Observational Study

In-hospital mortality of hepatorenal syndrome in the United States: Nationwide inpatient sample

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Abstract

BACKGROUND
Hepatorenal syndrome (HRS) is a life-threatening condition among patients with advanced liver disease. Data trends specific to hospital mortality and hospital admission resource utilization for HRS remain limited.

AIM
To assess the temporal trend in mortality and identify the predictors for mortality among hospital admissions for HRS in the United States.

METHODS
We used the National Inpatient Sample database to identify an unweighted sample of 4938 hospital admissions for HRS from 2005 to 2014 (weighted sample of 23973 admissions). The primary outcomes were temporal trends in mortality as well as predictors for hospital mortality. We estimated odds ratios from multi-level mixed effect logistic regression to identify patient characteristics and treatments associated with hospital mortality.

RESULTS
Overall hospital mortality was 32%. Hospital mortality decreased from 44% in 2005 to 24% in 2014 ($P < 0.001$), while there was an increase in the rate of liver transplantation ($P = 0.02$), renal replacement therapy ($P < 0.001$), length of hospital stay ($P < 0.001$), and hospitalization cost ($P < 0.001$). On multivariable analysis, older age, alcohol use, coagulopathy, neurological disorder, and need for mechanical ventilation predicted higher hospital mortality, whereas liver transplantation, transjugular intrahepatic portosystemic shunt, and abdominal paracentesis were associated with lower hospital mortality.

CONCLUSION
Although there was an increase in resource utilizations, hospital mortality among patients admitted for HRS significantly improved. Several predictors for hospital mortality were identified.

Key Words: Hepatorenal syndrome; Liver transplantation; Mortality; Nationwide; Big data; Hospitalization; Outcomes; Predictors

Core Tip: In this study, we utilized the national inpatient sample database to assess the temporal trend in mortality and identify predictors for mortality among hospital admissions for hepatorenal syndrome in the United States. We demonstrated that the overall hospital mortality was 32%. Hospital mortality decreased from 44% in 2005 to 24% in 2014. There was an increase in the rate of liver transplantation, renal replacement therapy, length of hospital stay, and hospitalization cost.

INTRODUCTION

Hepatorenal syndrome (HRS) is a serious complication of cirrhosis with an incidence as high as 32% among patients with advanced liver disease[1-7]. Previous studies have consistently demonstrated high morbidity, mortality, and resource utilizations[1,8-17]. Several factors have been associated with poor outcomes, including high model for end stage liver disease (MELD) score[18], degree of acute kidney injury (AKI)[11,19], extrahepatic organ failure[20], and sepsis[18,21].

In recent decades, there have been significant advances in knowledge, treatment, and optimal management of patients with HRS[1,7-17,22-24]. While terlipressin, a synthetic vasopressin analog with predominant vasopressin 1A receptor effect[25], has been used to treat HRS in many Asian and European countries, it is currently not yet available in the United States for the treatment of HRS[1,26]. Thus, currently available treatment options for HRS in the United States include albumin volume expansion, octreotide with or without midodrine, and intravenous cardiovascular medications like vasopressin and norepinephrine[1]. Nevertheless, there have been improvements in the overall care for patients with HRS, including liver transplantation and renal replacement therapy. In addition, several studies have suggested the use of transjugular intrahepatic portosystemic shunt (TIPS) for patients with HRS[27-29]. However, data specific to HRS, hospital mortality trends, and hospital admission resource utilization remain limited.

In this study, we aimed to evaluate patient characteristics, in-hospital treatments, mortality, and resource utilization during hospital admissions for HRS in the United States. We also assessed the temporal trend in mortality and identified the predictors for mortality.

MATERIALS AND METHODS

Study population

We conducted a retrospective cohort study of hospital admissions for HRS from 2005 to 2014 in the national inpatient sample (NIS) database. The detail of the NIS database was previously described[30]. We identified hospital admission with a primary discharge diagnosis using the international classification of disease-9 (ICD-9) diagnosis code of 572.4. The Mayo Clinic institutional review board approved this study (IRB number 21-007353 and date of approval; July 27, 2021) and exempted the need for informed consent because the data in NIS database was publicly available and deidentified.

Data collection

We abstracted patient and hospital characteristics, procedures, outcomes, and resource utilization from the database (Supplementary Table 1). Patient characteristics included age, sex, race, etiology of liver disease, medical comorbidity based on Elixhauser index [31], and admission day. Hospital characteristics included hospital size, ownership, location, teaching status, and region. Procedures included renal replacement therapy, liver transplantation, TIPS, abdominal paracentesis, and mechanical ventilation. Outcomes included hospital mortality, resource utilization, including length of hospital stay, and hospitalization cost. Since this study used data over 10 different calendar years, we adjusted hospitalization costs for inflation using the consumer price index and converted them to 2014 United States dollar equivalents.

Statistical analysis

The NIS database contains hospitalization data from a stratified sample of 20% of hospitals in the United States. As such, we used discharge weight provided by the Healthcare Cost and Utilization (HCUP) to estimate the total number of hospital admissions for HRS. We used descriptive statistics to summarize patient and hospital characteristics, procedures, outcomes, and resource use of HRS admission. We fitted logistic regression model for hospital mortality and liver transplantation, and standard least square linear regression for length of hospital stay, and hospitalization cost, using calendar years as the independent variable to assess the annual trend from 2005 through 2014. We estimated adjusted odds ratio (OR) for hospital mortality from multivariable multi-level mixed effect logistic regression, employing hospital identification number as random effect with patients-level characteristics clustered within hospital-level characteristics. We performed all statistical analyses using STATA, version 15 (StataCorp LP, College Station, TX, United States).

RESULTS

Patient characteristics, in-hospital treatments, outcomes, and resource use in hospital admission for HRS

There were 4938 hospital admissions with HRS as the primary diagnosis in the unweighted sample and 23973 admissions in the weighted sample. Table 1 shows patient and hospital characteristics of hospital admissions for HRS. The mean age was 58.8 ± 12.3 years, and the majority of patients were males (63%). Alcohol-related liver disease (46%) and viral hepatitis (25%) were the most common liver disease etiologies. Most patients were admitted to large urban teaching hospitals. Of those patients admitted for HRS, 21% received renal replacement therapy and 2% underwent liver transplant during their hospitalization. During this 10-year period, there was a 32% mortality observed for HRS admissions. The mean length of hospital stay was 8.8 d and the mean hospitalization cost was 73731 United States dollars.

Trends in hospital mortality, liver transplantation, length of stay, hospitalization cost in hospital admission for HRS

Table 2 showed the annual trend in hospital mortality, liver transplantation, length of hospital stay, and hospitalization cost in HRS admissions from 2005 to 2014.

There was a decreasing trend in hospital mortality from 44% in 2005 to 24% in 2014 among hospital admissions for HRS in the United States (OR: 0.92, 95%CI: 0.90-0.94 *per* year; *P* < 0.001) (Figure 1A).

Meanwhile, there was an increase in the rate of liver transplantation (OR: 1.11, 95%CI: 1.02-1.20 *per* year; *P* = 0.02) (Figure 1B) and renal replacement therapy (OR: 1.05, 95%CI: 1.02-1.08 *per* year; *P* < 0.001) (Figure 1C) performed in hospitalization for HRS.

There was an increasing trend in mean length of hospital stay (coefficient estimate 0.2 d *per* year; *P* < 0.001) (Figure 1D) and hospitalization cost (coefficient estimate 5778 United States dollars *per* year; *P* < 0.001) (Figure 1E) among hospitalization for HRS during 10-year period from 2005 to 2014.

Predictors for hospital mortality

In multivariable analysis (Table 3), older age (OR: 1.45 for 40-59 years, 1.77 for 60-79 years, 2.12 for ≥ 80 years, compared to 18-39 years; all *P* < 0.001), alcohol use (OR: 1.35; *P* < 0.001), coagulopathy (OR: 1.15; *P* = 0.001), and presence of a neurological disorder (OR: 1.38; *P* < 0.001) predicted higher hospital mortality.

Need for mechanical ventilation (OR: 9.24; *P* < 0.001) was associated with higher mortality, whereas liver transplantation (OR: 0.15; *P* < 0.001) and TIPS (OR: 0.23; *P* < 0.001), and abdominal paracentesis (OR: 0.48; *P* < 0.001) were associated with lower hospital mortality. Renal replacement therapy was not significantly associated with mortality risk.

DISCUSSION

In this study based on a large United States database of hospitalizations, the mortality rate for hospitalized patients with HRS decreased by approximately 50% during the 10-year study period. During the same period, there was a 2-fold increase in the incidence of HRS patients receiving a liver transplant and the incidence of in-hospital renal replacement therapy increased by 60%. Notably, there were also increase in length of hospital stay and a 2-fold increase in the estimated hospital cost, which is likely related to higher utilization of healthcare resources. This highlights the high economic burden of chronic liver disease in the United States[32,33].

The marked improvement in the in-hospital mortality rate for HRS is likely reflective of changes in both medical and surgical management during the study period. Our study shows that there was an apparent increase in the number of liver transplants and renal replacement therapy around 2007 to 2008. This trend coincided with overall changes in clinical practice over the preceding years[34]. Although the unique pathophysiology of HRS has long been recognized as a functional renal failure occurring as a result of advanced liver disease[35], its treatment, including the initiation of in-hospital dialysis, and the role for liver transplantation have signifi-cantly evolved[36]. Historically, the initiation of renal replacement therapy in patients with HRS was felt to be controversial and futile. Increasing experience with liver transplantation in the setting of HRS as well as improved access to continuous renal

Table 1 Patient characteristics, in-hospital treatments, outcomes, and resource use in hospital admission for hepatorenal syndrome (mean ± SD)

	Unweighted, *n* (%)	Unweighted % ± SE	Weighted, *n* (%)	Weighted % ± SE
Total, *n* (%)	4938		23973	
Sex				
Male	3130	63.39 ± 0.68	15183	63.33 ± 0.31
Female	1808	36.61 ± 0.68	8790	36.67 ± 0.31
Age (yr)		58.8 ± 12.3		58.8 ± 12.3
18-39	266	5.39 ± 0.32	1299	5.42 ± 0.15
40-59	2461	49.84 ± 0.71	11933	49.77 ± 0.32
60-79	1927	39.02 ± 0.69	9365	39.06 ± 0.31
≥ 80	284	5.75 ± 0.33	1376	5.74 ± 0.15
Race				
White	3098	72.23 ± 0.68	15050	72.12 ± 0.31
Black	421	9.81 ± 0.45	2055	9.85 ± 0.21
Hispanic	511	11.91 ± 0.49	2495	11.95 ± 0.22
Asian/Pacific islander	81	1.89 ± 0.21	395	1.89 ± 0.09
Native American	57	1.33 ± 0.17	280	1.34 ± 0.07
Other	121	2.82 ± 0.25	593	2.84 ± 0.11
Admission day				
Weekday	3955	80.09 ± 0.57	19223	80.18 ± 0.26
Weekend	983	19.91 ± 0.57	4751	19.82 ± 0.26
Liver disease etiology				
Alcoholic liver disease	2249	45.54 ± 0.71	10935	45.61 ± 0.32
Viral hepatitis	1218	24.66 ± 0.61	5915	24.67 ± 0.28
Comorbidities				
Diabetes Mellitus	1260	25.52 ± 0.62	6132	25.58 ± 0.28
Hypertension	1937	39.23 ± 0.69	9437	39.36 ± 0.32
Fluid/electrolyte disorders	3548	71.85 ± 0.64	17233	71.88 ± 0.29
Coagulopathy	2115	42.83 ± 0.70	10286	42.90 ± 0.32
Anemia	1937	39.23 ± 0.69	9422	39.30 ± 0.31
Weight loss	872	17.66 ± 0.54	4255	17.75 ± 0.25
Cancer	658	13.32 ± 0.48	3198	13.34 ± 0.22
Congestive heart failure	630	12.76 ± 0.47	3042	12.69 ± 0.21
Chronic pulmonary disease	613	12.41 ± 0.47	2973	12.40 ± 0.21
Obesity	456	9.23 ± 0.41	2218	9.25 ± 0.19
Neurological disorders	234	4.74 ± 0.30	1147	4.78 ± 0.14
Pulmonary circulation disorders	176	3.56 ± 0.26	847	3.53 ± 0.12
Valvular disease	164	3.32 ± 0.25	795	3.32 ± 0.12
Peripheral vascular disorders	119	2.41 ± 0.22	587	2.45 ± 0.10
Depression	413	8.36 ± 0.39	2002	8.35 ± 0.18
HIV/AIDS	36	0.73 ± 0.12	173	0.72 ± 0.05
Substance use				

Smoking	583	11.81 ± 0.46	2825	11.78 ± 0.21
Alcohol	1930	39.08 ± 0.69	9394	39.19 ± 0.31
Drug use	209	4.23 ± 0.29	1023	4.27 ± 0.13
Bed size				
Small	611	12.30 ± 0.50	2898	12.09 ± 0.21
Medium	1210	24.41 ± 0.66	5905	24.63 ± 0.28
Large	3117	63.28 ± 0.74	15171	63.28 ± 0.31
Location/Teaching status				
Rural	651	13.89 ± 0.53	3167	13.21 ± 0.22
Urban, non-teaching	1723	36.76 ± 0.74	8320	34.70 ± 0.31
Urban, teaching	2564	49.35 ± 0.77	12487	52.08 ± 0.32
Hospital region				
Northeast	984	20.24 ± 0.62	4817	20.09 ± 0.26
Midwest	1122	23.03 ± 0.65	5406	22.55 ± 0.27
South	1699	34.03 ± 0.73	8261	34.46 ± 0.31
West	1133	22.70 ± 0.64	5489	22.90 ± 0.27
Medical procedures/interventions				
Renal replacement therapy	1018	20.61 ± 0.58	4929	20.56 ± 0.26
Paracentesis	2226	45.08 ± 0.71	10843	45.23 ± 0.32
Mechanical ventilation	499	10.10 ± 0.43	2412	10.06 ± 0.19
TIPS	46	0.93 ± 0.14	218	0.91 ± 0.06
Liver transplantation	85	1.68 ± 0.18	404	1.68 ± 0.08
LTA	66	1.34 ± 0.16	321	1.34 ± 0.07
SLKT	19	0.38 ± 0.09	93	0.39 ± 0.04
Outcomes				
Mortality	1573	31.90 ± 0.66	7616	31.81 ± 0.30
Length of hospital stay (d)		8.8 ± 10.9		8.8 ± 11.0
Hospitalization cost (United States $)		735701 ± 135526		73731 ± 135876

SE: Standard error; HIV/AIDS: Human immunodeficiency virus/acquired immunodeficiency syndrome; TIPS: Transjugular intrahepatic portosystemic shunt; LTA: Liver transplant alone; SLKT: Simultaneous liver-kidney transplantation.

replacement have resulted in a change in practice and a decrease in mortality[37].

In 2007-2008, multiple randomized control trials on terlipressin were published and have influenced the medical management HRS as well as patient outcomes[9-11,14, 15]. Studies have shown potential beneficial effects of terlipressin, a potent selective splanchnic and extrarenal vasoconstrictor, on kidney function among patients with HRS[10,38,39]. Additionally, non-response to vasoconstrictors can also predict HRS mortality[40,41]. Unfortunately, as of 2020, the FDA has not yet approved the use of terlipressin for HRS in the United States. Results from the phase 3 trial terlipressin did not show any significant survival benefit and its use was associated with adverse events, such as respiratory failure[42,43]. Although terlipressin is currently not yet available in the United States[1,26], the observed findings of decreasing mortality trends for HRS in the Unites States are likely due to improvements in healthcare, increased access and acceptance of chronic intermittent hemodialysis for patients with liver disease as well as increased acceptance of liver transplantation for patients with acute decompensation[44].

In addition to liver transplantation, our study interestingly showed that TIPS and abdominal paracentesis were associated with lower hospital mortality among patients with HRS. Possible mechanisms underlying reduced mortality among patients who received paracentesis were that those who had abdominal paracentesis received more

Table 2 The annual trend in hospital mortality, liver transplantation, renal replacement therapy, length of hospital stay, hospitalization cost in hepatorenal syndrome admission from 2005 to 2014 (mean ± SD)

Year	Unweighted sample[1]	Weighted sample[1]	Hospital mortality weighted % ± SE	Liver transplantation weighted % ± SE	Renal replacement therapy weighted % ± SE	Length of stay (d)	Hospital cost (United States $)
Total	4931	23941	31.8 ± 0.7	1.7 ± 0.2	20.6 ± 0.6	8.8 ± 11.0	73731 ± 135876
2005	312	1471	43.8 ± 2.8	0.7 ± 0.5	13.8 ± 2.0	8.2 ± 8.6	42857 ± 67978
2006	330	1551	40.8 ± 2.7	0.6 ± 0.4	13.6 ± 1.9	7.2 ± 7.6	41841 ± 67254
2007	287	1358	36.7 ± 2.9	1.1 ± 0.6	17.0 ± 2.2	8.0 ± 8.9	49879 ± 77833
2008	367	1737	37.1 ± 2.5	1.9 ± 0.7	21.7 ± 2.2	8.6 ± 9.4	65419 ± 109901
2009	486	2363	31.1 ± 2.1	2.2 ± 0.7	20.8 ± 1.8	8.9 ± 11.3	71737 ± 123006
2010	610	2973	31.1 ± 1.9	0.9 ± 0.4	21.3 ± 1.7	9.3 ± 13.7	69778 ± 106971
2011	628	2934	30.3 ± 1.9	1.9 ± 0.5	23.3 ± 1.7	8.6 ± 9.6	82917 ± 154746
2012	603	3015	31.2 ± 1.9	2.0 ± 0.6	21.9 ± 1.7	9.1 ± 13.5	74951 ± 113671
2013	622	3110	28.3 ± 1.8	2.7 ± 0.7	21.4 ± 1.6	9.4 ± 12.1	95671 ± 210352
2014	686	3430	24.1 ± 1.6	1.7 ± 0.5	22.4 ± 1.6	9.0 ± 9.0	90829 ± 149495
P value			< 0.001	0.02	< 0.001	< 0.001	< 0.001

[1]Sample of hepatorenal syndrome patients having complete data on mortality status.

SE: Standard error.

aggressive treatments such as albumin and vasopressors, TIPS, and liver transplantation than those who received palliative care. Furthermore, abdominal paracentesis may have led to the diagnosis and treatment for spontaneous bacterial peritonitis[45]. The use of TIPS in patients with HRS remains controversial, although there is increasing data suggesting there may be benefit[24,29]. According to current best practice recommendations, the presence of HRS is not an absolute contraindication for TIPS and the presence of other indications, such as ascites, should guide decision making[29]. Specific to this topic, there is a clear need for additional randomized controlled trials, however, in the interim, there are an increasing number of small studies demonstrating positive outcomes in select HRS patients receiving TIPS[24,46, 47]. Since mortality in patients with HRS undergoing TIPS is driven mainly by poor liver function it may be possible that there was a population selection bias and these patients had initially better liver function resulting in better survival.

Our study also showed several risk factors associated with in-patient mortality for HRS. These factors include advanced age, history of alcohol use, coagulopathy and presence of a neurological disorder. It is well known that older age, coagulopathy, and neurological disorder are associated with poor outcomes in patients with HRS[11,18-21]. Hepatic encephalopathy is known to be associated with mortality[48], and thus this could be the underlying reason for association between neurological disorder and increased in-patient mortality for HRS. Although specific knowledge regarding the duration and timing of alcohol use prior to hospitalization is a limitation of this dataset, active alcohol use is a known decompensating event that can result in AKI and HRS. It is also possible that recent alcohol use prevented certain patients from being suitable for liver transplantation. In this foreseeable scenario, initiation of renal replacement therapy has increasingly been used as a bridge to liver transplant eligibility and liver compensation.

There are several limitations in our study. The NIS is a hospitalized database. Thus, we did not evaluate the long-term outcomes of HRS following hospitalization. Although our study showed a decreasing trend of in-hospital mortality rates, it should not be generalized to the overall survival of patients with HRS. Estimates of in-hospital mortality do not include deaths that occur after discharge. The database did not contain MELD score, which predicted mortality in HRS patients[48]. In addition, treatment of HRS was not assessed in this study[40,41]. Data on medications including midodrine, octreotide, vasopressor, albumin infusion were not available in the database. Thus, we could not assess the effects of these agents and the response to

Table 3 Clinical characteristics associated with in-hospital mortality

Characteristics	Univariable analysis		Multivariable analysis	
	Unadjusted OR (95%CI)	*P* value	Adjusted OR (95%CI)	*P* value
Female sex	0.96 (0.85-1.09)	0.52	0.91 (0.78-1.07)	0.27
Age (yr)				
18-39	1 (ref)	-	1 (ref)	-
40-59	1.21 (0.91-1.60)	0.19	1.45 (1.28-1.64)	< 0.001
60-79	1.24 (0.93-1.65)	0.14	1.77 (1.68-1.87)	< 0.001
≥ 80	1.68 (1.17-2.42)	0.005	2.12 (1.51-3.00)	< 0.001
Race				
White	1 (ref)	-	1 (ref)	-
Black	1.38 (1.11-1.71)	0.003	1.26 (0.91-1.75)	0.16
Hispanic	1.05 (0.86-1.29)	0.61	1.12 (0.78-1.61)	0.53
Asian/Pacific Islander	1.44 (0.91-2.27)	0.12	1.30 (0.98-1.73)	0.07
Native American	1.04 (0.59-1.84)	0.88	1.11 (0.86-1.43)	0.43
Other	0.88 (0.59-1.32)	0.55	0.93 (0.48-1.81)	0.84
Weekend admission	1.14 (0.98-1.32)	0.08	1.05 (0.82-1.34)	0.69
Liver disease etiology				
Alcohol-related	0.90 (0.80-1.01)	0.08	0.85 (0.71-1.01)	0.06
Viral hepatitis	0.98 (0.86-1.13)	0.83	1.00 (0.81-1.24)	1.00
Comorbidities				
Smoking	0.96 (0.79-1.16)	0.66	1.15 (0.83-1.60)	0.40
Alcohol use	0.98 (0.87-1.11)	0.79	1.35 (1.26-1.45)	< 0.001
Drug use	0.84 (0.62-1.14)	0.26	0.77 (0.55-1.08)	0.13
HIV/AIDS	1.02 (0.51-2.07)	0.95	0.81 (0.58-1.13)	0.22
Autoimmune arthritis	1.10 (0.64-1.91)	0.73	1.14 (0.54-2.41)	0.72
Congestive heart failure	1.05 (0.88-1.26)	0.59	0.99 (0.87-1.12)	0.84
Chronic pulmonary disease	1.00 (0.84-1.21)	0.96	0.95 (0.78-1.16)	0.63
Coagulopathy	1.01 (0.90-1.15)	0.82	1.15 (1.16-1.25)	0.001
Diabetes mellitus	0.78 (0.67-0.89)	< 0.001	0.87 (0.73-1.04)	0.12
Hypertension	0.76 (0.67-0.86)	< 0.001	0.83 (0.70-1.01)	0.06
Lymphoma	1.42 (0.68-2.96)	0.35	1.53 (0.42-5.60)	0.52
Fluid/electrolyte disorders	0.85 (0.74-0.97)	0.02	0.87 (0.75-1.01)	0.07
Cancer	1.34 (1.13-1.59)	0.001	1.40 (0.88-2.23)	0.15
Neurological disorders	1.29 (0.98-1.70)	0.07	1.38 (1.21-1.58)	< 0.001
Obesity	0.87 (0.70-1.07)	0.20	0.92 (0.62-1.38)	0.70
Peripheral vascular disorders	0.78 (0.51-1.18)	0.23	0.78 (0.42-1.46)	0.44
Psychoses	0.80 (0.55-1.16)	0.24	0.93 (0.78-1.12)	0.44
Pulmonary circulation disorders	0.75 (0.53-1.05)	0.10	0.68 (0.43-1.08)	0.11
Valvular disease	0.75 (0.53-1.07)	0.12	1.01 (0.64-1.60)	0.96
Weight loss	0.91 (0.78-1.07)	0.27	1.05 (0.97-1.13)	0.21
Medical procedure				
Renal replacement therapy	0.98 (0.85-1.14)	0.81	0.92 (0.68-1.25)	0.59

Liver transplantation	0.33 (0.23-0.46)	< 0.001	0.15 (0.11-0.21)	< 0.001
TIPS	0.40 (0.18-0.90)	0.03	0.23 (0.12-0.43)	< 0.001
Paracentesis	0.46 (0.41-0.53)	< 0.001	0.48 (0.43-0.53)	< 0.001
Mechanical ventilation	6.97 (5.66-8.59)	< 0.001	9.24 (7.90-10.81)	< 0.001

HIV/AIDS: Human immunodeficiency virus/acquired immunodeficiency syndrome; TIPS: Transjugular intrahepatic portosystemic shunt; OR: Odds ratio; 95%CI: 95% confidence interval.
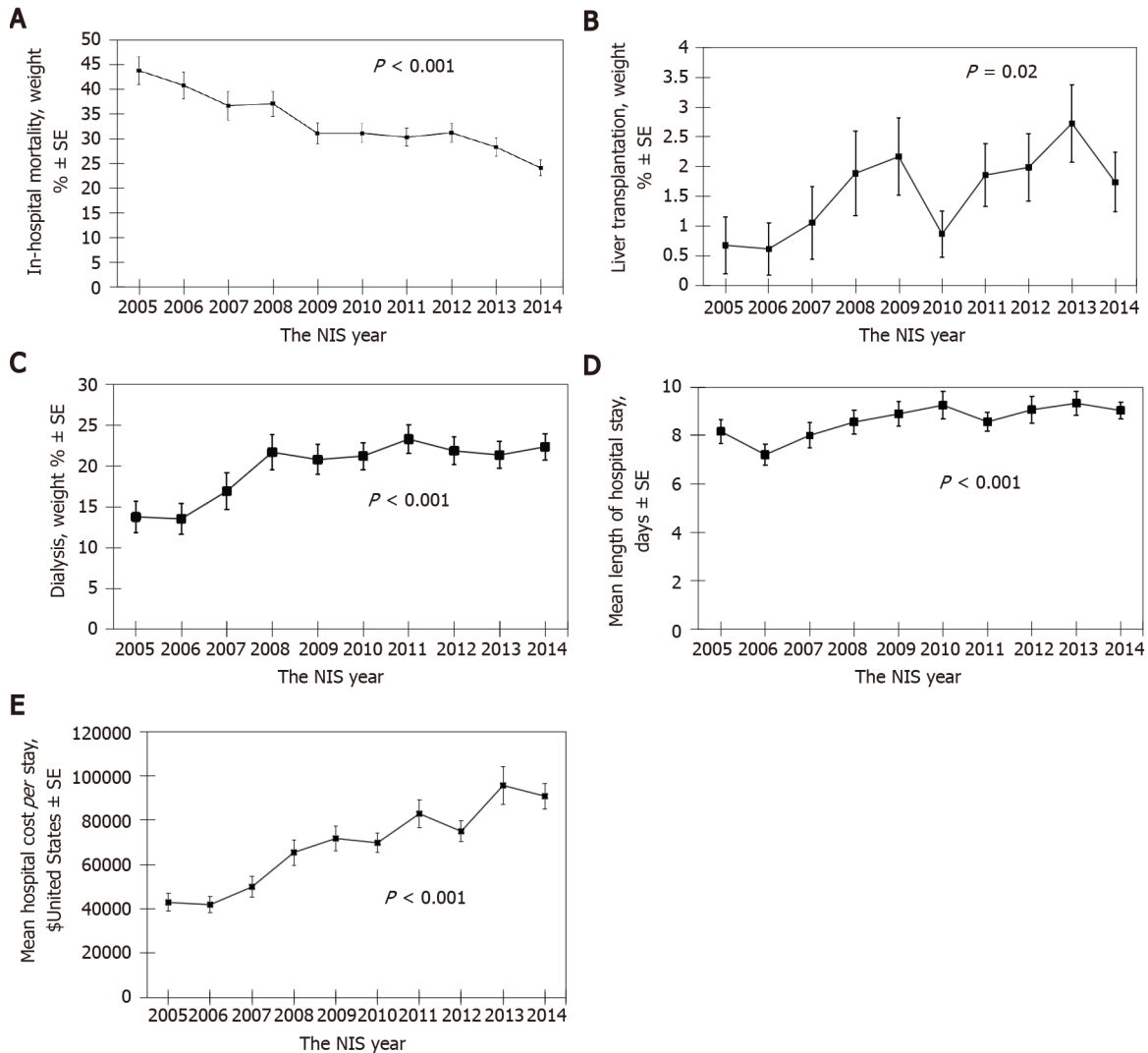
Figure 1 Data on admissions in the United States due to hepatorenal syndrome. A: Decreasing trend in hospital mortality among hospital admissions; B: Increase in the rate of liver transplantation among hospital admissions; C: Trend of renal replacement therapy among hospital admissions; D: Trend of mean length of hospital stay among hospital admissions; E: Trend of hospitalization cost among hospital admissions. NIS: National inpatient sample.

treatments on the outcomes of HRS. Lastly, HRS was identified by ICD-9 diagnosis code. Given definition of the HRS has changed over the years, these changes in definition may have affected the incidence of HRS in our study overtime.

CONCLUSION

In summary, our study showed a decreasing trend of in-hospital mortality rates in patients with HRS. These trends were likely related to advances in medicine, increased access and acceptance of renal replacement therapy, and increased utilization of liver transplantation which is the definitive treatment for HRS. Future studies are needed to

understand if these trends are impacted by other factors such as facility performance, patient care teams, health insurance reimbursement policies, or other factors.

ARTICLE HIGHLIGHTS

Research background

Hepatorenal syndrome (HRS) is a serious complication of cirrhosis, associated with high morbidity, mortality, and resource utilizations. In recent decades, there have been significant advances in knowledge, treatment and optimal management of patients with HRS.

Research motivation

There has been improvement in overall care for patients with HRS. Data on trends of hospital mortality and resource utilization in hospital admissions for HRS were limited.

Research objectives

We aimed to evaluate patient characteristics, in-hospital treatments, mortality, resource use among hospital admissions for HRS s in the United States. We also assessed the temporal trend in mortality and identified the predictors for mortality.

Research methods

We used the national inpatient sample database to identify unweighted sample of 4938 hospital admissions primarily for HRS from 2005 to 2014 (weighted sample of 23973 admissions). The primary outcome was the temporal trend in and predictors for hospital mortality. We estimated odds ratio from multi-level mixed effect logistic regression to identify patient characteristics and treatments associated with hospital mortality.

Research results

The overall hospital mortality was 32%. Hospital mortality decreased from 44% in 2005 to 24% in 2014 ($P < 0.001$), while there was an increase in the rate of liver transplantation ($P = 0.02$), renal replacement therapy ($P < 0.001$), length of hospital stay ($P < 0.001$), and hospitalization cost ($P < 0.001$). Multivariable analysis older age, alcohol abuse, coagulopathy, neurological disorder, and need for mechanical ventilation predicted higher hospital mortality, whereas liver transplantation, TIPs, and abdominal paracentesis were associated with lower hospital mortality.

Research conclusions

Although there was an increase in resource utilizations, hospital mortality among hospital admissions for HRS significantly improved.

Research perspectives

These trends were likely related to increased utilization of liver transplantation which is the definitive treatment for HRS. Future studies are needed to understand if these trends are impacted by other factors such as facility performance, patient care teams, health insurance reimbursement policies, or other factors.

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