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Risk Factors of Mortality in Patients with Liver Abscess Admitted Emergently

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Abstract

Background: Despite relatively low rates, liver abscesses if untreated adequately are associated with high morbidity and mortality and are on the rise. This study was undertaken in order to determine the underlying risk factors which may impact the mortality of patients who present with liver abscesses.

Methods: This retrospective study analyzed data from the National Inpatient Sample for patients who were admitted with a primary diagnosis of abscess of the liver from 2005 to 2014. Numerous factors of interest were utilized to stratify the data in order to determine risk factors associated in in-hospital mortality using statistical tests, including a multivariable generalized additive model (GAM).

Results: A total of 1,665 patients were admitted with the primary diagnosis of liver abscess. The mean and median age were both 58 years. Males and White race accounted for the majority of the patients admitted (57.5% and 64%, respectively). Overall mortality rate was 1.7%. The generalized additive model (GAM) revealed older female patients, patients managed with operation and those hospitalized for more than three weeks had higher odds of mortality. OR (95%CI) for age, female gender and operation were 1.07 (1.03, 1.10), 3.99 (1.56, 9.68), and 3.99 (1.71, 9.31), respectively. The estimated degree of freedom for hospital length of stay was 4.66 (P=0.01) which indicated a significant, non-linear association between mortality and hospital length of stay with the highest odds of mortality for patients hospitalized more than three weeks. Comorbidities that were flagged as possible risk factors included coagulopathy, diabetes (chronic complications), liver disease, and solid tumor.

Conclusion: The odds of mortality rate in patients with liver abscesses was 4 times higher in women than in men, and also it increased by 7% for every year increase in age. The odds of mortality increased significantly after three weeks of hospitalization. The odds of mortality were 4 times higher in those who underwent operative treatment as compared to those treated non-surgically.

Keywords: Liver abscess, morbidity, mortality, non-operative management, operative management, National Inpatient Sample, generalized additive model (GAM).

INTRODUCTION

Liver abscesses can be attributed to liver injuries, ischemia, or nearby bacterial, fungal, or parasitic infections.[1] Symptoms associated with this condition can include but are not limited to, fever, chills, upper right quadrant pain, nausea, and fatigue.[2] Liver abscesses are divided into different categories depending on the original cause, with polymicrobial pyogenic liver abscesses being the most prevalent type of liver abscess seen here in the United States.[1] Amebic liver abscess is more common in underdeveloped countries and also, in immigrants in developed countries, especially in refugees. Although one of the most common underlying causes today is biliary tract disease, there are other contributing factors that could increase the risk.

Despite being relatively uncommon (2.3 cases per 100,000 people),[1] liver abscess is associated with significant morbidity and mortality in untreated patients.[2] This has made it a growing concern for the healthcare system to identify and treat this condition. Owing to the variety of causes and complications associated with liver abscesses, they are best treated by an interdisciplinary team approach. Therefore, it is important to elucidate the risk factors associated with liver abscess mortality in order to minimize hospital stay and waste of resources, as well as streamline treatment efficiency.

Previous studies have noted that liver abscesses occur more frequently in men and that adults aged 40-60 are more susceptible to developing liver abscesses without any sort of inducing trauma.[1] Other risk factors associated with liver abscesses include diabetes, cirrhosis, immunocompromised states, and individuals with proton pump inhibitor usage.[1] Risk factors for amebic liver abscess which has a high mortality rate, include recent travel to a tropical region, alcoholism, immunosuppression, including HIV/AIDS infection, cancer, malnutrition, pregnancy and old age.[1]

While have been major technological advances in the diagnosis and management of liver abscesses, it is still unclear which form of treatment is the most favorable: operation (surgical), minimally invasive diagnostic/therapeutic procedure (non-surgical), or non-invasive treatment (radiological drainage). In the past, most cases were treated surgically, but today less invasive percutaneous and laparoscopic procedures are more common unless other complications arise. In rare circumstances, patients can also be treated solely with long-term antibiotics.[3]

Without adequate and timely treatment, liver abscesses can lead to sepsis, hepatic failure, and multiorgan failure, all of which have a high death rate. Proper identification of risk factors is key to detecting liver abscesses in the early stages before more complications arise leading to surgery or death. This study aims to identify these factors in patients admitted with a primary diagnosis of liver abscess. We specifically analyzed several factors including demographics, comorbidities, operative status, etc. with the purpose of improving outcomes for individuals diagnosed with a liver abscess.

METHODS

This study examined data from the National Inpatient Sample (NIS) repository for patients who were admitted with a primary diagnosis of abscess of the liver (ICD-9 code 572.0) from 2005-2014. The gathered information consisted of demographics (age, gender, race), income quartile (quartiles 1-4), insurance status (private insurance, Medicare, Medicaid, self-pay, no charge, other), hospital location (rural, urban teaching, urban non-teaching), and comorbidities outlined in Table 1.

Datta Analysis

The data were analyzed via stratification based on different factors of interest including sex, outcome (survived vs. deceased), and operation status (operation vs. no operation). After stratifying the data, statistical indicators were employed to pose our findings in tables that display the percentage for categorical variables and mean and standard deviation/confidence interval (95%) for continuous variables. The analysis utilized a chi-squared test and t-test, respectively. To evaluate the numerous risk factors when assessing mortality, univariable logistic regression analyses were constructed. Since hospital length of stay had non-linear association with mortality, a multivariable generalized additive model was built and the factors adjusted for included age, sex, time to operation (days), invasive diagnostic procedure, race, income quartile, insurance, hospital location, and comorbidities. For the above analyses, statistical significance was deemed as a p-value less than 0.05. R was used to complete this analysis.

RESULTS

In this sample population, 1,665 patients were admitted with a primary diagnosis of liver abscess. The mean and median age were both 58 years. Males and White race accounted for the majority of the patients admitted (57.5% and 64%, respectively). Overall mortality rate was 1.7%. In Table 1, factors were stratified by sex and compared. A significant proportion of both male and female populations self-identified as White. There was also a significant difference in the type of insurance used by the male and female populations. The majority of males used private insurance while the majority of females used Medicare. However, the data reveals no significant difference of income quartile between men and women. Additionally, of the 29 comorbidities analyzed, male patients were significantly more likely to present with alcohol or drug abuse. On the other hand, female patients were significantly more likely to present with deficiency anemias, chronic blood loss, depression, hypertension, hypothyroidism, and obesity than male patients. In this population sample, there was also a significant difference in average age between males and females. The average age was 55 years old for male patients and 62 years for female patients. Finally, the analysis also showed that the hospital length of stay was also significantly longer for female patients than for male patients.

Table 1. Characteristics of patients admitted with the primary diagnosis of liver abscess. Data was stratified according to sex categories, NIS 2005-2014.

Patient Characteristics, N=1,660		**N (%)**		
		Male	**Female**	***P***
All Cases		954 (57.5%)	706 (42.5%)	
Race	**White**	456 (61.7%)	347 (67.1%)	**0.03**
	Black	89 (12%)	61 (11.8%)	
	Hispanic	110 (14.9%)	71 (13.7%)	
	Asian/Pacific Islander	40 (5.4%)	27 (5.2%)	
	Native American	8 (1.1%)	1 (0.2%)	
	Other	36 (4.9%)	10 (1.9%)	
Income Quartile	**Quartile 1**	250 (27%)	201 (28.9%)	0.3
	Quartile 2	211 (22.8%)	176 (25.3%)	
	Quartile 3	229 (24.7%)	163 (23.5%)	
	Quartile 4	236 (25.5%)	155 (22.3%)	
Insurance	**Private Insurance**	430 (25.9%)	240 (14.5%)	**0.001**
	Medicare	295 (17.8%)	323 (19.5%)	
	Medicaid	70 (4.2%)	69 (4.2%)	
	Self-Pay	96 (5.8%)	42 (2.5%)	
	No Charge	16 (1%)	8 (0.5%)	
	Other	47 (2.8%)	23 (1.4%)	

Hospital Location	**Rural**	65 (6.8%)	50 (7.1%)	0.8
	Urban: Non-Teaching	412 (43.2%)	294 (41.6%)	
	Urban: Teaching	477 (50.0%)	362 (51.3%)	
Comorbidities	**AIDS**	3 (0.3%)	1 (0.1%)	0.5
	Alcohol Abuse	66 (6.9%)	11 (1.6%)	**0.001**
	Deficiency Anemias	238 (24.9%)	242 (34.3%)	**0.001**
	Rheumatoid Arthritis	17 (1.8%)	21 (3.0%)	0.1
	Chronic Blood Loss	5 (0.5%)	15 (2.1%)	**0.003**
	Congestive Heart Failure	50 (5.2%)	48 (6.8%)	0.2
	Chronic Pulmonary Disease	117 (12.3%)	102 (14.4%)	0.2
	Coagulopathy	65 (6.8%)	37 (5.2%)	0.2
	Depression	53 (5.6%)	68 (9.6%)	**0.002**
	Diabetes, Uncomplicated	180 (18.9%)	123 (17.4%)	0.4
	Diabetes, Chronic Complications	20 (2.1%)	11 (1.6%)	0.4
	Drug Abuse	25 (2.6%)	5 (0.7%)	**0.004**
	Hypertension	350 (36.7%)	329 (46.6%)	**0.001**
	Hypothyroidism	40 (4.2%)	89 (12.6%)	**0.001**
	Liver Disease	5 (0.5%)	2 (0.3%)	0.4
	Lymphoma	7 (0.7%)	3 (0.4%)	0.4
	Fluid/Electrolyte Disorders	264 (27.7%)	259 (36.7%)	**0.001**
	Metastatic Cancer	58 (6.1%)	43 (6.1%)	0.9
	Other Neurological Disorders	27 (2.8%)	31 (4.4%)	0.08
	Obesity	34 (3.6%)	49 (6.9%)	**0.002**
	Paralysis	6 (0.6%)	5 (0.7%)	0.9
	Peripheral Vascular Disorders	25 (2.6%)	20 (2.8%)	0.8
	Psychoses	16 (1.7%)	14 (2.0%)	0.6
	Pulmonary Circulation Disorders	6 (0.6%)	6 (0.8%)	0.6
	Renal Failure	52 (5.5%)	37 (5.2%)	0.8
	Solid Tumor	54 (5.7%)	36 (5.1%)	0.6
	Peptic Ulcer	1 (0.1%)	3 (0.4%)	0.2
	Valvular Disease	26 (2.7%)	31 (4.4%)	0.06
	Weight Loss	77 (8.1%)	74 (10.5%)	0.09
Other Factors	**Invasive Diagnostic Procedure**	836 (50.4%)	602 (36.3%)	0.2
	Surgical Procedure	158 (9.5%)	110 (6.6%)	0.6
	Invasive or Surgical Procedure	854 (51.4%)	616 (37.1%)	0.1
	Deceased	8 (0.84%)	21 (3%)	**0.001**
		Mean (SD)	**Mean (SD)**	**P**
	Age, Years	54.82 (17.47)	61.81 (18.11)	**0.001**
	Time to Invasive Diagnostic Procedure, Days	5.70 (0.53)	6.62 (0.71)	0.3
	Time to Surgical Procedure, Days	5.70 (0.53)	6.62 (0.71)	0.3
	Hospital length of Stay, Days	10.21 (8.13)	11.42 (10.40)	0.008
	Total Charges, Dollars	50,138	55,141	0.1

Table 2. Characteristics of patients admitted with the primary diagnosis of liver abscess. Data was classified according to outcome categories, NIS 2005-2014.

Patient Characteristics, N=1,664		N (%)		
		Survived	Deceased	*P*
All Cases		1635 (98.3%)	29 (1.7%)	
Sex	Female	684 (97%)	21 (3%)	**0.001**
	Male	946 (99.2%)	8 (0.8%)	
Race	White	785 (64%)	18 (72%)	0.7
	Black	147 (13%)	3 (12%)	
	Hispanic	177 (17%)	4 (16%)	
	Asian/ Pacific Islander	67 (5.3%)	0 (0%)	
	Native American	9 (0.7%)	0 (0%)	
	Other	46 (3.7%)	0 (0%)	
Income Quartile	Quartile 1	440 (27.1%)	12 (41%)	0.4
	Quartile 2	381 (23.4%)	6 (21%)	
	Quartile 3	386 (23.8%)	6 (21%)	
	Quartile 4	389 (23.9%)	5 (17%)	
Insurance	Private Insurance	667 (40.1%)	7 (24%)	**0.001**
	Medicare	596 (35.8%)	22 (76%)	
	Medicaid	139 (8.4%)	0 (0%)	
	Self-Pay	137 (8.2%)	0 (0%)	
	No Charge	24 (1.4%)	0 (0%)	
	Other	71 (4.3%)	0 (0%)	
Hospital Location	Rural	113 (6.8%)	2 (7%)	0.8
	Urban: Non-Teaching	695 (41.8%)	11 (38%)	
	Urban: Teaching	827 (49.7%)	16 (55%)	
Comorbidities	AIDS	4 (0.2%)	0 (0%)	0.8
	Alcohol Abuse	75 (4.5%)	2 (7%)	0.5
	Deficiency Anemias	472 (28.4%)	8 (27.6%)	0.9
	Rheumatoid Arthritis	36 (2.2%)	2 (7%)	0.09
	Chronic Blood Loss	20 (1.2%)	0 (0%)	0.5
	Congestive Heart Failure	93 (5.6%)	5 (17.2%)	**0.009**
	Chronic Pulmonary Disease	212 (12.7%)	7 (24%)	0.08
	Coagulopathy	97 (5.8%)	5 (17.2%)	**0.01**
	Depression	118 (7.1%)	3 (10.3%)	0.5
	Diabetes, Uncomplicated	299 (18.3%)	4 (14%)	0.5
	Diabetes, Chronic Complications	27 (1.6%)	4 (14%)	**0.001**
	Drug Abuse	29 (1.7%)	1 (3.4%)	0.5
	Hypertension	663 (39.8%)	16 (55%)	0.1
	Hypothyroidism	108 (7.7%)	1 (3.4%)	0.4
	Liver Disease	6 (0.4%)	1 (3.4%)	**0.01**
	Lymphoma	10 (0.6%)	0 (0%)	0.6
	Fluid/Electrolyte Disorders	508 (30.5%)	15 (52%)	**0.02**
	Metastatic Cancer	100 (6%)	1 (3.4%)	0.5
	Other Neurological Disorders	55 (3.3%)	3 (10.3%)	**0.04**
	Obesity	83 (5%)	0 (0%)	0.2

Comorbidities	Paralysis	11 (0.7%)	0 (0%)	0.6
	Peripheral Vascular Disorders	45 (2.7%)	0 (0%)	0.4
	Psychoses	30 (1.8%)	0 (0%)	0.4
	Pulmonary Circulation Disorders	11 (0.7%)	1 (3.4%)	0.08
	Renal Failure	84 (5%)	5 (17.2%)	**0.004**
	Solid Tumor	83 (5%)	7 (24%)	**0.001**
	Peptic Ulcer	4 (0.2%)	0 (0%)	0.8
	Valvular Disease	54 (3.2%)	3 (10.3%)	**0.04**
	Weight Loss	146 (8.8%)	5 (17.2%)	0.1
Other Factors	Invasive Diagnostic Procedure	1411 (84.8%)	28 (96%)	0.1
	Surgical Procedure	255 (15.3%)	10 (34.5%)	**0.006**
	Invasive or Surgical Procedure	1443 (86.7%)	28 (96%)	0.1
		Mean (SD)	Mean (SD)	P
	Age, Years	57.52 (18.03)	73.17 (11.17)	0.001
	Time to Invasive Diagnostic Procedure, Days	2.34 (3.12)	2.43 (2.45)	0.9
	Time to Surgical Procedure, Days	5.88 (6.40)	10.40 (5.68)	**0.03**
	Hospital length of Stay, Days	10.60 (8.94)	16.72 (17.24)	**0.001**
	Total Charges, Dollars	51,241	110,825	**0.001**

Table 3. Characteristics of patients admitted with the primary diagnosis of liver abscess. Data was stratified according to operation status, NIS 2005-2014.

Patient Characteristics, N=1,665		N (%)		
		Not Operated	Operated	*P*
All Cases		1397 (83.9%)	268 (16.1%)	
Sex	Female	596 (43%)	110 (41%)	0.6
	Male	796 (57%)	158 (59%)	
Race	White	661 (63.5%)	142 (66%)	0.1
	Black	118 (11.4%)	32 (15%)	
	Hispanic	161 (15.5%)	20 (9.3%)	
	Asian/ Pacific Islander	57 (5.5%)	10 (4.8%)	
	Native American	6 (0.5%)	3 (1.4%)	
	Other	38 (3.7%)	8 (3.7%)	
Income Quartile	Quartile 1	380 (28%)	72 (27%)	0.3
	Quartile 2	314 (23%)	73 (28%)	
	Quartile 3	338 (25%)	55 (21%)	
	Quartile 4	332 (24%)	62 (24%)	
Insurance	Private Insurance	564 (40.5%)	110 (41%)	0.06
	Medicare	536 (38.5%)	82 (30.5%)	
	Medicaid	107 (7.7%)	32 (11.9%)	
	Self-Pay	114 (8.2%)	24 (9%)	
	No Charge	19 (1.4%)	5 (1.9%)	
	Other	56 (4%)	15 (5.6%)	
Hospital Location	Rural	98 (7%)	17 (6.3%)	0.4
	Urban: Non-Teaching	602 (43.1%)	105 (39.2%)	
	Urban: Teaching	697 (49.9%)	146 (54.5%)	

	AIDS	4 (0.3%)	0 (0%)	0.4
	Alcohol Abuse	66 (4.7%)	11 (4.1%)	0.6
	Deficiency Anemias	399 (29%)	81 (30%)	0.6
	Rheumatoid Arthritis	32 (2.3%)	6 (2.2%)	0.9
	Chronic Blood Loss	16 (1.1%)	4 (1.5%)	0.6
	Congestive Heart Failure	71 (5.1%)	27 (10.1%)	**0.001**
	Chronic Pulmonary Disease	178 (12.7%)	41 (15.3%)	0.2
	Coagulopathy	82 (5.9%)	20 (7.5%)	0.3
	Depression	107 (7.7%)	14 (5.2%)	0.2
	Diabetes, Uncomplicated	252 (18%)	51 (19%)	0.7
	Diabetes, Chronic Complications	24 (1.7%)	7 (2.6%)	0.3
	Drug Abuse	25 (1.8%)	5 (1.9%)	0.9
	Hypertension	579 (41.4%)	100 (37.3%)	0.2
	Hypothyroidism	116 (8.3%)	13 (4.9%)	0.053
Comorbidities	**Liver Disease**	1 (0.1%)	6 (2.2%)	**0.001**
	Lymphoma	8 (0.6%)	2 (0.7%)	0.7
	Fluid/Electrolyte Disorders	432 (30.9%)	91 (34%)	0.3
	Metastatic Cancer	78 (5.6%)	23 (8.6%)	0.06
	Other Neurological Disorders	45 (3.2%)	13 (4.9%)	0.2
	Obesity	74 (5.4%)	9 (3.4%)]	0.2
	Paralysis	8 (0.5%)	3 (1.1%)	0.3
	Peripheral Vascular Disorders	41 (2.9%)	4 (1.5 %)	0.2
	Psychoses	24 (1.7%)	6 (2.2%)	0.5
	Pulmonary Circulation Disorders	7 (0.5%)	5 (1.9%)	**0.01**
	Renal Failure	65 (4.7%)	24 (9%)	**0.004**
	Solid Tumor	82 (5.9%)	8 (3%)	0.06
	Peptic Ulcer	4 (0.3%)	0 (0%)	0.4
	Valvular Disease	40 (2.9%)	17 (6.3%)	**0.004**
	Weight Loss	109 (7.8%)	42 (15.7%)	**0.001**
	Deceased	18 (1.30%)	11 (4.1%)	**0.004**
	Invasive Diagnostic Procedure	1204 (72.3%)	236 (88%)	0.4
		Mean (SD)	**Mean (SD)**	**P**
Other Factors	**Age, Years**	58.11 (18.14)	56 (17.58)	0.1
	Time to Invasive Diagnostic Procedure, Days	2.27 (3.03)	2.80 (3.54)	**0.03**
	Time to Surgical Procedure, Days	0.0 (0)	6.1156 (6.43)	**0.001**
	Hospital length of Stay, Days	9.44 (7.66)	17.34 (12.94)	**0.001**
	Total Charges, Dollars	42,572	102,379	**0.001**

In Table 2, factors were stratified by outcome (survived vs. deceased) and were then compared. Of the patients in this sample, those that survived had significantly higher rates of private insurance than those deceased. The statistical analysis showed no significant difference of race, income quartile, or hospital location between patients who survived and those who did not. A variety of comorbidities were also compared between the survivors and the deceased to possibly highlight underlying complications in treatment and outcome. Patients who survived had significantly lower frequencies of liver disease, congestive heart failure, fluid/electrolyte disorder, renal failure, diabetic chronic complications, solid tumors, valvular disease, or other neurological disorders than patients who died. Deceased patients had significantly longer hospital stays and were subsequently charged significantly higher than those who survived. Patients who survived were less likely to have a surgical procedure, however, deceased patients waited significantly longer for surgical procedures to be performed. Lastly, patients who died were also significantly older than those who survived.

Data was stratified according to operation status (operation vs. no operation) is presented in Table 3. In this data, many demographic variables such as age, sex, race, income, insurance, hospital location, and many comorbidities lacked significant differences between patients who received operations and those who did not. Some comorbidities were exceptional though. Patients who did not have an operation had significantly lower rates of congestive heart failure, pulmonary circulation disorders, liver disease, renal failure, valvular disease, and weight loss. They also had significantly shorter waits for invasive diagnostic procedures, shorter hospital length of stays, and consequently lower charges than patients who had an operation. Overall, patients who had no operation had significantly lower rates of the comorbidities mentioned above and shorter hospital length of stay and lower rate of mortality than those with operation.

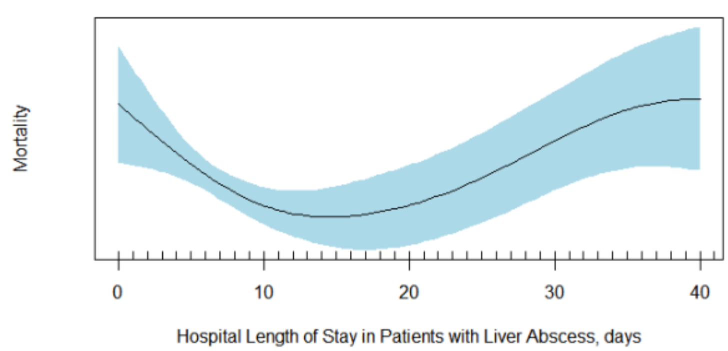
Table 4 depicts a multivariable generalized additive model used to evaluate the associations between mortality and different risk factors in patients who had a primary diagnosis of liver abscess. The model showed that patients who underwent an operation had four times higher odds of mortality than those who did not. There were also significant associations between mortality and age, sex, hospital length of stay, coagulopathies, diabetes with complications, liver disease, and solid tumors. The association in sex exemplified almost four times higher odds of mortality due to liver abscesses in women. Additionally, the association with age suggested that older patients have higher odds of mortality than younger adults. The data on the comorbidities like coagulopathy, chronically complicated diabetes, and solid tumors also implied that patients also diagnosed with these comorbidities had 4, 10- and 6.5-times higher odds of mortality when diagnosed with liver abscess than those patients without them, respectively. Specifically, for those with liver disease, the odds of mortality was 17 times higher than patients without liver disease.

Another significant variable was hospital length of stay. It exemplified a non-linear association with mortality which was U-shaped (Figure 1). The relationship's estimated degree of freedom (EDF) was 4.66 (P=0.01). As it clears in Figure 1, the risk of mortality was highest before day 10 and after day 20. There was a sharp drop in in-hospital mortality during the time period between 10 and 20 days, with a steady rise after this point. However, after three weeks the model suggests a significant increase in the risk of mortality for these patients.

Table 4. Associations between mortality and various factors in patients admitted with a primary diagnosis of liver abscess, analyzed by multivariable generalized additive model. Mortality was the dependent variable.

Patient Characteristics, N=1,559	OR (95%CI)	P
No Operation	3.99 (1.71, 9.31)	**0.001**
Age, Years	1.07 (1.03, 1.10)	**0.001**
Female Sex	3.99 (1.56, 9.68)	**0.003**
Coagulopathy	4.16 (1.40, 12.30)	**0.01**
Diabetes, Chronic Complications	10.24 (2.87, 36.58)	**0.001**
Liver Disease	17.48 (1.73, 176.38)	**0.015**
Solid Tumor	6.51 (2.43, 17.42)	**0.001**
Hospital Length of Stay, Days	EDF = 4.66	**0.01**
Race	**Removed**	
Income Quartile		
Insurance	**Via**	
Hospital Location		
Invasive Diagnostic Procedure	**Backward**	
Drug Abuse		
All Other Associated Comorbidities	**Elimination**	

Figure 1. Association of in-hospital mortality and hospital length of stay in patients admitted with a primary diagnosis of liver abscess in NIS database, 2005-2014, according to generalized additive model (GAM). The estimated degree of freedom of 4.66 (P=0.01) indicated a significant, non-linear association between in-hospital mortality and hospital length of stay after adjusting for age, gender, race, income quartile, health care insurance, hospital location and comorbidities. The odds of mortality increased significantly after three weeks of hospitalization. Age, sex, operation status and several comorbidities were also significantly associated with in-hospital mortality in multivariable GAM regression.



DISCUSSION

Age and Morality

This retrospective study, evaluation of risk factors for mortality in patients with liver abscesses by using data from the National Inpatient Sample (NIS) 2005-2014, found that for every year's increase in age, there is a 7% increase in odds of mortality. Although rates of liver abscess are relatively low in the United States, mortality rates in those presenting with liver abscesses continue to be a concern for healthcare professionals. As seen in previous studies, an increase in age has been shown to be correlated with higher mortality rates. For example, a retrospective study that included 8,424 patients admitted between 2008 and 2013 demonstrated that the rate of mortality increased with an increase in age; the mortality rate was approximately 4.8 times higher when patients were older than 60 years of age.[4] Similar to Poovorawan et al., we also noted an increase in mortality with an increase in age.

Sex and Mortality

Our study showed a higher prevalence of liver abscesses in men but higher mortality rates in women. Previous studies have solidified that liver abscesses, especially amebic liver abscesses, occur more in males.[5] According to a research study with mice, the higher prevalence in male mice is due to higher levels of testosterone in male mice.[6] When testosterone was removed from male mice the size of liver abscesses observed significantly decreased, while testosterone added to female mice caused higher occurrences of liver abscesses. Testosterone suppresses CDK4- natural killer T cells, which allows the *Entamoeba histolytica* infection to proliferate and results in a liver abscess in the host.[7]

Operation and Mortality

For patients who did undergo an operation, the odds of mortality in the current study was found to be almost four times higher than that in patients who did have an operation. The high rates of mortality in surgically managed patients are similarly exhibited in other studies, which aimed to evaluate the best treatments for liver abscesses. A review article on mortality trends in patients with liver abscesses noted numerous other studies in their discussion, most found a decreased mortality rate in those who were treated via percutaneous drainage as compared to surgical intervention.[8] However, a few other studies had contradictory findings when assessing the link between operation and mortality. For example, in a retrospective study, researchers found that there were more chance of deaths in the non-surgical drainage group compared to the surgical drainage group.[9] Due to these conflicting conclusions, the link between operation and mortality needs further investigations.

Comorbidities and Mortality

Some comorbidities including coagulopathy, diabetes, liver disease, and solid tumors proved to be significant risk factors for mortality in our patient population. In regards to diabetes, this pre-existing condition was found to be a risk for liver abscesses, specifically for pyogenic liver abscess (PLA). Studies showed that individuals with type 2 diabetes mellitus have an increased hazard for PLA. Poor control of blood glucose levels impairs the activation of neutrophils and phagocytosis, which assists in the proliferation of pathogens in blood tissues.[10] This increases the risk of mortality in diabetic patients diagnosed with liver abscesses because the infection can more easily establish and spread. Liver disease, especially end-stage disease leading to cirrhosis, was found to have a significant correlation with liver abscess in our study. Cirrhosis is established medically as a risk factor for developing liver abscesses, as the immunodeficiency associated with cirrhosis allows for PLA to form and grow undetected.[11] Previous medical insight aligns with our findings of liver disease as an increased risk factor for mortality in liver abscess patients. Coagulopathy also arose as a significant comorbidity. Coagulopathy is a common complication of blood infection, or sepsis, which is known to be a major source of liver abscess infections.[12] This may explain our data highlighting coagulopathy as an increased risk factor for mortality in liver abscess patients. Finally, solid tumors were a significant factor in mortality in liver abscess patients. In some cases, liver abscesses are an early sign of hepato-biliary cancer.[13] Other cancers associated with liver abscesses include colorectal cancers, which, like hepatobiliary cancers, develop as solid carcinomas.[14] Due to the extensive radiation and chemotherapy regimens usually indicated for these cancers, patients may be more susceptible to severe infections, which could increase the mortality of liver abscesses.

Hospital Length of Stay and Mortality

Owing to the non-linear association between hospital length of stay (HLOS) and mortality, a multivariable analysis was conducted to adjust for additional variables like age, sex, time to operation, invasive diagnostic procedure, race, income quartile, insurance, hospital location, and comorbidities. To the best of our knowledge, this was the first published analysis of the nonlinear association between hospital length of stay and in-hospital mortality in patients with liver abscess through generalized additive regression models. The results revealed a U-shaped curve, with mortality relatively high at initial presentation, bottoming out between inpatient days 10 and 20, and rising again continuously from there. The linear relationship between HLOS and mortality demonstrated after inpatient day 20 is in line with previous literature examining these variables in patients admitted for a diverse range of emergent diagnoses including anorectal abscess, gastric/duodenal ulcers, hemorrhoids, paralytic ileus, ventral hernia, blunt chest wall trauma, rectosigmoid malignancy, and gastroparesis.[15,16,17,18,19,20,21,22,23] This may be due to the fact that patients with longer HLOS are more likely to have experienced unforeseen complications such as empyema, rupture, or sepsis. Conversely, the relatively high rate of mortality immediately after admission is probably heavily influenced by acutely decompensating patients who presented to the hospital with more advanced disease. Though the NIS data does not allow us to account for the course of disease prior to hospital admission, it can be reasonably assumed that many patients were unaware of their underlying liver abscesses, and presented only after becoming symptomatic due to worsening disease. The sharp drop in mortality between admission and inpatient day 20 may be explained by a variety of factors. A similar U-shaped association between HLOS and mortality was observed in elderly patients with colon cancer, for whom the odds of mortality increased by 1.8% per day for each additional day after inpatient day 15.[24] Similarly, patients admitted for thrombophlebitis, pancreatitis, and *C. Difficile* colitis experienced initially high rates of mortality immediately followed by periods of decreased risk, which subsequently increased linearly after day 4 for thrombophlebitis and day 6 for pancreatitis and *C. Difficile* colitis.[25,26,27] In concert with the previous literature, our study supports the idea that increased length of hospital stay, following initial stabilization after admission, is a modifiable risk factor for mortality that should be limited whenever possible.

AUTHORS' DISCLOSURES

The authors declare that there is no conflict of interest.

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