017 dollars during the time period was $94440

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and the annual percentage change increased by 1.15% (95%CI: 0.35%, 1.96%, P = 0.005) from $95515 in 1998 to $103850 in 2017.

CONCLUSION
The in-hospital mortality rate for patients admitted with BCS in the United States has reduced between 1998 and 2017 and this may a reflection of better management of these patients.

Key Words: National Inpatient Sample; Budd Chiari syndrome; Mortality; Length of stay; Total charges

Core Tip: Using a large administrative database, we were able to analyze the mortality and socioeconomic impact of Budd Chiari syndrome hospitalizations in the United States over a 19-year period with a high degree of granularity. We were able to show that while the mortality rate and length of stay has declined significantly, total charges continue to show an upward trend.

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INTRODUCTION

The Budd Chiari syndrome (BCS) is a rare but potentially fatal disorder that results from partial or complete obstruction of the hepatic venous outflow in the absence of right heart failure. Unlike Asian countries, the incidence and prevalence of BCS in Western countries is thought to be lower, but there are no large epidemiological studies[1]. BCS is a heterogeneous disease with a protean clinical presentation ranging from asymptomatic or chronic forms to fulminant liver failure[2,3]. Prognosis of BCS is highly variable and studies from large academic centers have reported mortality rates ranging anywhere between 13%-36%[4-9]. These wide ranges of mortality are more likely related to small sample size, variability in follow up period and publication selection bias. Risk factors such as ascites, hepatic encephalopathy, coagulopathy, elevated creatinine or bilirubin are considered to be independent risk factors for mortality[4-8]. A stepwise management approach consisting of anticoagulation, endovascular venoplasty, transjugular intrahepatic portosytemic shunts (TIPS) and liver transplantation (LT) has been proposed for the management of BCS[3,9-12]. However, this approach may not be applicable to all patients because of varying severity of presentation, the extent of venous occlusion and other serious comorbidities.

There are multiple studies that had investigated the mortality and economic burden of decompensated liver cirrhosis in the United States, but there is a paucity of data regarding the mortality burden and health care utilization for patients with BCS. The primary objective of our study was to assess the trends in in-hospital mortality, length of stay (LOS) and resource utilization among inpatients with BCS using the National Inpatient Sample (NIS) database.

MATERIALS AND METHODS

Study design and data source

This was a retrospective study where data were extracted from the NIS from 1998 to 2017. The NIS is the largest publicly available all-payer inpatient administrative database developed by the Agency for Healthcare Research and Quality (AHRQ) for

the Health Care cost and Utilization Project (HCUP). It represents approximately 20% stratified sample of discharges from community hospitals, but excludes long term acute care hospitals and rehabilitation facilities and contains information of more than 7 million hospital discharges annually. The number of states participating in the NIS grew from 8 in 1988 to 48 in 2017. The database captures information about primary and secondary diagnoses during each hospital stay as well as information about procedures. NIS also contains other valuable information such as severity and comorbidity measures, hospital characteristics (size, region, bed size, teaching/non-teaching), payment source (Medicare/Medicaid/private), total charges and length of hospital stay. In 2012, NIS revised the sample design so as to represent a sample of discharges rather than a sample of hospitals. This new strategy is expected to make the estimates more precise by reducing the sampling error. Starting October 1, 2015 all hospitals in the United States adopted International Classification of Diseases (ICD) 10 codes for disease classification as well as for procedures. The calendar year for 2016 and 2017 which is included in this study uses ICD 10 CM/PCS codes.

Population

Data were extracted from the NIS to identify patients ≥ 18 years of age using all listed diagnosis (primary or secondary diagnosis) of BCS from 1998 to 2017. The diagnosis of BCS was captured using the codes 453.0 (ICD-9) and I82.0 (ICD-10).

Variables

We obtained information on patient demographics (age, sex, race) and hospital characteristics (region of the country, bed-size, teaching status), patient disposition and insurance status (Medicare, Medicaid and private insurance). Study outcome included changes in inpatient mortality, LOS and total charges with time. We investigated if important complications such as acute liver failure, acute kidney injury, cirrhosis, ascites, hepatic encephalopathy, esophageal varices, portal vein thrombosis, inferior vena cava (IVC) thrombosis and spontaneous bacterial peritonitis had an impact on outcome. We also analyzed inpatient procedures such as liver biopsy, upper gastrointestinal endoscopy, paracentesis, TIPS and LT using appropriate ICD codes (Supplementary Table 1 shows the list of ICD-9 and ICD-10 codes). Severity of illness was measured using the Elixhauser comorbidity index after excluding liver diseases and this included 29 major Elixhauser comorbidity conditions[13].

Statistical analyses

Descriptive statistics are used to summarize patients' characteristics, hospital characteristics and utilization, comorbidities, complications, procedures and the outcome by using the weighted survey methods. Data are presented as mean and standard error for continuous variables, percentage and standard error for categorical variables. Standard errors of percentage or mean were estimated using Taylor series linearization method. To make inferences regarding the national estimates for the total number of BCS discharges across the study period, sample weights were applied to each admission per recommendations from the NIS. For the years from 1993-2011, AHRQ had developed discharge trend weights, specifically the NIS Trend Weight Files. Therefore, in our study for trend analyses spanning 2012 and earlier, NIS data trend weights were used to make estimates comparable to the new 2012 NIS design. We used the trend weight in place of the original discharge weights to create national estimates for trend analysis to make the data similar for the entire study period. For 2012 or later data, no trend weights were necessary and the discharge weight supplied on the NIS files were used directly[14]. We calculated BCS discharges rate per 1000000 US populations by dividing the estimated total BCS discharges by projected US population from the Census Bureau.

The annual percentage change (APC) was derived to compare the patients' characteristics, hospitals' characteristics and outcomes over time by using Poisson regression for categorical variables and linear regression with natural logarithm transformation for continuous variables. *P* value for APC was used to determine if the trends in the annual percentage change was significantly different from zero, the change was considered as statistically significant with *P* value of 0.05 or less.

The hierarchical generalized linear mixed model with hospitals as random effects was performed to evaluate the effects of potential associations between outcomes (mortality, length of stay and total charges) and patients' demographics (age, gender, and race), patient-level hospitalization variables (primary payer, disposition of patient), hospital-level variables (hospital region, bed size, location and teaching status), comorbidities, complications and procedures separately. Since race was not

available in some states, a dummy variable was created for missing data in the models to prevent the observation from being dropped. For mortality, binomial distribution and logit link was used. For length of stay, negative binomial distribution and log links were used. When analyzing the total charges, final total charges were adjusted to 2017 dollars based on medical care Consumer Price Index in US city average provided by the Bureau of Labor Statistics. We specified the models using gamma distributions and log links. A variable with *P* value of 0.05 or less was retained in the model and considered as statistically significantly associated with outcomes. All analyses were performed with SAS version 9.4 (SAS Institute, Cary, NC, United States)

RESULTS

Between 1998 and 2017, we identified a total of 8435 hospitalizations related to BCS. The mean age of the cohort was 50.5 years, 55% were women and 56 % were white. Nearly half (52%) the patients were covered by government funded health insurance (Medicare and Medicaid) (Table 1). A majority of the patients (59%) were discharged home, and an additional 13.5% were discharged with home health services. While the number of routine home discharges remained the same, there was a 3.31% increase in utilization of home health services ($P < 0.0001$) (Table 2).

Hospital mortality

Between 1998 and 2017, the in-hospital mortality was 8.74% ($n = 737$). Using the sample weights provided by HCUP, this corresponded to 3591 deaths (Table 2). Despite a significant increase in the comorbidity score during the time period, overall, in-hospital mortality rate among BCS patients decreased significantly by 4.41% per year ($P < 0.0001$) from 18% in 1998 to 8% in 2017, with the mortality rate being the lowest in 2015 (5%) (Figure 1A). There were no gender differences in mortality, but those who died were older than those were discharged from the hospital (mean age 58.7 years *vs* 49.7 years, $P < 0.001$). Of the patients who died, 53% were Caucasians, 13% were African Americans and 10% were Hispanics. Most deaths occurred in large hospitals (73%) or urban teaching hospitals (71%) (Supplementary Table 2). On multivariate analysis, older age, higher comorbidity score, acute liver failure, acute kidney injury (AKI), acute respiratory failure, hepatic encephalopathy, hepatorenal syndrome, intestinal infarct, IVC thrombosis, sepsis/septic shock and cancer were associated increased risk of mortality (Table 3).

Length of stay

The average of LOS was 8.8 days and it consistently decreased by 2% (95%CI: -2.67%, -1.41%, $P < 0.001$) per year from 12.7 d in 1998 to 7.6 d in 2017 (Figure 1B). The LOS in patients who died was longer compared to those who survived (13.54 d *vs* 8.38 d, $P < 0.0001$). On multivariate analysis primary payer, and hospital characteristics had impact on LOS. Important complications that had impact on LOS included AKI, acute liver failure, acute respiratory failure, ascites, spontaneous bacterial peritonitis, IVC thrombosis, comorbidity score and cancer (Table 4). Compared to the West, hospitals in the North East, Midwest and South had longer inpatient stays. LOS in urban teaching hospitals was significantly higher than urban non-teaching hospitals ($P < 0.0001$) (Supplementary Table 3).

Hospital costs

The average total charges after adjusted for Medical Care Consumers Price Index to 2017 dollars during the time period was $94440, and the APC increased by 1.15% (95%CI: 0.35%, 1.96%, $P = 0.005$) per year from $95515 in 1998 to $103850 in 2017 (Figure 1C). The hospital charge was higher in patients who died compared to those who survived ($190724 *vs* $85071, $P < 0.0001$). The charge was also higher in urban teaching hospitals than urban non-teaching hospitals ($P < 0.0001$). When stratified by different regions of the country, the charges were higher in the West compared to every other region in the country ($P < 0.001$, Supplementary Table 4). On multivariate analysis, race, hospital characteristics, number of procedures, length of stay, and comorbidity score were associated with total charges. Important complications that had an effect on total charges included AKI, acute respiratory failure, HRS, IVC thrombosis, cancer, and anemia due to acute blood loss (Table 5).

Table 1 Characteristics of patients and hospitals and individual effects on mortality, length of stay and total charges

Study time period	1998-2017	Individual effect (Type III test, *P* value)		
		Mortality	Length of stay	Total charges
BCS patients' characteristics				
Age	50.50 (0.19)	< 0.001	0.052	< 0.001
Female	55.19 (0.54)	0.003	0.001	< 0.001
Race		0.138	0.013	< 0.001
1: White	56.03 (0.54)			
2: Black	13.26 (0.37)			
3: Hispanic	9.56 (0.32)			
4: Asian/Pacific Islander	2.56 (0.17)			
6: Other	3.65 (0.2)			
9: Unknown	14.93 (0.39)			
Primary payer		< 0.001	0.002	< 0.001
1: Medicare	33.17 (0.52)			
2: Medicaid	18.42 (0.42)			
3: Private insurance	40.20 (0.54)			
6: Other	8.21 (0.3)			
Hospital characteristics				
Hospital size		0.014	< 0.001	< 0.001
1: Small	9.81 (0.32)			
2: Medium	18.92 (0.43)			
3: Large	71.27 (0.49)			
Hospital location and teaching status		0.195	< 0.001	< 0.001
1: Rural	6.89 (0.28)			
2: Urban nonteaching	24.24 (0.47)			
3: Urban teaching	68.87 (0.51)			
Hospital region		0.533	0.010	< 0.001
1: Northeast	21.84 (0.45)			
2: Midwest	22.15 (0.46)			
3: South	33.45 (0.52)			
4: West	22.57 (0.46)			
Clinical characteristics				
Ascites	29.93 (0.5)	< 0.001	< 0.001	< 0.001
Acute kidney injury	18.84 (0.43)	< 0.001	< 0.001	< 0.001
Hepatic cirrhosis with no mention of alcohol	18.65 (0.43)	0.901	0.031	0.838
Cancer	17.26 (0.41)	< 0.001	0.002	0.010
Portal hypertension	16.57 (0.41)	0.029	0.898	0.000
Hepatic encephalopathy	9.59 (0.32)	< 0.001	< 0.001	< 0.001
Portal vein thrombosis	7.92 (0.3)	0.006	0.372	0.073
Esophageal varices without bleeding	7.44 (0.29)	0.002	0.324	0.091
Acute respiratory Failure	7.03 (0.28)	< 0.001	< 0.001	< 0.001
HCC	6.93 (0.28)	< 0.001	< 0.001	0.543

Acute blood loss anemia/hemorrhagic	6.62 (0.27)	0.008	< 0.001	< 0.001
IVC thrombosis	6.39 (0.27)	< 0.001	< 0.001	< 0.001
Sepsis	6.10 (0.26)	< 0.001	< 0.001	< 0.001
Alcoholic cirrhosis	5.73 (0.25)	0.113	0.731	0.140
Acute liver failure	5.60 (0.25)	< 0.001	< 0.001	< 0.001
Hepatorenal syndrome	3.29 (0.2)	< 0.001	< 0.001	< 0.001
Variceal bleeding	3.20 (0.19)	0.107	0.160	0.001
Spontaneous bacterial peritonitis	2.83 (0.18)	< 0.001	< 0.001	< 0.001
Intestinal infarct/acute vascular insufficiency	2.11 (0.16)	< 0.001	< 0.001	< 0.001
Elixhauser Comoridity Score excluding liver disease	9.38 (0.12)	< 0.001	< 0.001	< 0.001

All data are presented as percentage (SE) for categorical variables and mean (SE) for continuous variables. BCS: Budd Chiari syndrome; HCC: Hepatocellular carcinoma IVC: Inferior vena cava.

Utilization of procedures

During their in-patient stay, patients underwent an average of 2.64 procedures per hospitalization. Paracentesis was the most frequent procedure (18.4%) followed by upper gastrointestinal endoscopy (10.9%), liver biopsy (6.2%), TIPS (3.6%) and LT (1.9%) (Table 2). Subgroup analysis showed that out of the 307 patients who underwent TIPS, 145 (47%) had LT.

While total number of procedures performed remained stable during the study period, there was a significant and notable reduction in the number of liver biopsies (APC: -4.01%, 95%CI: -5.42%, -2.58%, $P < 0.0001$), TIPS (APC: -4.95%, 95%CI: -6.78%, -3.09%, $P < 0.0001$) and LT (APC: -2.68%, 95%CI: -5.26%, -0.02%, $P = 0.05$). Hispanics underwent more procedures than Caucasians ($P < 0.001$) and Blacks ($P < 0.001$). Patients admitted to urban teaching hospitals underwent more procedures than urban non-teaching hospitals ($P < 0.0001$) and rural hospitals ($P < 0.0001$) (Supplementary Table 5).

DISCUSSION

In this large population-based study from the United States, we found that the overall in-patient mortality rate for an unselected group of patients with BCS was 8%. The mortality rates and LOS reduced significantly from 1998 to 2017, but total hospital charges, however, increased during the study period. The patients who survived hospitalization were younger than those who died (49.7 years *vs* 58.6 years), but race, hospital teaching status and hospital region did not impact survival. The reduction in mortality was multifactorial and possibly could be related to earlier detection of BCS, advances in therapeutic options and a better overall inpatient care.

To our knowledge, there are no prior studies that have exclusively analyzed inpatient mortality secondary to BCS, but multicenter studies in the recent era that investigated prognosis of BCS have reported improvement in survival rates with time [9,10]. A European study that consisted of 157 BCS patients, who were managed using a stepwise treatment algorithm over a median duration of 50 mo reported a mortality of 23%[9]. A majority of these patients succumbed to liver failure (33%) and the median time to death for the cohort was 10 mo. The study found that age, bilirubin and creatinine were independent risk factors for survival. Most patients (88.5%) in their study were on long term anticoagulation and those who did not respond to medical management were treated with percutaneous angioplasty/thrombolysis (n = 22), TIPS (n = 62) and LT (n = 20) in a step wise manner. Due to inherent limitations of the NIS dataset we were unable to determine how many patients in our study were on anticoagulation.

Overall, less than 5% of the patients underwent invasive procedures such as TIPS and LT. There were no significant differences in mortality between patients who underwent these procedures and those who did not. However, 89% of patients who underwent TIPS and 92% who had LT during their inpatient stay survived hospitalization. We also noticed a downward trend in the number of TIPS and LT in hospitalized BCS patients, perhaps because these procedures were done after patients were

Table 2 Trends in outcomes of interest

	1998-2017 (unweighted: 8435, weighted: 41119)	1998 (unweighted: 262, weighted: 1367)	2017 (unweighted: 680, weighted: 3400)	APC (95%CI)	*P* value for APC
Procedures					
Number of procedures	2.64 (0.03)	3.09 (0.20)	2.42 (0.13)	-0.51% (-1.09%, 0.06%)	0.082
Paracentesis	18.41 (0.42)	28.56 (2.82)	16.47 (1.42)	-1.67% (-2.53%, -0.81%)	0.000
Upper endoscopy	10.94 (0.34)	13.08 (2.06)	11.91 (1.24)	-0.17% (-1.31%, 0.97%)	0.766
Liver biopsy	6.24 (0.26)	10.35 (1.9)	5.15 (0.85)	-4.01% (-5.42%, -2.58%)	< 0.0001
Portosystemic shunt/TIPS	3.63 (0.2)	6.12 (1.54)	2.94 (0.65)	-4.95% (-6.78%, -3.09%)	< 0.0001
Liver transplantation	1.9 (0.15)	1.29 (0.75)	2.06 (0.54)	-2.68% (-5.26%, -0.02%)	0.048
Disposition of patient					
1: Discharged to home or selfcare	58.8(0.54)	50.71 (3.12)	55.96 (1.91)	-0.28% (-0.77%, 0.21%)	0.262
6: Home health care	13.49 (0.37)	12.04 (2.04)	17.23 (1.45)	3.31% (2.20%, 4.43%)	< 0.0001
5: Transfer: other type of facility	11.12 (0.34)	10.21 (1.89)	12.08 (1.25)	1.87% (0.70%, 3.06%)	0.002
20: Died in hospital	8.74 (0.31)	18.17 (2.44)	7.66 (1.02)	-4.31% (-5.50%, -3.10%)	< 0.0001
2: Transfer: short-term hospital	6.8 (0.28)	8.25 (1.71)	5.6 (0.88)	-1.26% (-2.66%, 0.17%)	0.084
7: Against medical advice	1 (0.11)	0.61 (0.43)	1.47 (0.46)	2.94% (-1.02%, 7.07%)	0.148
Outcomes					
Number of deaths	737 (Unweighted); 3591 (Weighted)	46 (Unweighted); 249 (Weighted)	52 (Unweighted); 260 (Weighted)		
Mortality rate per 1000000 United States populations		0.9	0.8	-0.29% (-0.86%, 0.27%)	0.309
Mortality rate per 1000000 inpatients		8.87	8.55	0.34% (-0.23%, 0.92%)	0.243
Mortality rate among BCS inpatients	0.09	0.18	0.08	-4.41% (-4.95%, -3.88%)	< 0.0001
Length of stay (d)	8.84 (0.13)	12.73 (1.01)	7.64 (0.36)	-2.04% (-2.67%, -1.41%)	< 0.0001
Average total charges in 2017 dollars	94440.04 (1996.06)	95515.01 (9483.24)	103850.98 (8183.79)	1.15% (0.35%, 1.96%)	0.005

All data are presented as percentage (SE) for categorical variables and mean (SE) for continuous variables. Annual percentage change (APC) > 0 means increasing, < 0 means decreasing. *P* value for APC measures if APC is significantly different from zero. *P* value ≤ 0.05 means the change is significant. BCS: Budd Chiari syndrome; APC: Annual percentage change.

discharged and hence was not captured by the NIS database. Nearly half (47%) the patients who had TIPS underwent LT, and it possible that TIPS was done in these patients as a bridge to LT, or perhaps they had more complications such as variceal bleeding or refractory ascites.

A management strategy that consists of a stepwise invasive treatment algorithm guided by response to prior treatment have resulted in better short- and long-term outcome in BCS patients[3,9-12,15]. This consists of early and prompt initiation of anticoagulation with low molecular weight heparin to prevent extension of thrombosis, referral to a hematologist for treatment of specific underlying clotting disorders and treatment of portal hypertension related complications. Patients who

Table 3 Multivariate model on mortality

	Response	Beta estimate	Standard error	*P* value for beta	Odds ratio (95%CI)
Age		0.024	0.003	< 0.0001	1.024 (1.019, 1.029)
Acute respiratory Failure	Yes (reference = No)	1.652	0.109	< 0.0001	5.219 (4.211, 6.468)
Intestinal infarct/acute vascular insufficiency	Yes (reference = No)	1.422	0.201	< 0.0001	4.143 (2.795, 6.142)
Acute liver failure	Yes (reference = No)	1.286	0.119	< 0.0001	3.617 (2.864, 4.567)
Hepatorenal syndrome	Yes (reference = No)	1.123	0.147	< 0.0001	3.072 (2.302, 4.101)
Cancer	Yes (reference = No)	0.882	0.098	< 0.0001	2.415 (1.993, 2.927)
Acute kidney injury	Yes (reference = No)	0.803	0.092	< 0.0001	2.232 (1.862, 2.675)
Sepsis/severe sepsis/septic shock	Yes (reference = No)	0.635	0.122	< 0.0001	1.886 (1.484, 2.398)
Hepatic encephalopathy	Yes (reference = No)	0.280	0.117	0.020	1.323 (1.052, 1.662)
Elixhauser Comorbidity Score excluding liver disease		0.026	0.004	< 0.0001	1.027 (1.019, 1.034)

deteriorate despite optimal medical management are considered for percutaneous or transhepatic angioplasty, TIPS and/or LT. The NIS data set did not include data on venoplasty or stenting perhaps because many of these procedures are done in the outpatient setting. Several studies have reported excellent outcome following LT in patients with BCS. In a previous study, using United Network of Organ Sharing (UNOS) datasets, we had reported 85% 3-year survival in patients with BCS who underwent LT in the United States[16]. Our group recently analyzed outcome of LT in 55 BCS patients who presented with fulminant hepatic failure using the UNOS database and found that expeditious LT in this subset of patients was associated with excellent long-term patient and graft survival. We also found that despite the presence of 3 or more organ failures, LT in these patients was associated with good outcome. They also achieved excellent post LT functional status as determined by the Karnofsky performance status scores[17]. A European series that investigated outcome of LT in 248 patients report actuarial survival of 76% at 1 year, 71% at 5 years and 68% at 10 years, with majority of the deaths occurring in the first 3 mo[18].

In our study we found that the average LOS was 9 d and this reduced consistently with an APC of 2% during the 19-year period. The reduction is consistent with nationwide efforts to reduce LOS for hospitalized patients. Multivariate analysis showed significant association between LOS and complications such as AKI, acute liver failure, acute respiratory failure, SBP and IVC thrombosis. The LOS was longer in medium and large sized hospitals compared to smaller hospitals probably because these hospitals were tertiary care centers and BCS patients admitted in those hospitals were perhaps more sicker requiring prolonged inpatient stay. This would also explain why urban hospitals had a longer LOS compared to hospitals in rural areas. Longer LOS in such hospitals was associated with higher total charges as expected. We also noticed a geographical variation in the LOS, as hospitals in the North East, Midwest and South had longer inpatient stays compared to the West. Although it is difficult to explain this particular finding, a similar observation was made by the HCUP report on US hospital LOS variation by region in 2016 and could be related to physician practice patterns, access to health care services, treatment preferences and cost of living that varies by geographic location in a diverse country like United States[19].

The average total costs for BCS hospitalizations between 1998 and 2017 was $94440 and this continued to show a significant upward trend. We found that compared to the West, hospitals in the Northeast, Midwest and South of United States had lower total charges. We do not have a good explanation for this finding. The increasing financial burden of BCS hospitalizations to the US health care system in our study, despite a reduction in the average LOS, is consistent with other studies that have analyzed the economic impact of hospitalizations related to decompensated cirrhosis and can be attributed to the increasing hospitalization rate as well as increasing severity of disease burden as indicated by comorbidity score[20,21].

Our study has a few limitations most of which are inherent to the use of a large administrative database. The use of ICD codes to capture the diagnosis of BCS could result in coding errors potentially resulting in misclassification. We could not perform a sensitivity analysis because of the absence of patient identifiers in the datasets. Another major shortcoming is that the NIS reports every hospitalization as a separate

Table 4 Multivariate model on length of stay

	Response	Beta estimate	Standard error	*P* value for Beta	*P* value for type 3 test
Primary payer	1: Medicare (reference)	0.000	-	-	0.022
	2: Medicaid	0.053	0.037	0.144	
	3: Private insurance	0.084	0.030	0.005	
Hospital bed size	1: Small (reference)	0.000	-	-	< 0.0001
	2: Medium	0.113	0.049	0.021	
	3: Large	0.293	0.042	<.0001	
Hospital location and teaching status	1: Rural (reference)	0.000	-	-	< 0.0001
	2: Urban nonteaching	0.206	0.054	<.0001	
	3: Urban teaching	0.433	0.050	<.0001	
Hospital region	1: Northeast	0.171	0.038	<.0001	< 0.0001
	2: Midwest	0.017	0.038	<.0001	
	3: South	0.055	0.034	<.0001	
	4: West (reference)	0.000			
Complications					
Acute liver failure	Yes (reference = No)	0.223	0.057	< 0.0001	< 0.0001
Acute respiratory Failure	Yes (reference = No)	0.380	0.052	< 0.0001	< 0.0001
Acute kidney injury	Yes (reference = No)	0.255	0.035	< 0.0001	< 0.0001
Ascites	Yes (reference = No)	0.118	0.028	< 0.0001	< 0.0001
Spontaneous bacterial peritonitis	Yes (reference = No)	0.480	0.076	< 0.0001	< 0.0001
IVC thrombosis	Yes (reference = No)	0.138	0.052	0.008	0.008
Intestinal infarct/acute vascular insufficiency	Yes (reference = No)	0.383	0.088	< 0.0001	< 0.0001
cancer	Yes (reference = No)	-0.278	0.036	< 0.0001	< 0.0001
Elixhauser Comorbidity Score excluding liver disease		0.019	0.001	< 0.0001	< 0.0001

IVC: Inferior vena cava.

encounter and not as a unique patient. It is possible that many of these patients were readmitted and were counted more than once. We were also unable to obtain information regarding therapeutic data with respect to anticoagulation and specific pharmacological agents used to treat underlying thrombophilia. Nonetheless, the NIS database is considered to be a powerful research tool providing robust clinical data about real world scenarios and its reliability has been extensively validated[22].

CONCLUSION

In conclusion, this is the first study from the United States to illustrate reducing mortality related to BCS hospitalizations as well as a reduction in the average LOS. While these findings are reassuring, BCS continues to have a significant economic impact as indicated by the rising healthcare costs.

Table 5 Multivariate model on total charges

	Response	Estimate	Standard error	*P* value for beta	*P* value for type 3 test
Race	1: White (reference)	0.000	-	-	< 0.0001
	2: Black	-0.037	0.026	0.162	
	3: Hispanic	0.015	0.031	0.613	
	4: Asian/Pacific Islander	0.136	0.058	0.019	
	6: Other	0.082	0.046	0.077	
	9: Unknown	-0.185	0.025	< 0.0001	
Hospital bed size	1: Small (reference)	0.000	-	-	< 0.0001
	2: Medium	0.080	0.034	0.018	
	3: Large	0.169	0.029	< 0.0001	
Hospital location and teaching status	1: Rural (reference)	0.000	-	-	< 0.0001
	2: Urban nonteaching	0.428	0.037	< 0.0001	
	3: Urban teaching	0.552	0.034	< 0.0001	
Hospital region	1: Northeast	-0.195	0.027	< 0.0001	< 0.0001
	2: Midwest	-0.333	0.027	< 0.0001	
	3: South	-0.330	0.024	< 0.0001	
	4: West (reference)	0.000	-	-	
Complications					
Acute liver failure	Yes (reference = No)	0.078	0.039	0.044	0.044
Acute respiratory Failure	Yes (reference = No)	0.204	0.036	< 0.0001	< 0.0001
Acute kidney injury	Yes (reference = No)	0.146	0.025	< 0.0001	< 0.0001
Hepatorenal syndrome	Yes (reference = No)	-0.132	0.050	0.008	0.009
IVC thrombosis	Yes (reference = No)	0.075	0.035	0.035	0.035
Acute blood loss anemia/ hemorrhagic	Yes (reference = No)	0.155	0.035	< 0.0001	< 0.0001
Cancer	Yes (reference = No)	-0.052	0.025	0.037	0.037
Elixhauser Comoridity Score excluding liver disease		0.005	0.001	< 0.0001	< 0.0001
Other variables					
Number of procedures		0.118	0.004	< 0.0001	< 0.0001
Length of stay		0.054	0.001	< 0.0001	< 0.0001

IVC: Inferior vena cava.

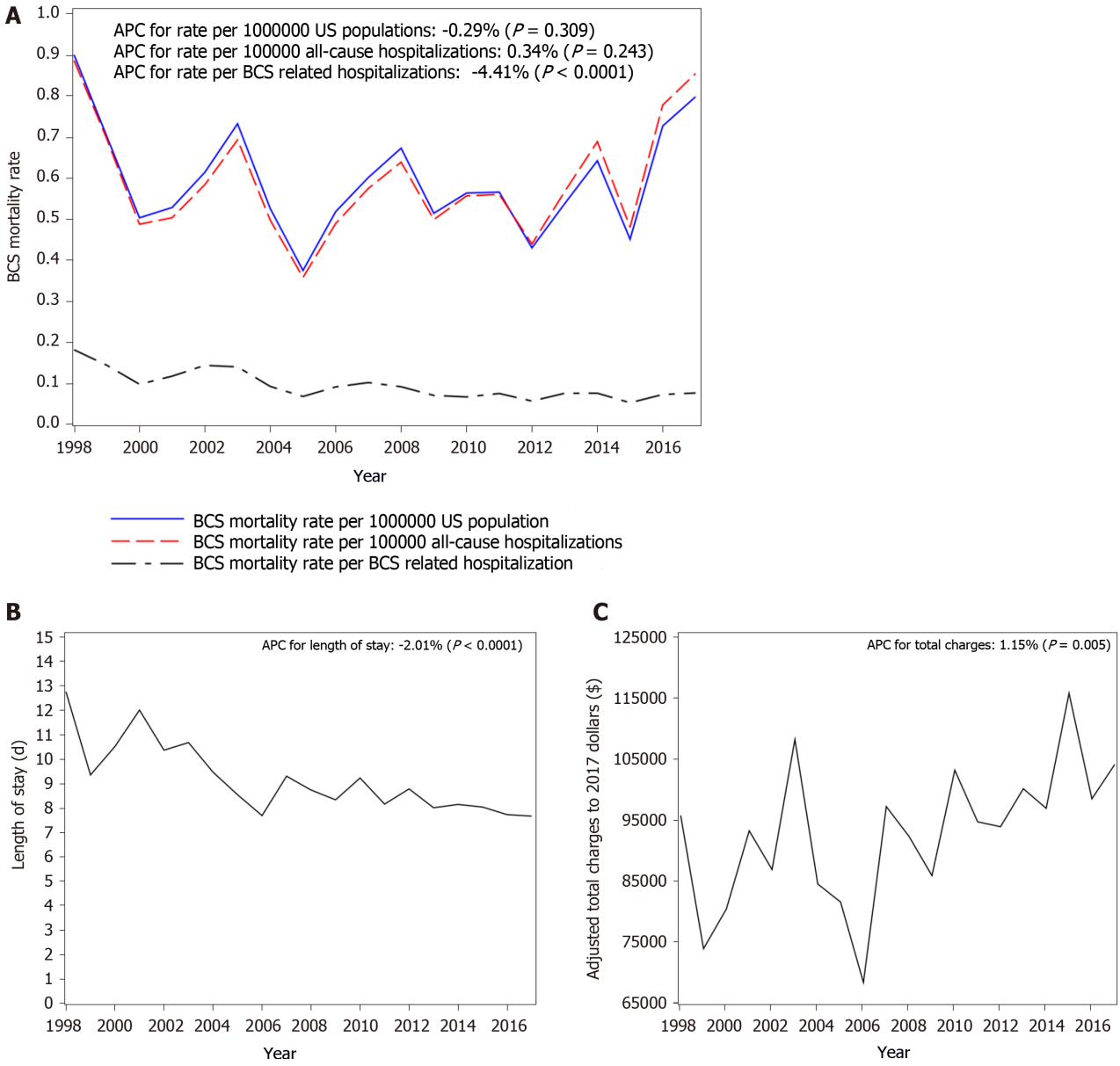

Figure 1 Annual percentage changes. A: Annual percentage change for mortality in patients with Budd Chiari syndrome (BCS) (per 1000000 United States population, per 100000 all cause hospitalizations and BCS related hospitalizations; B: Length of hospital stay for patients with BCS from 1998 to 2017; C: Adjusted (charges adjusted to 2017 dollars) hospital charges from 1998 to 2017 in patients with BCS. APC: Annual percentage change; BCS: Budd Chiari syndrome; US: United States.

ARTICLE HIGHLIGHTS

Research background

The Budd Chiari syndrome (BCS) is a rare disorder that results from partial or complete obstruction of the hepatic venous outflow in the absence of right heart failure.

Research motivation

There is a paucity of data on the in-hospital mortality of BCS as well its economic impact on the United States health care system.

Research objectives

This study aimed to evaluate trends in mortality, length of hospital stays and resource utilization among inpatients with BCS.

Research methods

Retrospective study where data were extracted from the National Inpatient Sample

(NIS) from 1998 to 2017. To make inferences regarding the national estimates for the total number of BCS discharges across the study period, sample weights were applied to each admission per recommendations from the NIS.

Research results

During the study period, there were 3591 (8.73%) in-patient deaths. The overall in-hospital mortality rate among BCS patients decreased from 18% in 1998 to 8% in 2017; the mortality decreased by 4.41% every year. The average of length of stay was 8.8 d and it consistently decreased by 2.04% from 12.7 d in 1998 to 7.6 d in 2017.The average total charges during the time period was $94440 and the annual percentage change increased by 1.15%

Research conclusions

The in-hospital mortality rate for patients admitted with BCS in the United States has reduced between 1998 and 2017 while total charges continued to increase.

Research perspectives

Using a large national database, we analyzed the mortality and socioeconomic impact of BCS hospitalizations in the United States with a high degree of granularity.

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