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Risk Factors of Mortality in Patients with Liver Necrosis from National Inpatient Sample Data Base (2005-2014) United States

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Abstract

Background: Liver necrosis represents a growing health and economic burden in the United States. This study aims to explore risk factors associated with mortality among hospital patients with liver necrosis.

Methods: Data from the National Inpatient Sample database (2005-2014) was analyzed. Demographics, clinical data, and outcomes were collected. Multivariable logistic regression models were used to investigate the association between various risk factors and mortality.

Results: The study included 10,476 adult and 3,207 elderly patients with acute or subacute liver necrosis. Mortality rates were 13% for adults and 19% for elderly patients. Females accounted for 53% of the sample in both age groups. In operatively treated patients, invasive diagnostic procedures significantly reduced mortality (OR = 0.690, 95% CI: 0.534-0.890). Age was a significant risk factor for higher mortality in adults (OR = 1.016, 95% CI: 1.004-1.027). For non-operated patients, medical/surgical complications increased mortality odds by 2.6 times in adults (OR = 2.665, 95% CI: 1.470-4.831) and 4.3 times in elderly patients (OR = 4.331, 95% CI: 1.932-9.705). Longer hospital stays increased mortality in adults (OR = 1.013, 95% CI: 1.004-1.022) but decreased it in elderly patients (OR = 0.966, 95% CI: 0.944-0.988). Invasive diagnostic procedures were protective in non-operated patients (OR = 0.714, 95% CI: 0.586-0.871 for adults; OR = 0.552, 95% CI: 0.385-0.790 for elderly). Being female reduced mortality odds by 36% in non-operated adults (OR = 0.638, 95% CI: 0.556-0.731).

Conclusion: Age, medical/surgical complications, and prolonged hospital stays are significant risk factors for mortality in liver necrosis patients. Invasive diagnostic procedures and being female reduce mortality odds, suggesting targeted interventions can improve outcomes.

Keywords: liver necrosis; in-hospital mortality; risk factors; epidemiology

Introduction

Necrosis is a form of cellular injury that results in the premature death of cells. Necrosis can occur as a normal and regulated physiological event. However, in most cases it

is caused by pathological stimuli such as hypoxia, trauma, radiation, pathogens, and chemical agents.[1] Certain pathological stimuli are more likely to result in necrosis in specific cell types, and hepatic (liver) cells have been found to be susceptible to necrosis from a wide range of causes including viral hepatitis, acetaminophen toxicity, chronic alcohol abuse, autoimmune disorders and localized ischemia.[2]

In clinical settings, a diagnosis of liver necrosis is appropriate in cases where liver cell death results in symptomatic liver dysfunction, with the possible addition of the modifiers 'acute' or 'subacute' to indicate the extent and severity of liver damage.[3] Early symptoms of liver necrosis include persistent nausea, weakness, fatigue and abdominal pain, progressing to jaundice, cirrhosis and fulminant liver failure as necrosis affects larger amounts of tissue.[4]

Although liver necrosis is a relatively rare condition, it is responsible for considerable economic and health burdens in the United States (US). The year-over-year prevalence of cirrhosis, which is a sequela of liver necrosis,[5] provides a significant example of this burden that also demonstrates how quickly it is growing. From 2001 to 2011, hospital admissions for cirrhosis in the U.S. nearly doubled from 371,000 to 659,000 with associated inpatient costs growing from $4.8 billion to $9.8 billion over that same period, while patients suffered an in-hospital fatality rate between 7-10%.[6] Acute liver necrosis also directly accounted for 4.2% (243/5748) of all adult liver transplants performed in the U.S. in 2009,[7] at an estimated cost of $48.6 million.[8]

The substantial and growing burden of liver necrosis has spurred significant efforts in liver necrosis research, which have been especially productive in the field of cellular biology. Studies such as those by Jaeschke et al.[9] and Bantel and Schulze-Osthoff[10] were able to elaborate on the physiological differences between apoptosis and necrosis in the liver at the cellular level and identify many of the intracellular chemical signaling pathways that are involved in the biological process of necrosis. These and similar breakthroughs in cellular research have contributed to the development of improved pharmaceutical agents and treatment modalities, but to further improve clinical and public health practice on this topic more contributions are required from the field of epidemiology.

Currently, there is large gap in knowledge regarding the behavioral and clinical risk factors for liver necrosis, making it difficult to investigate the underlying causes. Studies have been published that demonstrate a relationship between liver necrosis and other disease processes, but these are often limited in scope and focus on narrow clinical presentations rather than providing a wider epidemiological picture.[11] Further emphasizing the need for greater research efforts in this area, studies in forensic pathology have found that current science is generally inadequate to allow for the determination of an exact cause for liver necrosis even in laboratory settings due to complex and often overlapping etiologies.[12]

This study aims to address this gap in the literature by performing a thorough epidemiological analysis of the risk factors associated with liver necrosis in the US. Using longitudinal data from a large, representative sample, this analysis will generate new insight into the existing association between liver necrosis and a wide range of possible risk factors, creating a foundation for future studies on causality and improving clinical and public health practice.

Methods

The National Inpatient Sample (NIS) database is currently considered the largest publicly available all-payer inpatient healthcare database in the US. Data was extracted from the NIS, which contains discharge data from a 20% stratified sample of community hospitals and is a part of the Healthcare Cost and Utilization Project (HCUP), sponsored by the Agency for Healthcare Research and Quality.[13] The database provides data regarding an array of measurements, including patient demographic, primary payer, hospital characteristics, principal diagnosis, up to 24 secondary diagnoses, and procedural diagnoses.[14] Nationally, it estimates more than 35 million weighted hospitalizations annually, and is perceived as an accurate representation of US in-patient population.[15, 16] Using the HCUP-NIS data from 2005 - 2014, we identified adult patients (>18 years old) admitted with the primary diagnosis of acute and subacute necrosis of liver (n = 10,476). The ICD-9 code utilized to identify patients with acute and subacute necrosis of the liver was 570. Data was used to obtain patient characteristics, including age, gender, race, income quartile, insurance status, operation status; days to operation; hospital length of stay; total charges and the associated comorbidities (e.g., AIDS, alcohol abuse, deficiency anemias, psychoses, solid tumor, renal failure). The Westchester Medical Center (WMC) Institutional Review Board approved this study, and informed consent was waived because the study is based on a review of a de-identified database.

Modified frailty index score calculation

The NIS database does not contain all the variables required to calculate the items included in the 5-item modified frailty index,[17] nor does it specify the duration of the comorbidity prior to admission. To include frailty in the study, we estimated the 5-item modified frailty index with the variables available in the database (Table 1). Functional health status was not available in the dataset and had to be estimated based on available variables. If a patient had comorbidity of a solid tumor, renal failure, metastatic cancer, paralysis, lymphoma, coagulopathy, or weight loss, it was assumed they were partially or totally dependent and therefore functionally dependent. Diabetes Mellitus was estimated to be present if either comorbidity of diabetes uncomplicated or diabetes with chronic complications was indicated. History of chronic obstructive pulmonary disease (COPD) was estimated using the comorbidity of chronic pulmonary disease. History of congestive heart failure was assumed to be present if the congestive heart failure comorbidity was indicated. The use of medication to control hypertension could not be determined from the data set, so it was estimated by the indication of hypertension.

Table 1. Comparison of variables used for estimating 5-Item Modified Frailty Index (mFI) Score

Subramaniam 5-Item mFI Factors	NIS Variable for Our Modified 5-Item mFI Estimate
Functional Health Status (Partially or Totally)	Presence of at least 1: Solid Tumor, Renal Failure, Metastatic Cancer, Paralysis, Lymphoma, Coagulopathy, Weight Loss
Diabetes Mellitus (non/insulin)	Diabetes (Uncomplicated) or Diabetes (Chronic Complications)
History of COPD	Chronic Pulmonary Disease
History of Congestive Heart Failure	Congestive Heart Failure
Hypertension requiring Medication	Hypertension (Un/Complicated)

Both instruments assign one point to each item if the comorbidity item was present. The items were summed to create an estimated modified frailty score. The scale still ranged from 0 to 5, with 0 being not frail, to 5 being very frail. For adults, the average modified frailty score was 1.05, with a standard deviation of 1.00, and a range of 0 to 5. For the elderly, the average was 1.98, with a standard deviation of 1.17, and a range of 0 to 5.

Statistical Analysis

Descriptive statistics were first calculated for the study variables among our sample and were expressed as either categorical or continuous data. Categorical data are expressed as count (%), and continuous data are expressed as mean ±SD or median and interquartile range for skewed data. Chi-square and t-tests were used to compare categorical and continuous variables, respectively. In univariable logistic regression analysis, patient characteristics were stratified based on sex categories (male vs. female); outcome categories (survived vs. deceased); and operation status (no operation vs. operation). Multivariable logistic regression analyses were used to investigate the associations between mortality and different factors in emergency admitted patients with the primary diagnosis of acute and subacute necrosis of liver and either undergoing an operation or not undergoing an operation. Backward stepwise regression was used to find the final predictors of in-hospital mortality in the adjusted model. Both multivariable models were adjusted for the following attributes of patients and hospitals: age, sex, race; income quartile, severity of illness subclass, and the associated comorbidities of diabetes, drug abuse, hypertension, hypothyroidism, liver disease, lymphoma, fluid/electrolyte disorders, metastatic cancer, other neurological disorders, other neurological disorders, obesity, paralysis, peripheral vascular disorders, pulmonary circulation disorders, renal failure, solid tumor, peptic ulcer, valvular disease, weight loss. The P values less than 0.05 were considered significant. All analyses were done by SPSS software version 24,[18] and R statistical software.[19]

Results

Gender Differences

The stratified analysis, based on age and gender, are presented in Table 2. A total number of 10,476 adults and 3,207 elderly patients were emergently admitted to the hospital with the primary diagnosis of acute and subacute necrosis of the liver, during the 10-year study period of 2005-2014. 53% of the sample were females among both the adult and the elderly groups. The mean (SD) age of the male adult group was 1.73 years older than the female adult group, while in the elderly group, the mean (SD) age of the male group was 1.23 years younger than the female group (Table 2). Furthermore, a total number of 1,971 patients died during the study period, among which 780 were males (15.9%) and 574 were females (10.3%) in the adult group, while 322 were males (21.4%) and 295

were females (17.3%) in the elderly group. Irrespective of gender, most patients were white. While in the adult group private insurance was dominant, most patients in the elderly group were insured by Medicare (Table 2). Moreover, more than half of the adult patients were admitted to urban teaching hospitals and only 12% to rural hospitals (Table 2). A slight difference in hospital location was present among the elderly group, where more than half of the patients were admitted to either rural or urban non-teaching hospitals. Major comorbidities in both age groups were fluid/electrolyte disorders, coagulopathy, hypertension, deficiency anemia, and diabetes uncomplicated. Among adults, alcohol and drug abuse were more prevalent compared to the elderly group. In the elderly group, compared to adults, congestive heart failure, renal failure, chronic pulmonary disease, metastatic cancer, pulmonary circulation disorders, and peripheral vascular disorders were more reported as comorbidities. In both age groups, females had higher rates of hypothyroidism, depression, psychoses, and other neurological disorders (Table 2).

Table 2. Characteristics of emergency admitted patients with the primary diagnosis of acute and subacute necrosis of liver (NIS 2005-2014). Data were stratified according to sex categories.

		Adult, N (%)			Elderly, N (%)		
		Male	Female	P	Male	Female	P
All Cases		**4,918 (46.9)**	**5,558 (53.1)**		**1,502 (46.8)**	**1,705 (53.2)**	
Race	**White**	2,824 (66.2)	3,137 (66.5)	**0.009**	1,013 (75.8)	1,092 (74.9)	0.3
	Black	547 (12.8)	699 (14.8)		106 (7.9)	141 (9.7)	
	Hispanic	516 (12.1)	525 (11.1)		96 (7.2)	116 (8.0)	
	Asian/Pacific Islander	142 (3.3)	139 (2.9)		65 (4.9)	57 (3.9)	
	Native American	54 (1.3)	59 (1.3)		7 (0.5)	11 (0.8)	
	Other	184 (4.3)	156 (3.3)		49 (3.7)	41 (2.8)	
Income Quartile	**Quartile 1**	1,473 (31.0)	1,705 (31.5)	0.1	420 (28.5)	478 (28.7)	0.7
	Quartile 2	1,310 (27.5)	1,389 (25.6)		376 (25.5)	439 (26.4)	
	Quartile 3	1,099 (23.1)	1,265 (23.4)		372 (25.3)	390 (23.4)	
	Quartile 4	874 (18.4)	1,057 (19.5)		305 (20.7)	359 (21.5)	
Insurance	**Private Insurance**	1,835 (37.5)	2,335 (42.1)	**<0.001**	144 (9.6)	133 (7.8)	0.053
	Medicare	700 (14.3)	725 (13.1)		1,297 (86.5)	1,500 (88.1)	
	Medicaid	1,089 (22.3)	1,457 (26.3)		26 (1.7)	42 (2.5)	
	Self-Pay	885 (18.1)	734 (13.2)		17 (1.1)	14 (0.8)	
	No Charge	81 (1.7)	50 (0.9)		0 (0)	3 (0.2)	
	Other	303 (6.2)	247 (4.5)		16 (1.1)	10 (0.6)	
Hospital Location	**Rural**	592 (12.0)	666 (12.0)	0.8	259 (17.2)	285 (16.7)	0.6
	Urban: Non-Teaching	1,617 (32.9)	1,860 (33.5)		560 (37.3)	665 (39.0)	
	Urban: Teaching	2,709 (55.1)	3,032 (54.6)		683 (45.5)	755 (44.3)	
COMORBIDITIES	**AIDS**	99 (2.0)	35 (0.6)	**<0.001**	2 (0.1)	0 (0)	0.2
	Alcohol Abuse	1,798 (36.6)	1,162 (20.9)	**<0.001**	196 (13)	74 (4.3)	**<0.001**
	Deficiency Anemias	913 (18.6)	1,172 (21.1)	**0.001**	373 (24.8)	414 (24.3)	0.7
	Rheumatoid Arthritis	50 (1.0)	228 (4.1)	**<0.001**	25 (1.7)	110 (6.5)	**<0.001**
	Chronic Blood Loss	59 (1.2)	53 (1.0)	0.2	18 (1.2)	16 (0.9)	0.5
	Congestive Heart Failure	369 (7.5)	247 (4.4)	**<0.001**	465 (31)	400 (23.5)	**<0.001**
	Chronic Pulmonary Disease	477 (9.7)	731 (13.2)	**<0.001**	333 (22.2)	365 (21.4)	0.6

		Adult, N (%)			Elderly, N (%)		
		Male	Female	P	Male	Female	P
All Cases		4,918 (46.9)	5,558 (53.1)		1,502 (46.8)	1,705 (53.2)	
COMORBIDITIES	Coagulopathy	1,734 (35.3)	1,623 (29.2)	**<0.001**	481 (32)	429 (25.2)	**<0.001**
	Depression	385 (7.8)	913 (16.4)	**<0.001**	94 (6.3)	216 (12.7)	**<0.001**
	Diabetes, Uncomplicated	593 (12.1)	624 (11.2)	0.2	379 (25.2)	405 (23.8)	0.3
	Diabetes, Chronic Complications	155 (3.2)	124 (2.2)	**0.003**	107 (7.1)	92 (5.4)	**0.043**
	Drug Abuse	717 (14.6)	633 (11.4)	**<0.001**	13 (0.9)	12 (0.7)	0.6
	Hypertension	1,495 (30.4)	1,542 (27.7)	**0.003**	907 (60.4)	1,083 (63.5)	0.070
	Hypothyroidism	143 (2.9)	509 (9.2)	**<0.001**	146 (9.7)	368 (21.6)	**<0.001**
	Liver Disease	89 (1.8)	105 (1.9)	0.8	20 (1.3)	16 (0.9)	0.3
	Lymphoma	44 (0.9)	18 (0.3)	**<0.001**	39 (2.6)	18 (1.1)	**<0.001**
	Fluid/Electrolyte Disorders	2,467 (50.2)	2,846 (51.2)	0.3	863 (57.5)	923 (54.1)	0.060
	Metastatic Cancer	146 (3.0)	166 (3.0)	0.9	127 (8.5)	87 (5.1)	**<0.001**
	Other Neurological Disorders	263 (5.3)	424 (7.6)	**<0.001**	114 (7.6)	160 (9.4)	0.070
	Obesity	311 (6.3)	579 (10.4)	**<0.001**	111 (7.4)	124 (7.3)	0.9
	Paralysis	53 (1.1)	40 (0.7)	0.051	25 (1.7)	30 (1.8)	0.8
	Peripheral Vascular Disorders	94 (1.9)	83 (1.5)	0.1	137 (9.1)	118 (6.9)	**0.022**
	Psychoses	272 (5.5)	493 (8.9)	**<0.001**	36 (2.4)	61 (3.6)	0.051
	Pulmonary Circulation Disorders	87 (1.8)	131 (2.4)	**0.035**	86 (5.7)	102 (6.0)	0.7
	Renal Failure	482 (9.8)	343 (6.2)	**<0.001**	428 (28.5)	342 (20.1)	**<0.001**
	Solid Tumor	142 (2.9)	64 (1.2)	**<0.001**	97 (6.5)	56 (3.3)	**<0.001**
	Peptic Ulcer	1 (0)	2 (0.0)	0.6	1 (0.1)	1 (0.1)	0.9
	Valvular Disease	104 (2.1)	134 (2.4)	0.3	167 (11.1)	160 (9.4)	0.1
	Weight Loss	522 (10.6)	572 (10.3)	0.6	205 (13.6)	203 (11.9)	0.1
Invasive Diagnostic Procedure		895 (18.2)	1,158 (20.8)	**<0.001**	245 (16.3)	278 (16.3)	0.9
Surgical Procedure		987 (20.1)	787 (14.2)	**<0.001**	257 (17.1)	194 (11.4)	**<0.001**
Invasive or Surgical Procedure		1,587 (32.3)	1,645 (29.6)	**0.003**	409 (27.2)	400 (23.5)	**0.014**
Medical/Surgical Complication*		64 (1.3)	73 (1.3)	0.9	27 (1.8)	20 (1.2)	0.1
Reoperation		70 (1.4)	66 (1.2)	0.2	20 (1.3)	8 (0.5)	**0.009**
Deceased		780 (15.9)	574 (10.3)	**<0.001**	322 (21.4)	295 (17.3)	**0.003**
		Mean (SD)	**Mean (SD)**	**P**	**Mean (SD)**	**Mean (SD)**	**P**
Age, Years		45.26 (12.32)	43.53 (12.37)	**<0.001**	74.91 (7.39)	76.14 (8.11)	**<0.001**
Modified Frailty Index Score		1.12 (1.03)	0.99 (0.98)	**<0.001**	2.10 (1.15)	1.88 (1.18)	**<0.001**
Time to Invasive Diagnostic Procedure, Days		3.97 (3.80)	4.25 (7.92)	0.3	4.17 (3.34)	4.15 (3.60)	0.9
Time to Surgical Procedure, Days		3.21 (5.01)	4.12 (5.86)	**<0.001**	3.79 (4.98)	4.15 (5.06)	0.4
Hospital Length of Stay, Days		6.55 (8.83)	6.51 (8.72)	0.8	6.58 (6.65)	6.20 (6.15)	0.1
Total Charges, Dollars		57,134 -115,876	57,944 -110,74	0.7	52,737 -96,236	45,572 -77,405	**0.023**

Mortality

Of all cases, 12.9% and 19.2% of adults and elderly patients died in hospitals, respectively. Patients who died were, on average, 6 years older than the survived patients in the adult group. However, in the elderly group, the deceased patients were at the same mean (SD) age compared to those patients who survived (Table 3). Several differences in terms of comorbidities can be noted when comparing patients in relation to their mortality outcomes. For instance, the deceased patients manifested significantly higher rates of congestive heart failure, coagulopathy, fluid/electrolyte disorders, metastatic cancer, renal failure, solid tumors, and weight loss than patients who survived in both age groups (Table 3). Among adults, in addition to the mentioned common comorbidities, significantly higher rates of alcohol abuse, chronic blood loss, liver disease, lymphoma, and pulmonary circulation disorders were manifested among the deceased (Table 3). In the elderly group, but not in adults, significantly higher rates of chronic pulmonary disease and peripheral vascular disorders were manifested in the deceased as comorbidities (Table 3).

Table 3. Characteristics of emergency admitted patients with the primary diagnosis of acute and subacute necrosis of liver (NIS 2005-2014). Data were classified according to outcome categories.

		Adult, N (%)			Elderly, N (%)		
		Survived	Deceased	p	Survived	Deceased	P
All Cases		**9,125 (87.1)**	**1,355 (12.9)**		**2,589 (80.8)**	**617 (19.2)**	
Sex, Female		4,982 (54.6)	574 (42.4)	**<0.001**	1,409 (54.4)	295 (47.8)	**0.003**
Race	**White**	5,199 (66.4)	760 (65.8)	0.3	1,715 (76)	390 (72.5)	0.4
	Black	1,074 (13.7)	172 (14.9)		195 (8.6)	52 (9.7)	
	Hispanic	914 (11.7)	127 (11.0)		169 (7.5)	43 (8.0)	
	Asian/Pacific Islander	250 (3.2)	31 (2.7)		93 (4.1)	29 (5.4)	
	Native American	92 (1.2)	21 (1.8)		16 (0.7)	2 (0.4)	
	Other	296 (3.8)	44 (3.8)		68 (3.0)	22 (4.1)	
Income Quartile	**Quartile 1**	2,782 (31.4)	397 (30.1)	**0.021**	744 (29.4)	153 (25.3)	0.2
	Quartile 2	2,311 (26.1)	387 (29.4)		657 (25.9)	158 (26.2)	
	Quartile 3	2,052 (23.2)	314 (23.8)		601 (23.7)	161 (26.7)	
	Quartile 4	1,714 (19.3)	220 (16.7)		532 (21.0)	132 (21.9)	
Insurance	**Private Insurance**	3,692 (40.6)	483 (35.8)	**<0.001**	205 (7.9)	72 (11.7)	**<0.001**
	Medicare	1,190 (13.1)	235 (17.4)		2,286 (88.5)	510 (82.7)	
	Medicaid	2,214 (24.3)	333 (24.7)		56 (2.2)	12 (1.9)	
	Self-Pay	1,416 (15.6)	203 (15.0)		20 (0.8)	11 (1.8)	
	No Charge	111 (1.2)	20 (1.5)		2 (0.1)	1 (0.2)	
	Other	473 (5.2)	75 (5.6)		15 (0.6)	11 (1.8)	
Hospital Location	**Rural**	1,144 (12.5)	114 (8.4)	**<0.001**	465 (18.0)	79 (12.8)	**<0.001**
	Urban: Non-Teaching	3,094 (33.9)	386 (28.5)		1,002 (38.7)	223 (36.1)	
	Urban: Teaching	4,887 (53.6)	855 (63.1)		1,122 (43.3)	315 (51.1)	
COMORBIDITIES	**AIDS**	116 (1.3)	18 (1.3)	0.8	1 (0.0)	1 (0.2)	0.4
	Alcohol Abuse	2,425 (26.6)	532 (39.3)	**<0.001**	206 (8.0)	64 (10.4)	0.052
	Deficiency Anemias	1,788 (19.6)	296 (21.8)	0.053	636 (24.6)	151 (24.5)	0.9
	Rheumatoid Arthritis	255 (2.8)	24 (1.8)	**0.029**	115 (4.4)	20 (3.2)	0.2
	Chronic Blood Loss	86 (0.9)	26 (1.9)	**0.001**	24 (0.9)	10 (1.6)	0.1

		Adult, N (%)			Elderly, N (%)		
		Survived	Deceased	p	Survived	Deceased	P
All Cases		9,125 (87.1)	1,355 (12.9)		2,589 (80.8)	617 (19.2)	
COMORBIDITIES	Congestive Heart Failure	498 (5.5)	118 (8.7)	**<0.001**	656 (25.3)	208 (33.7)	**<0.001**
	Chronic Pulmonary Disease	1,067 (11.7)	141 (10.4)	0.1	528 (20.4)	170 (27.6)	**<0.001**
	Coagulopathy	2,580 (28.3)	775 (57.2)	**<0.001**	641 (24.8)	268 (43.4)	**<0.001**
	Depression	1,195 (13.1)	103 (7.6)	**<0.001**	260 (10.0)	50 (8.1)	0.1
	Diabetes, Uncomplicated	1,092 (12.0)	125 (9.2)	**0.003**	657 (25.4)	126 (20.4)	**0.010**
	Diabetes, Chronic Complications	247 (2.7)	32 (2.4)	0.5	158 (6.1)	41 (6.6)	0.6
	Drug Abuse	1,246 (13.7)	104 (7.7)	**<0.001**	21 (0.8)	4 (0.6)	0.8
	Hypertension	2,674 (29.3)	361 (26.6)	**0.044**	1,663 (64.2)	327 (53.0)	**<0.001**
	Hypothyroidism	596 (6.5)	56 (4.1)	**<0.001**	424 (16.4)	90 (14.6)	0.3
	Liver Disease	153 (1.7)	41 (3.0)	**<0.001**	30 (1.2)	6 (1.0)	0.6
	Lymphoma	43 (0.5)	18 (1.3)	**<0.001**	50 (1.9)	7 (1.1)	0.1
	Fluid/Electrolyte Disorders	4,318 (47.3)	995 (73.4)	**<0.001**	1,345 (5.02)	441 (71.5)	**<0.001**
	Metastatic Cancer	183 (2.0)	129 (9.5)	**<0.001**	136 (5.3)	78 (12.6)	**<0.001**
	Other Neurological Disorders	583 (6.4)	103 (7.6)	0.090	220 (8.5)	54 (8.8)	0.8
	Obesity	782 (8.6)	107 (7.9)	0.4	187 (7.2)	48 (7.8)	0.6
	Paralysis	76 (0.8)	17 (1.3)	0.1	47 (1.8)	8 (1.3)	0.4
	Peripheral Vascular Disorders	149 (1.6)	28 (2.1)	0.3	191 (7.4)	63 (10.2)	**0.019**
	Psychoses	710 (7.8)	54 (4.0)	**<0.001**	83 (3.2)	14 (2.3)	0.2
	Pulmonary Circulation Disorders	173 (1.9)	45 (3.3)	**<0.001**	148 (5.7)	40 (6.5)	0.5
	Renal Failure	642 (7.0)	182 (13.4)	**<0.001**	599 (23.1)	171 (27.7)	**0.017**
	Solid Tumor	137 (1.5)	69 (5.1)	**<0.001**	111 (4.3)	42 (6.8)	**0.008**
	Peptic Ulcer	2 (0.0)	1 (0.1)	0.3	2 (0.1)	0 (0)	0.9
	Valvular Disease	201 (2.2)	37 (2.7)	0.2	260 (10)	67 (10.9)	0.6
	Weight Loss	878 (9.6)	215 (15.9)	**<0.001**	303 (11.7)	104 (16.9)	**<0.001**
Invasive Diagnostic Procedure		1,816 (19.9)	238 (17.6)	**0.043**	443 (17.1)	80 (13.0)	**0.012**
Surgical Procedure		1,401 (15.4)	370 (27.3)	**<0.001**	350 (13.5)	101 (16.4)	0.070
Invasive or Surgical Procedure		2,722 (29.8)	508 (37.5)	**<0.001**	668 (25.8)	141 (22.9)	0.1
Medical/Surgical Complication		108 (1.2)	29 (2.1)	**0.004**	31 (1.2)	16 (2.6)	**0.010**
Reoperation		106 (1.2)	30 (2.2)	**0.001**	22 (0.8)	6 (1.0)	0.8
		Mean (SD)	**Mean (SD)**	**P**	**Mean (SD)**	**Mean (SD)**	**P**
Age, Years		43.52 (12.44)	49.85 (10.39)	**<0.001**	75.55 (7.81)	75.63 (7.79)	0.8
Modified Frailty Index Score		1.01 (1.01)	1.33 (0.92)	**<0.001**	1.94 (1.17)	2.14 (1.16)	**<0.001**
Time to Invasive Diagnostic Procedure, Days		4.08 (6.50)	4.50 (6.26)	0.4	4.20 (3.54)	3.93 (3.14)	0.5
Time to Surgical Procedure, Days		3.61 (5.47)	3.65 (5.24)	0.9	3.93 (4.00)	4.00 (4.89)	0.9
Hospital Length of Stay, Days		6.25 (8.35)	8.37 (11.02)	**<0.001**	6.41 (6.27)	6.21 (6.87)	0.5
Total Charges, Dollars		50,937 -104,731	102,105 -151,414	**<0.001**	45,350 -82,118	63,979 -102,963	**<0.001**

Operation vs. No Operation

The stratified analysis based on operation status (e.g., operation vs. no operation) is presented in Table 3. Only 1,774 (16.9%) of adults and 451 (14.1%) of elderly patients had an operation. In both age groups, females had a significantly lower rate of operation (Table 4). The mean (SD) age of the group with an operation was 4.6 years older than the group with no operation among adults, but 2.2 years younger among the elderly age group (Table 4). In both age groups, most patients were white, and more than half were admitted to the urban teaching hospitals except elderly males (42.8%). Most of the adults were funded by private insurance, following by Medicaid, but the elderly operations were mainly funded by Medicare. Among participants who underwent an operation, the rates of alcohol abuse, coagulopathy, liver disease, fluid/electrolyte disorders, solid tumor, and weight loss were significantly higher when compared to participants who did not undergo an operation, regardless the age. In addition, among both the adult and elderly group who underwent operation, the rate of deficiency anemias, chronic blood loss, metastatic cancer, and renal failure, were significantly higher than in the group without operation. In addition, among the elderly group who underwent an operation, the rate of obesity was significantly higher than in the group without operation (Table 4).

Table 4. Characteristics of emergency admitted patients with the primary diagnosis of acute and subacute necrosis of liver (NIS 2005-2014). Data were stratified according to operation status.

		Adult, N (%)			Elderly, N (%)		
		No Operation	Operation	P	No Operation	Operation	P
All Cases		8,711 (83.1)	1,774 (16.9)		2,756 (85.9)	451 (14.1)	
Sex, Female		4,771 (54.8)	787 (44.4)	**<0.001**	1,511 (54.8)	194 (43)	**<0.001**
Race	**White**	4,899 (66.0)	1,062 (68.2)	**0.007**	1,797 (75.0)	308 (77.4)	0.8
	Black	1,076 (14.5)	170 (10.9)		219 (9.1)	28 (7.0)	
	Hispanic	859 (11.6)	182 (11.7)		182 (7.6)	30 (7.5)	
	Asian/Pacific Islander	229 (3.1)	52 (3.3)		105 (4.4)	17 (4.3)	
	Native American	89 (1.2)	24 (1.5)		16 (0.7)	2 (0.5)	
	Other	272 (3.7)	68 (4.4)		77 (3.2)	13 (3.3)	
Income Quartile	**Quartile 1**	2,700 (31.9)	479 (27.9)	**0.004**	783 (29.0)	115 (26.0)	0.052
	Quartile 2	2,245 (26.5)	454 (26.4)		715 (26.5)	100 (22.6)	
	Quartile 3	1,934 (22.9)	434 (25.3)		637 (23.6)	125 (28.3)	
	Quartile 4	1,583 (18.7)	351 (20.4)		562 (20.8)	102 (23.1)	
Insurance	**Private Insurance**	3,462 (39.9)	714 (40.4)	**<0.001**	229 (8.3)	48 (10.6)	0.4
	Medicare	1,186 (13.7)	239 (13.5)		2,409 (87.6)	388 (86.0)	
	Medicaid	2,047 (23.6)	500 (28.3)		61 (2.2)	7 (1.6)	
	Self-Pay	1,411 (16.3)	210 (11.9)		28 (1.0)	3 (0.7)	
	No Charge	113 (1.3)	18 (1.0)		3 (0.1)	0 (0)	
	Other	464 (5.3)	86 (4.9)		21 (0.8)	5 (1.1)	
Hospital Location	**Rural**	1,130 (13.0)	128 (7.2)	**<0.001**	504 (18.3)	40 (8.9)	**<0.001**
	Urban: Non-Teaching	2,961 (34.0)	521 (29.4)		1,073 (38.9)	152 (33.7)	
	Urban: Teaching	4,620 (53.0)	1,125 (63.4)		1,179 (42.8)	259 (57.4)	
COMORBIDITIES	**AIDS**	115 (1.3)	19 (1.1)	0.4	1 (0.0)	1 (0.2)	0.3
	Alcohol Abuse	2,163 (24.8)	797 (44.9)	**<0.001**	203 (7.4)	67 (14.9)	**<0.001**
	Deficiency Anemias	1,576 (18.1)	509 (28.7)	**<0.001**	660 (23.9)	127 (28.2)	0.054
	Rheumatoid Arthritis	249 (2.9)	30 (1.7)	**0.005**	117 (4.2)	18 (4.0)	0.8

		Adult, N (%)			Elderly, N (%)		
		No Operation	Operation	P	No Operation	Operation	P
All Cases		8,711 (83.1)	1,774 (16.9)		2,756 (85.9)	451 (14.1)	
COMORBIDITIES	Chronic Blood Loss	78 (0.9)	34 (1.9)	**<0.001**	29 (1.1)	5 (1.1)	0.9
	Congestive Heart Failure	532 (6.1)	84 (4.7)	**0.025**	778 (28.2)	87 (19.3)	**<0.001**
	Chronic Pulmonary Disease	1,057 (12.1)	151 (8.5)	**<0.001**	621 (22.5)	77 (17.1)	**0.009**
	Coagulopathy	2,490 (28.6)	867 (48.9)	**<0.001**	748 (27.1)	162 (35.9)	**<0.001**
	Depression	1,130 (13.0)	168 (9.5)	**<0.001**	280 (10.2)	30 (6.7)	**0.019**
	Diabetes, Uncomplicated	995 (11.4)	222 (12.5)	0.2	677 (24.6)	107 (23.7)	0.7
	Diabetes, Chronic Complications	227 (2.6)	52 (2.9)	0.4	174 (6.3)	25 (5.5)	0.5
	Drug Abuse	1,228 (14.1)	122 (6.9)	**<0.001**	24 (0.9)	1 (0.2)	0.2
	Hypertension	2,512 (28.8)	525 (29.6)	0.5	1,745 (63.3)	245 (54.3)	**<0.001**
	Hypothyroidism	546 (6.3)	106 (6.0)	0.6	449 (16.3)	65 (14.4)	0.3
	Liver Disease	31 (0.4)	163 (9.2)	**<0.001**	9 (0.3)	27 (6.0)	**<0.001**
	Lymphoma	50 (0.6)	12 (0.7)	0.6	47 (1.7)	10 (2.2)	0.5
	Fluid/Electrolyte Disorders	4,154 (47.7)	1,160 (65.4)	**<0.001**	1,502 (54.5)	284 (63.0)	**<0.001**
	Metastatic Cancer	244 (2.8)	68 (3.8)	**0.020**	176 (6.4)	38 (8.4)	0.1
	Other Neurological Disorders	604 (6.9)	83 (4.7)	**<0.001**	242 (8.8)	32 (7.1)	0.2
	Obesity	750 (8.6)	140 (7.9)	0.3	189 (6.9)	46 (10.2)	**0.012**
	Paralysis	82 (0.9)	11 (0.6)	0.2	50 (1.8)	5 (1.1)	0.3
	Peripheral Vascular Disorders	145 (1.7)	32 (1.8)	0.7	229 (8.3)	26 (5.8)	0.060
	Psychoses	678 (7.8)	87 (4.9)	**<0.001**	90 (3.3)	7 (1.6)	**0.049**
	Pulmonary Circulation Disorders	159 (1.8)	59 (3.3)	**<0.001**	171 (6.2)	17 (3.8)	**0.041**
	Renal Failure	631 (7.2)	194 (10.9)	**<0.001**	657 (23.8)	113 (25.1)	0.6
	Solid Tumor	144 (1.7)	62 (3.5)	**<0.001**	110 (4.0)	43 (9.5)	**<0.001**
	Peptic Ulcer	3 (0.0)	0 (0)	0.4	1 (0.0)	1 (0.2)	0.3
	Valvular Disease	206 (2.4)	32 (1.8)	0.2	293 (10.6)	34 (7.5)	**0.044**
	Weight Loss	708 (8.1)	387 (21.8)	**<0.001**	307 (11.1)	101 (22.4)	**<0.001**
Invasive Diagnostic Procedure		1,459 (16.7)	595 (33.5)	**<0.001**	358 (13.0)	165 (36.6)	**<0.001**
Medical/Surgical Complication		59 (0.7)	78 (4.4)	**<0.001**	28 (1.0)	19 (4.2)	**<0.001**
Reoperation		0 (0)	136 (7.7)	**<0.001**	0 (0)	28 (6.2)	**<0.001**
Deceased		985 (11.3)	370 (20.9)	**<0.001**	516 (18.7)	101 (22.4)	0.070
		Mean (SD)	**Mean (SD)**	**p**	**Mean (SD)**	**Mean (SD)**	**P**
Age, Years		43.56 (12.55)	48.19 (10.71)	**<0.001**	75.88 (7.83)	73.66 (7.34)	**<0.001**
Modified Frailty Index Score		1.01 (1.01)	1.23 (0.94)	**<0.001**	2.00 (1.17)	1.88 (1.17)	**0.046**
Time to Invasive Diagnostic Procedure, Days		3.60 (6.26)	5.48 (6.80)	**<0.001**	3.95 (3.14)	4.62 (4.10)	0.080
Hospital Length of Stay, Days		5.28 (6.52)	12.64 (14.18)	**<0.001**	5.61 (5.04)	11.07 (10.45)	**<0.001**
Total Charges, Dollars		40,65	140,778	**<0.001**	39,058	109,467	**<0.001**
		-65,647	-215,228		-51,473	-182,462	

Risk Factors of Mortality

Multivariable logistic regression analyses were used to investigate the associations between mortality and different risk factors in emergency admitted patients with the primary diagnosis of acute and subacute necrosis of the liver. Analyses were performed in both age groups (e.g., adults and elderly) either undergoing an operation or not undergoing an operation. Backward stepwise regression was used to find the final predictors of in-hospital mortality in the adjusted model. Both multivariable models were adjusted for the following attributes of patients and hospitals: age; sex; race; income quartile; insurance; hospital location; invasive diagnostic procedure and medical/surgical complications. Time to surgery was added to the regression model built for patients with operations. Hospital length of stay in days was added to the model built for the group with no operation. Among adult patients who underwent an operation, age was the main risk factor for mortality whereas invasive diagnostic procedure was the main protective factor. Invasive diagnostic surgeries decreased the odds of mortality by 31% (Table 5). Among patients with no operation, medical/surgical complications and modified frailty index were the main risk factors for mortality in both age groups. Medical/surgical complications increased the odds of mortality by more than 2 times (2.665 in adults while 4.331 in the elderly patients). Increased hospital length of stay increased mortality in adults and decreased it in the elderly patients. Similar to operated patients, invasive diagnostic procedure was the main protective factor in non-operated patients. Being male increased the odds of mortality by about 36% among adults who did not undergo an operation (Table 5).

Table 5. Backward logistic regression analysis to evaluate the associations between mortality and different factors in emergency admitted patients with the primary diagnosis of acute and subacute necrosis of liver and undergoing an operation. Mortality was the dependent variable, NIS 2005-2014.

	Adults with Operation		Elderly with Operation	
	N = 1,771	R^2 = 0.015	N = 451	R^2 = 0.009
	OR (95% CI)	P	OR (95% CI)	P
Age, Years	1.016 (1.004, 1.027)	**0.006**	0.988 (0.958, 1.020)	0.5
Invasive Diagnostic Procedure	0.690 (0.534, 0.890)	**0.004**	**Removed**	
Sex, Female			0.168 (0.458, 1.145)	0.2
Time to Operation, Days				
Modified Frailty Index Score				
Medical/Surgical Complication	**Removed Via Backward Elimination**		**Removed Via Backward Elimination**	
Race				
Income Quartile				
Insurance				
Hospital Location				

Table 6. Backward logistic regression analysis to evaluate the associations between mortality and different factors in emergency admitted patients with the primary diagnosis of acute and subacute necrosis of liver and not undergoing an operation. Mortality was the dependent variable, NIS 2005-2014.

	Adults Not Operated		Elderly Not Operated	
	N = 8,700	R^2 = 0.090	N = 2,755	R^2 = 0.029
	OR (95% CI)	P	OR (95% CI)	P
Hospital Length of Stay, Days	1.013 (1.004, 1.022)	**0.005**	0.966 (0.944, 0.988)	**0.003**
Medical/Surgical Complication	2.665 (1.470, 4.831)	**0.001**	4.331 (1.932, 9.705)	**<0.001**
Invasive Diagnostic Procedure	0.714 (0.586, 0.871)	**<0.001**	0.552 (0.385, 0.790)	**0.001**

	Adults Not Operated		Elderly Not Operated	
	N = 8,700	R^2 = 0.090	N = 2,755	R^2 = 0.029
	OR (95% CI)	P	OR (95% CI)	P
Modified Frailty Index Score	1.168 (1.092, 1.249)	**<0.001**	1.201 (1.104, 1.306)	**<0.001**
Age, Years	1.046 (1.039, 1.053)	**<0.001**	**Removed Via**	
Sex, Female	0.638 (0.556, 0.731)	**<0.001**	**Backward**	
Race	**Removed Via**		**Elimination**	
Income Quartile	**Backward**			
Insurance	**Elimination**			
Hospital Location				

Discussion

This study sought to investigate risk factors for mortality among patients admitted with a diagnosis of acute or subacute liver necrosis in the US. Through an analysis of the 2005-2014 NIS dataset containing 10,476 individual cases of acute or subacute liver necrosis, this study was able to generate new insights regarding risk factors associated with mortality among liver necrosis patients at the U.S. population level. Our study revealed several important findings. Firstly, elderly patients had approximately 6% higher rate of mortality when compared to adult patients. Additionally, increased hospital length of stay was shown to be correlated with mortality rates, and this correlation differed among different age groups (e.g., adults vs. elderly). Furthermore, invasive diagnostic procedures had a protective role for mortality among patients. Finally, marked differences in patient outcomes based on gender were also noted, with a diagnosis of acute or subacute liver necrosis being associated with a disproportionately higher risk of death for men compared to women, and significant differences in the presence of specific comorbidities between genders.

Age Differences

Increased age was shown to be a risk factor for mortality among patients. In line with previous literature,[20-22] elderly patients in our sample had a higher mortality rate (19%) compared to adult patients' mortality rate (13%). This difference in mortality rates among age groups may be explained by the presence of different comorbidities in the elderly patients as compared to adult patients. A comparison between age groups highlighted the increased prevalence of behavioral risk factors, such as alcohol and drug use, among younger liver necrosis patients. On the other hand, liver necrosis in elderly patients tended to be correlated with a variety of medical comorbidities including congestive heart failure, chronic pulmonary disease, and cancer. Furthermore, our findings showed that among both the adult and elderly age groups, several comorbidities are correlated with a higher incidence of death, the most prominent of which are fluid/electrolyte disorders, congestive heart failure, coagulopathy, cancer, weight loss and renal failure. The prevalence of certain comorbidities among liver necrosis patients across different age reported in this study are consistent with previous findings in the literature, including findings reported by Yorke[23] regarding thyroid disorders and liver dysfunction, as well as Kim et al.'s research on aging and liver disease.[24] Work by Xanthopolous et al.[11] reported similar correlations between liver dysfunction, coagulopathy, heart failure and mortality, while an earlier study by Wilkinson et al.[25] demonstrated the high prevalence of fluid/electrolyte disorders and renal failure in patients with fulminant liver failure. The concordance of this study's findings with the broader scientific literature is not surprising given the extent of general medical knowledge on the topic, but it does serve to reinforce the validity of the NIS dataset and the chosen analytical framework.

Hospital Length of Stay

Among our analyzed sample, the HLOS among adults and elderly population was similar, around 6.5 and 6.4 days, respectively. Moreover, HLOS was shown to be associated with mortality rates differently among adults and elderly without an operation. Among adults, increased HLOS was shown to be associated with increased mortality rates. The risk of mortality increased by 1.3% for every extra day spent at the hospital for adults. These findings are consistent with the literature, where previous research has shown that prolonged HLOS is associated

with an increased risk of mortality among hospitalized patients.[20, 26-28] This is likely due to several factors, including the development of complications during extended hospitalization, such as infections or blood clots, as well as a decline in physical and cognitive function due to bed rest. For instance, Elola-Olaso et al., demonstrated the association of prolonged hospital length of stay with surgical site infection among a sample of 2332 patients who underwent hepatectomy.[29] Similarly, among another sample of patients who underwent liver resection, nosocomial infections were associated with increased length of hospital stay.[30] Additionally, prolonged HLOS may also indicate a delay in diagnosis or treatment, which can negatively impact patient outcomes. In a retrospective review of patients undergoing resection for hepatocellular carcinoma (HCC), Prolonged (>10 days) HLOS was independently associated with impaired hepatic function and pre-existing morbidities.[31]

Despite those findings, our results indicated that increased HLOS was a protective factor against mortality for elderly patients. For every extra day spent at the hospital, the risk of mortality decreased by 3.4% for elderly patients among our sample. These findings can be explained by the prevalence of medical comorbidities among elderly patients that require further care and management, including congestive heart failure, chronic pulmonary disease, and cancer. In such cases, Increased hospital length of stay may lead to better mortality outcomes because it allows for more comprehensive and thorough care. A longer stay in the hospital can provide more opportunities for monitoring and treating complications, as well as more time for the patient to recover. Additionally, a longer stay may also allow for more time for patient education and follow-up care, which can improve outcomes after discharge.

The Role of Invasive Diagnostic Procedures

Our results indicate that among adults, regardless of their operation status, as well as elderly who did not go through an operation, invasive diagnostic procedures had a protective role in relation to mortality odds. This finding is in line with previous literature demonstrating the protective role of invasive diagnostic procedures in other conditions, including patients with emergent paralytic ileus and rectal or rectosigmoid junction malignancy.[32, 33] To the best of our knowledge, no study has investigated this relationship among patients admitted with liver diseases. Our findings provide encouraging evidence toward the continued increase in utilization of invasive diagnostic procedures. However, due to the lack of literature relating to liver necrosis patients, further research is encouraged, especially randomized control trials, to determine the efficacy invasive diagnostic procedures in comparison to traditional treatment plans among admitted liver necrosis patients.

Gender Differences

The stratified data presented in this research demonstrate that at the population level, liver necrosis can have a significantly different underlying etiology depending on a patient's biological gender. Based on all adult patients diagnosed with liver necrosis in the NIS database, females are disproportionately more likely to present with depression, psychoses, and hypothyroidism than adult men, who are in turn more likely to present with hypertension, coagulopathy, and drug and alcohol abuse. Possibly due in part to these differing comorbidity patterns, mortality rates following a diagnosis of liver necrosis also appear to be skewed based on gender. Of all the adult patients in this study who died following diagnosis, only 42.4% were female even though females comprise 53.1% of the overall sample, meaning that adult men are disproportionately more likely to die following a diagnosis of liver necrosis than women.

Many of these correlational comorbidities can be explained by the overarching health differences that exist between genders in the general population. However, the significant difference in mortality, along with the finding that males are more likely to receive surgical intervention following diagnosis, raises questions about how certain comorbidities may contribute to a more severe pathological progression of liver necrosis in different demographic groups. Further research is required to develop a thorough understanding of these epidemiological patterns. In particular, the marked gender difference in the prevalence of alcohol and drug use and its potential association with more severe liver necrosis may represent a high-value target for future study. A deeper evidence base on the intersection of these topics would allow for the development of more effective public health interventions for addressing these behavioral risk factors and improving health outcomes.[34]

Public Health Implications

This study's value does not come from its concordance with existing knowledge but rather from the scale and scope of its dataset and analysis and its presentation

of a range of correlational comorbidities for liver necrosis that surpasses the breadth of any earlier work on the topic. The wide range of information presented here can not only serve as a foundational starting point for future research on liver necrosis and its risk factors but also as a catalyst for several valuable avenues of discussion. These include a consideration of current public health policy based on comorbidity differences between genders, the implications of aging and comorbidity prevalence for clinical best practices, and the economic relevance of reducing mortality from liver necrosis.

The results of this study provide important insights into the progression of liver necrosis across different groups with different comorbidities, which may have further implications for best practices in the clinical setting. As an example, the finding that in the rate of obesity in elderly patients who required surgical intervention was significantly higher than among elderly patients who did not receive surgery highlights the possible value of emphasizing exercise and dietary regimens for overweight elderly patients to help prevent severe disease progression requiring surgery. The correlations between increased mortality, fluid/electrolyte imbalance, invasive diagnostic procedures and medical/surgical complications are also of strong clinical relevance and demand further research efforts. With a better understanding of how these issues arise and impact disease progression, clinicians may be able to update best practices for liver necrosis management that can further reduce mortality rates.

Further development of our understanding of this topic through further research is also highly relevant from an economic perspective. This study found that adult patients who survived following a diagnosis of liver necrosis incurred significantly lower costs than those who died ($50,937 vs. $102,105). While some of these cost differences can likely be attributed to differences in mean age (43.52 vs 49.85), length of hospital stay (6.25 days vs. 8.37) and the typically increased costs observed during a person's last year of life,[35] there are likely additional preventable cost factors specific to the management of liver necrosis. This is emphasized by the observed cost difference between elderly survivors and deceased ($45,350 vs. $63,979) despite the lack of significant difference in mean age or length of hospital stay between the two groups. Although rudimentary, these figures offer an estimate of the potential economic benefit to be achieved through a reduction in mortality rates from liver necrosis and can contribute to more in-depth economic analyses that should be conducted as part of the spectrum of further research into this topic.

Strengths and limitations

This study and its methodology have several strengths, starting with its use of a large sample from a recognized and trusted dataset, the NIS. This large sample allowed for the presentation of stratified data across numerous relevant categories, which to the authors' best knowledge has not yet been done at this scale on the topic of liver necrosis. This study also implemented multivariable logistic regression analyses which provided additional insight into the data regarding risk factors and mortality. These strengths allow this study to provide standalone scientific value, although its limitations must also be considered. As a primarily descriptive study, the findings reported are a direct reflection of the available data, meaning that they can not necessarily be generalized to under-represented populations such as non-white groups or those who do not access hospital care. This study is also limited to reporting correlations found in the data and cannot offer causal explanations for the trends observed, although these trends do serve to highlight promising areas for future research with this objective in mind. Furthermore, other major limitations of this data base is that crucial data such as the cause of acute necrosis, which operative treatments, which invasive diagnostic procedures, and what treatment was used.

Conclusions

In the United States, liver necrosis represents a significant health and economic burden that appears to be growing over time. Previous studies have explored the association between liver necrosis and the presence of other specific health conditions, but none have presented such a broad analysis of the disease as is presented in this study. Using a large national dataset, the findings of this paper provide valuable insights on a wide array of comorbidities and risk factors for mortality associated with liver necrosis. The study's conclusions highlight the critical role of age, medical/surgical complications, and the protective effects of invasive diagnostic procedures, offering targeted insights for improving patient outcomes in liver necrosis care. Through its descriptive data analysis, this work provides standalone scientific value for researchers and clinicians seeking to better understand liver necrosis and offers important insight into possible directions for future research.

Acknowledgments

Conflict of Interest

The authors have no conflict of interest to declare

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