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Liver Transplantation Recipients are at Increased Risk for Hospital Acquired Conditions

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Abstract

Background: Transplant recipients are at increased risk for hospital acquired conditions (HACs) which are avoidable complications that worsen patient and hospital outcomes.

Methods: Utilizing the Nationwide Inpatient Sample, a retrospective database analysis was performed between 2002 and 2013 including adult liver transplant recipients. Liver transplant recipients were evaluated based on the presence of HACs. Multivariable analysis was performed to determine factors associated with HACs and the effect on outcomes.

Results: 60,408 liver transplant recipients were evaluated including 1,008 (1.7%) patients that experienced a HAC. The most common HAC was vascular catheter associated infection (35.2%). HACs increased yearly (aOR:1.13; 95% 1.08-1.18). HACs were associated with increased comorbidities [aOR:2.30; 95% CI: 1.69-3.13] and receiving care at small hospitals [aOR:1.84; 95% CI: 1.12-2.33]. Patients with hepatocellular carcinoma were less likely to experience a HAC [aOR:0.43; 95% CI: 0.29-0.64]. Transplant recipients with HACs had an increased risk of inpatient mortality [OR:2.53; 95% CI:1.63-3.92], longer length of stay [23.53 days; 95% CI: 16.88-30.18] and higher cost of admission [$85,052; 95% CI: $65,240-$104,863].

Conclusions: HACs after liver transplantation are increasing and are associated with increased hospital utilization and worse patient outcomes. Patients at risk of developing HACs should be intervened upon early to improve outcomes.

Keywords: Length of stay; Inpatient mortality; Cost of admission; Quality improvement; Hospital acquired conditions

Introduction

The Centers for Medicare and Medicaid Services (CMS) defined specific conditions considered to be high cost that can be reasonably prevented through the application of evidence-based guidelines. These conditions are known as hospital acquired conditions (HACs) and include 14 diagnoses: foreign object retained after surgery, air embolism, blood incompatibility, stage 3 and 4 pressure ulcers, falls and trauma, manifestations of poor glycemic control, catheter associated urinary tract infection, vascular catheter associated infections, surgical site infection following coronary artery bypass graft, surgical site infection following certain orthopedic procedures, surgical site infection following bariatric surgery for obesity, surgical site infection following cardiac implantable electronic devices, deep vein thrombosis and pulmonary embolism following certain orthopedic procedures and iatrogenic pneumothorax with venous catheterization [1].

These complications cost Medicare more than $146 million dollars a year in potentially preventable spending [2]. Given higher health care costs, longer lengths of stay, and higher rates of inpatient mortality in patients experiencing HACs, multiple incentive programs and interventions were initiated in order to minimize or prevent unnecessary complications including publicizing each hospital's complication rates and decreasing reimbursement to hospitals with the highest rates of HACs [3]. A recent study completed by the Agency for Healthcare Research and Quality determined these efforts to be successful given the number of HACs experienced in 2015 decreased by 21% saving approximately $28 billion dollars [4].

Liver transplantation is one of the most complicated surgeries performed in the United States on a regular basis [5]. Despite this complex surgery being performed on patients with decompensated cirrhosis, acute liver failure and hepatocellular carcinoma (HCC), medical and surgical advancements have improved the one year survival rate after transplantation to greater than 90% [6]. However, multiple complications are more likely to occur after liver transplantation including post-operative hemorrhage, vascular and biliary tract complications, graft dysfunction and infection. Liver transplant recipients are also at risk for HACs [7].

Previous studies have evaluated specific HACs in liver transplant recipients, specifically the risk of hospital acquired infections. Over the past 15 years, there has been a significant increase in the number of infections post transplant most of which are from nosocomial, multidrug-resistant organisms [8]. There have been no large, multicenter studies evaluating all CMS defined HACs after liver transplant.

We aim to evaluate the incidence of HACs after liver transplantation, determine patient and hospital factors associated with HACs and evaluate the effect of these complications on hospital and patient outcomes.

Methods

Data Source: A retrospective database analysis using the Nationwide Inpatient Sample (NIS) was performed between 2002 and 2013. The NIS is part of the Healthcare Cost and Utilization Project. This database represents information from over 7 million hospital discharges annually from hospitals across the United States and is one of the largest publicly available databases. Information obtained from this database includes primary and secondary diagnoses, procedures, and demographic information for the patient and the hospital [9]. This information is de-identified to protect the privacy of the patients, the physician involved in care, and the hospital in which care was received; therefore, this study is exempt from review by The Ohio State University Institutional Review Board.

Study sample

Patients were identified using the International Classification of Disease, Ninth Revision, Clinical Modification (ICD-9) codes for liver transplantation [10]. Transplant recipients were grouped based on the presence of at least one HAC. Patients were excluded if they were under the age of 18. Outcomes of Interest and Description of Variables: The primary outcome of interest was to determine the prevalence of HACs in liver transplant recipients. While CMS defines 14 conditions, only HACs relevant to liver transplant were evaluated including foreign objected retained after surgery, air embolism, blood incapability, pressure ulcer stage 3 and 4, falls and trauma, catheter associated urinary tract infection, vascular catheter associated infection, manifestations of poor glycemic control and iatrogenic pneumothorax with venous catherization. Hospital acquired conditions not evaluated in this study included surgical site infection following coronary artery bypass graft, surgical site infection following certain orthopedic procedures, surgical site infection following bariatric surgery for obesity, surgical site infection following cardiac implantable electronic devices, deep vein thrombosis and pulmonary embolism following certain orthopedic procedures

Relevant HACs were evaluated during the studied time; however, the codes for pressure ulcers were available in the NIS starting in 2008 and the codes for vascular catheter associated infections were available in the NIS starting in 2007. HACs were represented by the appropriate ICD-9 codes and these codes have been verified in previous studies. [1, 11]

Additional outcomes of interest included the association of patient and hospital factors with a higher rate of HACs. Evaluated factors included age, gender, payer, income, region care was received, presence of comorbid conditions represented by the Elixhauser comorbidities score and a diagnosis of hepatocellular carcinoma.

Finally, we aimed to evaluate the effect of HACs on hospital utilization and patient outcomes, specifically evaluating mortality, length of stay and cost of admission.

Statistical analysis

Associations between patients with and without HACs and factors of interest were evaluated using chi-square tests or t-tests, as appropriate. Multivariable logistic regression models were fit for experiencing a HAC and inpatient mortality while multivariable linear regression models were fit for length of stay and cost of admission. All models were adjusted for gender, age, race, income, payer, Elixhauser comorbidity score, hospital size, hospital type, hospital region, and HCC. The models for mortality, length of stay and cost further included whether or not the patient experienced a HAC. To evaluate if there was a significant trend in HACs over the years studied the multivariable model for HAC included year as a term in the model and interactions were examined to evaluate if the trend varied with gender, age, race, income, or payer. All analyses were performed using weighted data employing appropriate survey procedures to produce national estimates. Data was analyzed using SAS 9.4 (SAS Institute Inc. Cary, NC) and a p-value less than 0.05 was considered to be significant.

Results

A total of 59,400 patients underwent liver transplantation during the studied time. The majority of the transplant recipients were male (66.4%), 41-60 years old (65.3%), Caucasian (68.1%) and had private insurance (55.1%) (Table 1).

Hospital acquired conditions

A total of 1,008 (1.7%) transplant recipients experienced a HAC (Table 1). The majority of transplant recipients only experienced one HAC but 40 (4.9%) experienced two HACs during their admission. The most common complication was a vascular catheter associated infection with an incidence of 355. Other frequently encountered HACs included falls and traumas (269 events) and iatrogenic pneumothorax with venous catheterization (195 events) (Table 2).

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Table 1: Univariate analysis comparing patient demographics, hospital demographics and outcomes in transplant recipients with and without HACs.

	Overall (n=60,408)		No HAC (n=59,400)		HAC (n=1,008)		p-value
	n	%	n	%	n	%	
Patient / Hospital Characteristics							
Sex							0.012
Male	40,112	66.4	39,512	98.5	600	1.5	
Female	20,296	33.6	19,888	97.9	408	2	
Age							0.016
18-40	6,135	10.2	6,009	97.9	126	2.1	
41-60	39,454	65.3	38,883	98.6	570	1.5	
>60	14,819	24.5	14,508	97.9	312	2.1	
Race							0.322
White	34,516	68.1	33,962	98.4	554	1.6	
Black	4,006	7.9	3,920	97.8	87	2.2	
Hispanic	7,425	14.6	7,278	98	147	1.9	
Other	4,760	9.4	4,664	97.9	96	2	
Income quartile							0.486
First	12,577	21.5	12,358	98.3	218	1.7	
Second	14,322	24.4	14,046	98.1	277	1.9	
Third	15,390	26.3	15,162	98.5	229	1.5	
Fourth	16,304	27.8	16,052	98.5	251	1.5	
Type of insurance							0.064
Medicare	15,772	26.3	15,444	97.9	329	2.1	
Medicaid	8,237	13.7	8,083	98.1	154	1.9	
Private	33,089	55.1	32,601	98.5	488	1.5	
Other	2,906	4.8	2,873	98.9	32	1.1	
Elixhauser Comorbidity							<0.001
<3	30,519	50.5	30,196	98.9	324	1.1	
≥3	29,889	49.5	29,205	97.7	684	2.3	
Hospital Size							0.056
Small	1,425	2.4	1,381	96.9	44	3.1	
Medium	7,714	12.9	7,576	98.2	138	1.8	
Large	50,894	84.8	50,081	98.4	813	1.6	
Hospital Region							0.77
Northeast	10,032	16.6	9,892	98.6	140	1.4	
Midwest	13,265	21.9	13,030	98.2	234	1.8	
South	21,054	34.9	20,707	98.4	348	1.7	
West	16,057	26.6	15,772	98.2	286	1.8	
HCC							<0.001
Not Present	44,648	73.9	43,799	98.1	848	1.9	
Present	15,760	26.1	15,601	98.9	159	1	
Outcomes							
Mortality							<0.001
Not Present	57,281	94.9	56,387	98.4	894	1.6	
Present	3,054	5.1	2,940	96.3	114	3.7	
Length of Stay (mean, SE)	20.8	0.6	20.4	0.5	45.59	3	<0.001
Cost (mean, SE)	110,171	1,894	108,695	1,872	196,870	9,427	<0.001

HCC: Hepatocellular Carcinoma; SE: Standard Error

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Table 2: Hospital acquired conditions experienced by transplant recipients.

	Overall (n=60,408)	
Hospital Acquired Conditions	n	%
Foreign Object Retained after Surgery	39	0.06
Air Embolism	25	0.04
Blood Incompatibility	≤10	≤0.02
Pressure Ulcer Stages III & IV	62	0.1
Falls and Trauma	269	0.45
Catheter-Associated Urinary Tract Infection (UTI)	87	0.14
Vascular Catheter-Associated Infection	355	0.59
Manifestations of Poor Glycemic Control	≤10	≤0.02
Iatrogenic Pneumothorax with Venous Catheterization	195	0.32

Patient / hospital demographics associated with HACs

On univariate analysis multiple patient and hospital demographics were associated with HACs including female gender (p value 0.012), age greater than 60 years (p value 0.016), and patients without hepatocellular carcinoma (HCC) (p value <0.001) (Table 1). Greater than 3 comorbid conditions was associated with an increased risk of HACs (p value <0.001), specifically vascular disease (p value <0.001), coagulopathy (<0.001), fluid and electrolyte disorders (p value <0.001), paralysis (p value 0.009), renal failure (p value <0.001) and weight loss (p value <0.001) (Supplementary Table 1).

On multivariable analysis HACs were more likely to be seen in older patients [aOR:1.13; 95% CI1.08-1.18], patients with 3 or more comorbidities [aOR:2.30; 95% CI:1.69-3.13] and patients that received care at small hospitals [aOR:1.84; 95% CI:1.12-2.33]. Patients with HCC were less likely to experience a HAC [aOR:0.43; 95% CI: 0.29-0.64] (Table 3).

Trends in HACs over time

In 2002, less than 10 liver transplant recipients experienced a HAC; however, the number of patients with HACs increased to 145 in 2013 (p value <0.001) (Figure 1). On multivariable analysis, HACs significantly increased by year [aOR:1.13; 95% CI: 1.08-1.18]. The rising rate of HACs was not significantly different between genders, races, ages, incomes or payers (Table 3).

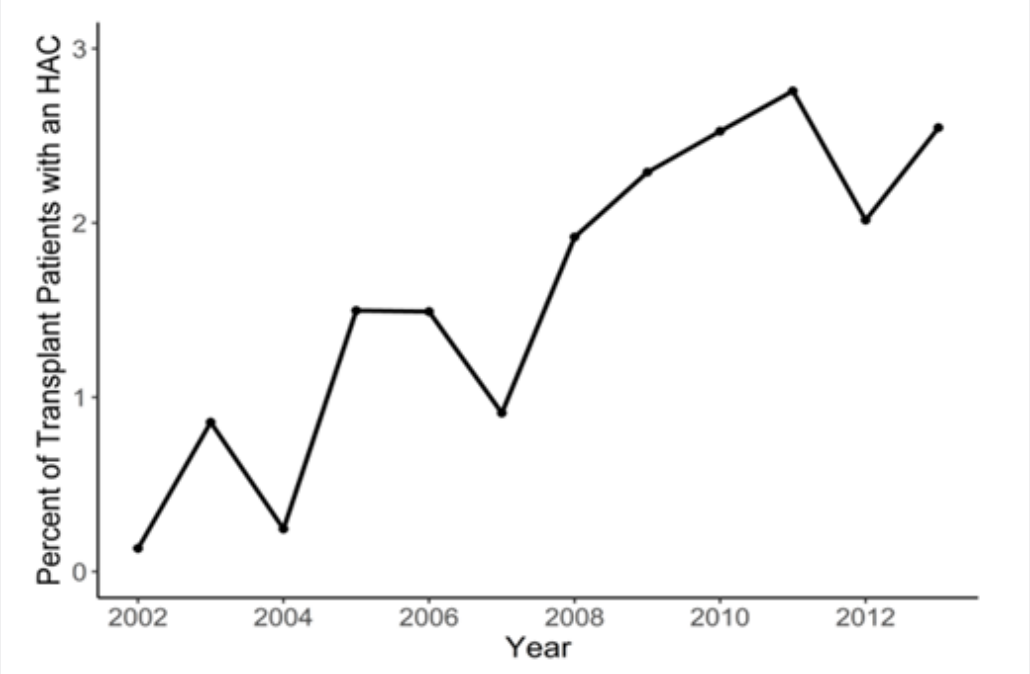

Figure 1: Trend in HACs.

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Table 3: Multivariable logistic regression model for experiencing a HAC.

	aOR	95% CI	p value
Year (1 year increase)	1.13	1.08-1.18	<0.001
Female sex	1.22	0.92-1.61	0.165
Age			**0.3**
18-40	Reference		
41-60	0.7	0.46-1.07	
>60	1.02	0.61-1.69	
Race			**0.239**
White	Reference		
Black	1.23	0.81-1.88	
Hispanic	1.17	0.84-1.63	
Other	1.63	1.00-2.68	
Income quartile			**0.425**
First	0.88	0.56-1.37	
Second	1.15	0.77-1.73	
Third	0.82	0.53-1.29	
Fourth	Reference		
Type of insurance			**0.152**
Private	Reference		
Medicare	1.21	0.91-1.62	
Medicaid	1.38	0.88-2.18	
Other	0.68	0.33-1.38	
Elixhauser Comorbidity*			**0.001**
<3	Reference		
≥3	1.71	1.25-2.34	
Hospital Size			0.092
Small	1.77	1.01-3.09	
Medium	0.91	0.63-1.33	
Large	Reference		
Hospital Type			**<0.001**
Rural /Urban Non-teaching	Reference		
Urban Teaching	1.74	1.33-2.33	
Hospital Region			**0.887**
Northeast	Reference		
Midwest	1.03	0.63-1.70	
South	0.98	0.58-1.64	
West	1.14	0.69-1.89	
Alcoholic Liver Disease	1.06	0.27-4.14	0.939
Hepatitis C	1.25	0.93-1.68	0.143
Hepatitis B	0.78	0.32-1.90	0.588
NAFLD	1.02	0.56-1.85	0.961
HCC	0.37	0.26-0.54	<0.001

aOR: Adjusted Odds Ratio; C: Confidence Intervals; HCC: Hepatocellular Carcinoma; NAFLD: Nonalcoholic Fatty Liver Disease

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HACs and the effect on patient outcomes and healthcare utilization

A total of 3,054 (5.1%) liver transplant recipients suffered inpatient mortality during the studied time including 114 (11.3%) patients that experienced a HAC (Table 1). On multivariable analysis, HACs were associated higher rates of inpatient mortality [aOR:2.53; 95% CI:1.63-3.92] (Table 4).

Table 4: Multivariable Analysis Evaluating Hospital Utilization and Patient Outcomes in Transplant Recipients Experiencing HACs.

Outcome	aOR / Coefficient	95% CI	p Value
Inpatient Mortality	2.53	1.63-3.92	<0.001
Length of Stay	23.53	16.88-0.18	<0.001
Cost of Admission	$85,052	$65,240-$104,863	<0.001

aOR: Adjusted Odds Ration; CI: Confidence Interval

The mean length of stay was 20.8 days; however, transplant recipients that experienced a HAC had a significant increase in length of stay to 45.6 days (p value <0.001) (Table 1). On multivariate analysis, HACs were associated with longer length of stay [23.5 days; 95% CI:16.88-30.18] (Table 4).

The mean cost for admission for liver transplant recipients was $110,171. Recipients that experienced a HAC had a significant higher cost of admission at $196,870 (p value <0.001) (Table 1). On multivariable analysis, HACs were associated with higher costs during admission a[$85,052; 95% CI: $65,240-$104,863] (Table 4).

Discussion

Hospital acquired conditions are associated with worse patient outcomes and increased utilization of hospital resources, including increased inpatient mortality, higher costs of admission and longer length of stay. Through careful and diligent patient care, these events should never occur during hospitalization. Given liver transplant recipients have significant underlying liver disease, more medical comorbidities and undergo complex surgical intervention, these patients are at highest risk of developing a HAC. It is crucial to evaluate and prevent HACs after this major surgical intervention in order to improve patient and graft outcomes. This study determined the rate of HACs has been increasing in the last 10 years, correlating with the increased complexity of patients undergoing liver transplantation. Once a transplant recipient experiences a HAC, they have worse outcomes. Due to the increasing number of liver transplantations being performed in critically ill patients, it is crucial to recognize and prevent HACs given their association with worse patient and hospital outcomes.

Hospital acquired complications have been extensively studied in other chronic medical conditions and after surgery, including kidney transplant. Previous studies have highlighted that HACs are more likely to occur in patients admitted with chronic medical problems given that these patients are hospitalized with higher frequency for longer periods of time and they are most susceptible to drug toxicity and infections [11]. Patients that underwent surgery, specifically more complex surgeries like renal transplant and malignancy were also at higher risk of developing HACs post operatively [12,13]. This study shows that liver transplant recipients also have a significant risk for developing HACs which is likely due to the complexity of the surgery, severity of underlying disease and medical comorbidities.

We also found that the rate of HACs significantly increased during the studied time which correlated with the increase in comorbidities in transplant recipients and patients with higher MELD scores undergoing transplant [14]. Risk factors for development of HACs included increased comorbidities and receiving care at an urban medical center. While standardized care and protocol have been initiated post operatively to minimize the risk of these complications, these known risk factors for HACs cannot be easily modified given the increase in medical problems in United States and location where transplantations are performed. Previous studies have highlighted that specific patient populations, including African American patients and those with government funded insurance were more likely to present with advanced stages of disease, metastatic HCC and less likely to undergo transplantation. However, this study determined that when African-Americans undergo liver transplantation they are not at a higher risk of HACs post operatively compared to non-minority patients [15,16]. This is likely due to diligent and standardized care initiated after transplant in order to prevent any complications, such as early removal of Foley catheters and central venous access [17,18].

This analysis also highlights that patients with HCC are less likely to experience a HAC after liver transplantation compared to patients with other indications for transplant, including cirrhosis from alcohol, viral hepatitis and nonalcoholic fatty liver disease. While the rates of HACs increased during the studied time, there was a significant decrease in HCC patients that experienced one of these complications. Liver transplant is an ideal and effective treatment for HCC within Milan Criteria [19]. In 2002, MELD exemption points were granted to patients listed for liver transplantation with the intention of offering these patients curative therapy prior to developing metastatic or more aggressive malignancy as the MELD score was thought to not accurately represent the likelihood of mortality in these patients [20,21]. These patients may be less likely to experience HACs after transplant given lower native MELD scores.

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Patient that undergo a liver transplantation and experience a HAC have increased healthcare utilization and worse patient outcomes including longer length of stay, higher cost of admission and increased risk of inpatient mortality. When these specific complications occur, such as a catheter associated urinary tract infection or vascular catheter infection, these patients will require therapy and intervention for these complications in addition to their post-operative management [22]. Unfortunately, many patients that have undergone a liver transplant have higher rates of multidrug resistant organisms which can lead to longer length of treatment with perhaps more expensive antibiotics and this would subsequently increase length of stay and cost during admission [8,23]. Hospital acquired complications lead to worse outcomes not only in patients with significant liver disease undergoing transplantation, but also patients that are admitted to the hospital for low risk procedures, such as knee arthroscopies and spinal fusions, proving that all HACs can significantly alter hospital outcomes in any patient [24]. In order to minimize unfavorable patient and hospital outcomes due to potentially preventable complications, interventions should be implemented, such as strict fall protocols with nursing staff and prompt removal of unnecessary lines and catheters to prevent infections.

This study has significant strengths. Given that HACs after liver transplantation are rare, performing this study with a large database like the NIS allows for an analysis that could not have been completed with a single center or multicenter analysis. However, the use of administrative databases does have some limitations. Patients were included in this study based on ICD-9 codes and while these codes have been verified in other studies, each patient's individual chart could not be reviewed to confirm accuracy. In addition, due to the cross-sectional analysis of this study, only associations not causation could be determined. Given laboratory results are not available in this database, we were unable to determine the patient's MELD score prior to transplantation and patients with high MELD scores and more comorbidities at the time of transplant would be at higher risk of HACs.

Conclusions

HACs after liver transplantation are increasing due to patients with higher MELD scores and more comorbidities undergoing this complex surgical intervention. Further research should be performed to determine interventions that can minimize HACs in transplant recipients given the association with worse hospital outcomes including length of stay, inpatient mortality and hospital costs.

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