Title

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Racial and ethnic disparities among patients hospitalized for acute cholangitis in the United States

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Abstract

Goals: We sought to determine whether race/ethnicity is associated with hospitalization outcomes among patients admitted with acute cholangitis.

Background: Few studies have evaluated the association between race and outcomes in patients with acute cholangitis.

Study: We analyzed United States hospitalizations from 2009–2018 using the Nationwide Inpatient Sample (NIS). We included patients ≥ 18 years old admitted with an ICD-9/10 diagnosis of cholangitis. Race/ethnicity was categorized as White, Black, Hispanic, or Other. We used multivariable regression to determine the association between race/ethnicity and in-hospital outcomes of interest, including endoscopic retrograde cholangiopancreatography (ERCP), early ERCP (<48 hours from admission), length of stay (LOS), and in-hospital mortality.

Results: Of 116,889 hospitalizations for acute cholangitis, 70% identified as White, 10% identified as Black, 11% identified as Hispanic, and 9% identified as Other. The proportion of non-White patients increased over time. On multivariate analysis controlling for clinical and sociodemographic variables, compared to White patients, Black patients had higher in-hospital mortality (aOR 1.4, 95% CI 1.2–1.6, p<0.001). Black patients were also less likely to undergo ERCP, more likely to undergo delayed ERCP, and had longer LOS (p<0.001 for all).

Conclusions: In this contemporary cohort of hospitalized patients with cholangitis, Black race was independently associated with fewer and delayed ERCP procedures, longer LOS, and higher mortality rates. Future studies with more granular social determinants of health data should further explore the underlying reasons for these disparities to develop interventions aimed at reducing racial disparities in outcomes among patients with acute cholangitis.

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Keywords

Acute cholangitis; Race; Disparity; Hospital outcomes

Introduction

Acute cholangitis is a common infection that is often treatable with antibiotics and biliary drainage, but when associated with delays in treatment, can lead to high mortality rates.[1–6] About 10,000 to 200,000 cases of acute cholangitis are diagnosed annually in the United States; with appropriate biliary drainage, the mortality rate is less than 10%.[2, 7, 8] The Tokyo Guidelines were developed in 2007 and revised in 2013 and 2018 to improve management of acute cholangitis. These guidelines recommend antibiotic therapy in patients with mild acute cholangitis but more aggressive therapy including early and urgent endoscopic retrograde cholangiopancreatography (ERCP) in patients with moderate and severe acute cholangitis respectively to improve outcomes.[1, 9] After implementation of these guidelines, inpatient admissions for acute cholangitis increased, early ERCP rates increased, and mortality associated with acute cholangitis decreased.[7]

There are well-documented racial differences in the incidence of gallstone-related disease and acute cholangitis.[2] Additionally, studies from before the publication of the Tokyo Guidelines documented evidence of racial and ethnic disparities among outcomes for patients hospitalized with acute cholangitis.[10, 11] Despite recognition of these disparities in the literature, the Tokyo Guidelines did not specifically address racial/ethnic considerations in the management of cholangitis.[1, 12] Of particular concern is the Tokyo Guideline's focus on early ERCP for optimal management of acute cholangitis. Previous literature has shown significant racial/ethnic disparities in other disease processes that require timely medical intervention, such as management of myocardial infarction, sepsis, and cancer treatment.[13–15] These disparities have not been fully explained by socioeconomic status or disease severity and have been hypothesized to be multifactorial, related to racism not fully explained by conventional variables. Thus, while the Tokyo guidelines may have resulted in overall improvements in cholangitis-associated outcomes, we hypothesize that racial/ethnic disparities in the disease course and clinical outcomes of acute cholangitis may persist, or may even have worsened, in the post-Tokyo guidelines era because of the need for a time-sensitive advanced medical intervention.

Thus, in the present study, we aimed to determine whether race or ethnicity affect hospitalization outcomes, including rates of ERCP, rates of early ERCP, hospital length of stay, and mortality, among a contemporary cohort of hospitalized patients with acute cholangitis.

Methods

Data for this study were obtained from the National Inpatient Sample (NIS), a database developed under the Healthcare Cost Utilization Project (HCUP) by the Agency for Healthcare Research and Quality (AHRQ). NIS is an all-payer inpatient healthcare database in the United States, including both regional and national data among patients with public,

private, and other insurance types that uses a complex dynamic sampling design that varies over time. The data includes sociodemographic variables, hospitalization diagnoses, procedures, hospital length of stay, and inpatient mortality.[16]

We examined all hospitalizations between 2009 and 2018 among patients ≥18 years old with a primary or secondary diagnosis of acute cholangitis, identified by the International Classification of Diseases, 9th Revision (ICD9) code 576.1 or the International Classification of Diseases 10th Revision (ICD10) code K830.[11, 17, 18] Non-White patients included patients identifying as Black, Hispanic, and/or Other race/ethnicity.

Covariates included demographic data (available in the NIS dataset), common etiologies of cholangitis (gallstone disease, liver/biliary/pancreatic malignancy), related diagnoses (e.g. bacteremia, pancreatitis, sepsis), and comorbidities (e.g. Charlson Comorbidity index, diabetes, hypertension). ICD9 and ICD10 codes used to define these covariates are provided in Table, Supplemental Digital content 1, ICD codes. ICD9 and ICD10 procedure codes were used to identify inpatient procedures, including diagnostic and/or therapeutic ERCP, cholecystectomy, and percutaneous biliary drainage (Table, Supplemental Digital Content 2, ICD codes). NIS also provides data on timing of procedures by hospital day.

Our primary outcome was inpatient mortality, which is a variable provided in the NIS dataset. Secondary outcomes included diagnostic/therapeutic ERCP, early ERCP (within 48 hours), and hospital length of stay.

Descriptive categorical variables were analyzed using Chi-square test and continuous variables using one-way ANOVA testing. To account for sampling, regression analyses were completed using survey-specific analyses (STATA svy package). Univariable and multivariable regression analyses were used to associate race/ethnicity with our outcomes of interest. For our primary outcome of inpatient mortality and secondary outcomes of ERCP and early ERCP (within 2 days of admission), we used logistic regression analysis. For hospital length of stay, we used zero-truncated Poisson regression. Sociodemographic and clinical factors hypothesized to be associated with primary and secondary outcomes were defined *a priori*. Factors that were statistically significant on univariable analysis ($p<0.05$) were included in multivariable models, and backward selection was used to develop final models. For all models, we tested for interactions between race and all other covariates. P-value of <0.05 was considered statistically significant. All statistical analyses were completed using STATA (Version 16.0, College Station, TX). This study was approved by the institutional review board at University of California San Francisco.

Results

Of 116,889 patients hospitalized with acute cholangitis 2009–2018, 81,473 (70%) identified as White, 11,247 (10%) identified as Black, 13,323 (11%) identified as Hispanic, and 10,846 (9%) identified as Other race/ethnicity. The proportion of non-White patients increased over time (Figure 1). Approximately 46% of White patients were female, compared to 52% of non-White patients (Table 1). Black and Hispanic patients were younger and had lower median household incomes than White patients. Hispanic patients, but not Black or

Other race/ethnicity patients, were significantly more likely than White patients to have public insurance. Compared to White patients, non-White patients were more likely to be hospitalized in urban teaching and non-teaching hospitals than rural hospitals. There were also geographic differences in racial/ethnic makeup of acute cholangitis admissions, as shown in Table 1.

Regarding clinical characteristics, Black patients had higher mean Charlson Comorbidity Index scores compared to White patients [Black 2.0 (SD: 2.9), vs. White: 1.7 (SD: 2.5)]. Compared to White patients, Black patients were less likely to have gallstone disease and more likely to have liver/biliary/pancreatic malignancy. Although Black patients were less likely than White patients to present with most cholangitis-associated complications, (e.g. pancreatitis and bacteremia), they were more likely to develop sepsis during hospitalization. Other race/ethnicity, but not Hispanic, patients had higher rates of bacteremia ($p<0.001$ and $p=0.73$, respectively), and both had higher rates of pancreatitis and sepsis compared to White patients.

Compared to White patients, Black patients had significantly longer hospital stays, fewer ERCPs, fewer early ERCPs, and higher in-hospital mortality, as shown in Table 2. Black patients also had higher rates of percutaneous drain placement and lower rates of cholecystectomy during hospitalization compared to White patients. All of these outcomes were similar between White and other non-White patients (i.e. Hispanic and Other).

On univariable logistic regression Black race was associated with significantly increased odds of in-hospital mortality compared with White race (OR 1.6, 95% CI 1.4–1.8, $p<0.001$, Table 3). On multivariable logistic regression, even after adjustment for age, gender, insurance type, Charlson severity index, etiology of cholangitis, hospital setting, and complications, Black patients had 40% increased mortality compared to White patients (aOR 1.4, 95%CI 1.2–1.6, $p<0.001$; Figure 2). Hispanic and Other race/ethnicity patients had similar mortality rates to White patients. On interaction analysis, after controlling for confounders, Hispanic patients with severe Charlson Severity Index scores experienced significantly increased risk of mortality than any other race/ethnicity group in the severe Charlson category (aOR 1.6, 95%CI 1.0–2.5, $p = 0.03$). And among patients with private insurance, Hispanic race/ethnicity was associated with lower mortality compared with other races/ethnicities with private insurance (aOR 0.5, 95%CI 0.3–1.0, $p = 0.03$). There were no other significant interactions, including no significant interactions between Black race and disease severity, insurance status, hospital type, hospital region, or gender.

The output of our multivariable regression analysis for secondary outcomes is also shown in Figure 1. After adjustment for demographics and comorbidities, Black patients were 22% less likely than White patients to undergo ERCP (See Table, Supplemental Digital Content 3, regression analysis for ERCP), 25% less likely to undergo early ERCP (See Table, Supplemental Digital Content 4, regression analysis for early ERCP), and had significantly longer hospital length of stay (See Table, Supplemental Digital Content 5, regression analysis for length of stay). In evaluating other racial/ethnic groups, Hispanic and Other race/ethnicity patients had similar mortality rates and rates of early ERCP compared

to White patients, but were 18% and 15% *more* likely to undergo ERCP and had longer length of hospital stay compared to White patients.

Discussion

Racial and ethnic disparities have been documented in the morbidity and mortality of multiple disease processes, including most gastrointestinal conditions.[19] Few contemporary studies have assessed associations between race/ethnicity and hospital outcomes in patients admitted with acute cholangitis, particularly since the publication of the Tokyo Guidelines in 2015. In this study, we aimed to characterize the racial and ethnic disparities among patients hospitalized with acute cholangitis using a national contemporary database. We found that despite a rising proportion of non-White patients with acute cholangitis, Black race is independently associated with longer hospital length of stay, reduced rates of both ERCP and early ERCP, and higher mortality.

Several older studies have documented evidence of racial and ethnic disparities among patients hospitalized with acute cholangitis.[10, 11] These studies found that non-White patients hospitalized for acute cholangitis had higher mortality rates, prolonged hospital length of stay, and incurred higher healthcare costs for acute cholangitis.[10] Black patients, in particular, had higher mortality rates and were less likely to undergo biliary drainage than White patients.[11] Since the publication of these studies, the Tokyo Guidelines have been released and updated twice, providing guidance on the diagnosis and management of patients with acute cholangitis.[1, 2, 17] As a result, mortality from acute cholangitis has decreased overall.[20] Unfortunately, our findings suggest that despite advances in the management of acute cholangitis, these advances are inequitable—Black patients remain at risk of suboptimal outcomes.

What explains our observed racial disparity in patients hospitalized with acute cholangitis? To understand any racial disparity, race must be viewed as a social construct that measures the effects of racism in our society on multiple levels. We believe that our findings are a result of the combined effects of structural and interpersonal racism in the management of patients with acute cholangitis. A key premise of the Tokyo Guidelines is that delaying ERCP is associated with increased mortality,[3, 21, 22] and morbidity, including increased rates of organ failure and longer hospital length of stay.[3, 8, 22] Our finding that Black patients were both less likely to undergo any ERCP and early ERCP likely contributes in part to our observed differences in mortality. But why were Black patients less likely to undergo ERCP and why were these procedures more likely delayed?

Differences in rates and timing of ERCP may be secondary to either delays in hospital presentation, or to differences in the care provided during the course of hospitalization. Previous studies have demonstrated delays in care among Black patients for a myriad of health conditions. [9, 15, 23] These studies hypothesize that delays in care among Black patients are due at least in part to structural disparities between Black and White patients, such as differences in education level, insurance, and occupation, leading to differences in timely presentation to the hospital. Yet even after controlling for some of these variables, racial disparities persist, suggesting additional differences (e.g., material economic hardship

that creates transportation barriers) not captured in clinical datasets.[11, 13–15] Additionally, it is possible that Black patients are more likely to present to hospitals with decreased availability of advanced endoscopy services or other center-specific practices that results in decreased procedure rates.[24–26] While we were unable to adjust for specific hospital or provider, Black patients in our cohort were *more* likely to be seen at teaching hospitals, which usually have *more* access to advanced endoscopists. Additionally, we did not find a significant interaction between race and hospital type or region on our ERCP outcomes; this disparity persisted across all types of hospitals. Together, these findings would support the notion that some degree of unmeasured bias or interpersonal racism impacts the decision to intervene with ERCP.

It is also possible that etiology of cholangitis, other comorbidities, or severity of cholangitis may make ERCP riskier in Black patients, leading to avoidance or delay in ERCP. In fact, we found that Black patients were more likely have a malignant obstruction as the cause of their cholangitis, compared to gallstones. While hepatobiliary malignancy was associated with higher mortality than gallstone disease, it was also associated with increased rates of early ERCP, making the racial disparity in early ERCP even more striking. Black patients also had more severe Charlson Comorbidity Index scores than non-Black patients in our cohort, but the difference in ERCP rates persisted despite adjustment for this. The Tokyo Guidelines and prior studies have also demonstrated early and urgent ERCP is particularly important among patients with moderate and severe cholangitis respectively.[1, 27] While we could not measure disease severity, Black patients presented with a different were less likely to present with bacteremia or pancreatitis, perhaps resulting in delayed diagnosis of acute cholangitis and subsequent delay in ERCP. However, they were more likely than patients of other races to develop sepsis, possibly suggesting more severe disease. However, this would suggest that Black patients would benefit even more than patients of other races from early ERCP.

The disparity we observed in mortality persisted even after adjustment for early ERCP and other covariates, suggesting other factors are at play. Race-specific inequities are often a marker of “racism-related exposures”.[19, 28] Our data suggest that there were no differential odds of death for Black patients compared to other patients by hospital type, Charlson severity index, insurance status, or gender, suggesting that the racial disparities are due to other factors that cannot be easily captured in clinical datasets. We hypothesize that these disparities are also due to other social determinants of health not captured in traditional clinical data such as neighborhood segregation and deprivation, social adversity (e.g. toxic stress, material economic hardship), interpersonal racism, health care literacy, and provider perceptions of patient symptoms may also contribute to racial inequities.[28]

While this study is the largest contemporary study of outcomes among patients hospitalized with acute cholangitis, there are several limitations to consider. First, this administrative dataset based on ICD coding lacks clinical granularity to confirm the validity of acute cholangitis diagnosis and its etiology and to classify disease severity at presentation and additional details of patients’ hospital course. Additionally, data regarding cause of in-hospital mortality was not available within this cohort of patients hospitalized with a primary or secondary diagnosis of acute cholangitis. The NIS database specifically relies on

billing codes and may underestimate the cholangitis or race data due to missclassifications or missing data in certain regions of the country. Secondly, robust sociodemographic data were not available to rigorously assess the possible mechanisms by which interpersonal and institutional racism may operate within this patient population. Hospital- and provider-specific data was also not available, limiting our ability to understand differences in specialist availability, racial congruence, provider experience, or provider preference. Finally, given our large sample size, it is possible that differences that are statistically significant may not be clinically significant.

Nevertheless, this study furthers our understanding of the prevalence of racial inequities in the management and outcomes of hospitalized patients with acute cholangitis—a condition which has seen significant overall improvements in care and declining mortality over the last decade.[7, 26, 29] Future studies should explore the relative contributions of interpersonal and structural racism to the observed differences in health outcomes among patients with acute cholangitis. Better understanding the underlying mechanism will provide opportunities to narrow these disparities, reduce hospital costs, and improve quality of care for all patients hospitalized with acute cholangitis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Abbreviations:

AHRQ	Agency for Healthcare Research and Quality
NIS	National Inpatient Sample
ICD-9	International Classification of diseases, 9th Revision- Clinical Modification
ICD10	International Classification of diseases, 10th Revision- Clinical Modification
ERCP	endoscopic retrograde cholangiopancreatography
LOS	length of stay
CI	confidence interval
aOR	adjusted odds ratio
aIRR	adjusted incidence rate ratio
IQR	interquartile range

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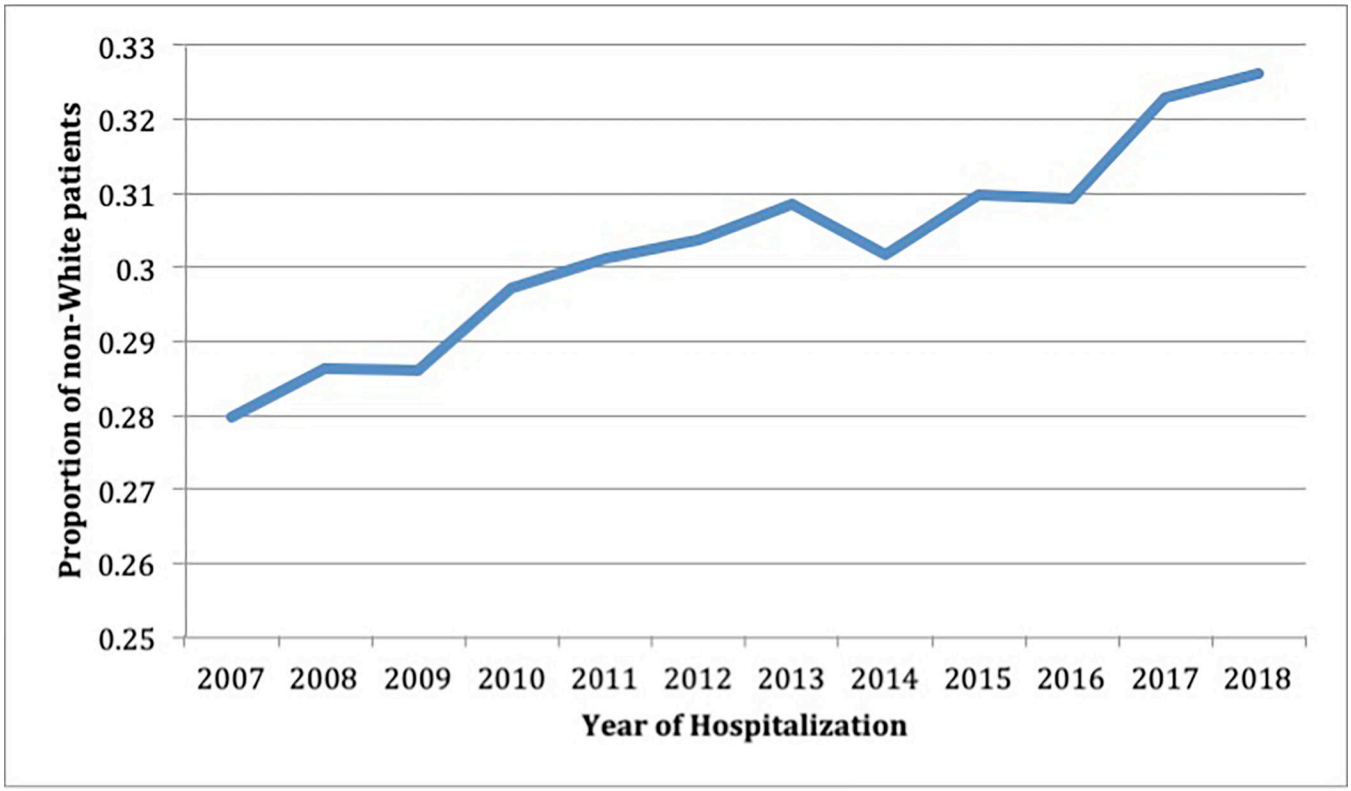

Figure 1.
Proportion of acute cholangitis hospitalizations among non-White patients by year, 2007–2018.

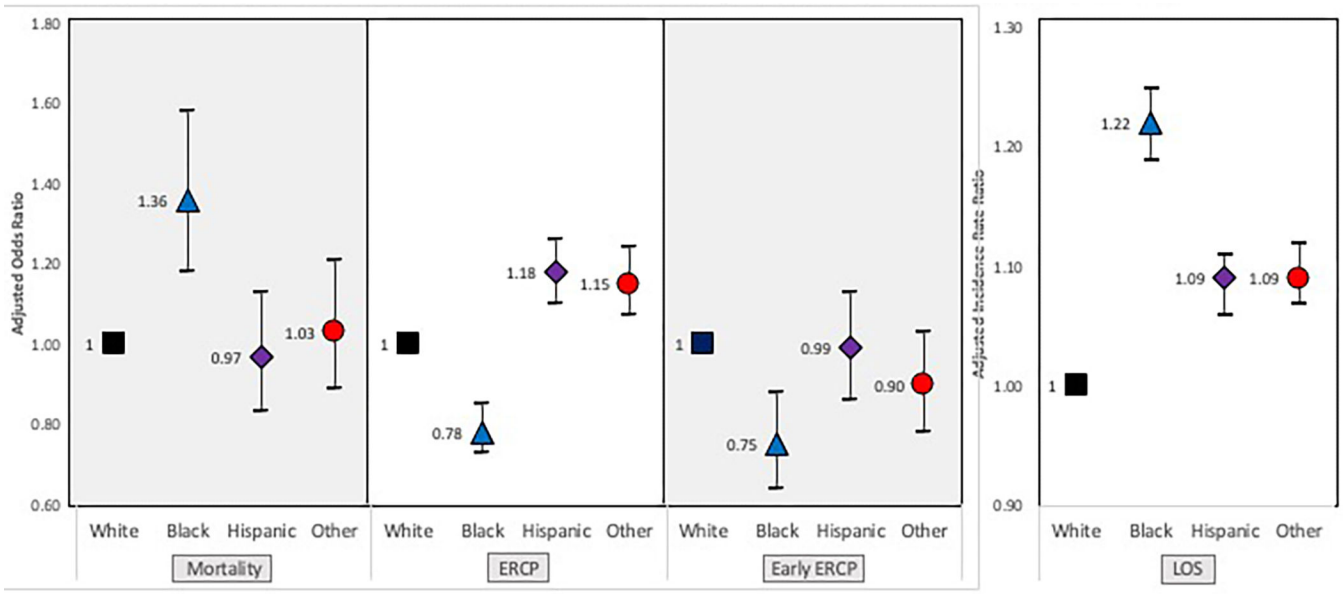

Figure 2.

Adjusted Risk of Hospital Outcomes in Patients with Acute Cholangitis by Race / Ethnicity including ERCP, early ERCP, hospital length of stay (LOS), and in-hospital mortality.

Table 1.

Baseline Sociodemographic, Hospital, and Clinical Characteristics in Patients Hospitalized with Cholangitis based on Race/Ethnicity, 2009–2018 (n = 116,889)

Variables	White 81,473, 70%	Black 11,247, 10%	Hispanic 13323, 11%	Other 10846, 9%	p-value
Demographics					
Sex (%)					<0.001
Male	54	45	47	53	
Female	46	55	53	47	
Age (%)					<0.001
< 65 years old	40	62	55	43	
≥ 65 years old	60	38	45	57	
Primary Expected Payer (%)					<0.001
Public (Medicaid or Medicare)	67	64	74	65	
Private	29	27	23	27	
Other (Self-pay or Other)	5	9	13	8	
Median Household Income Quartile (%)					<0.001
Quartile 1	20	46	36	19	
Quartile 1	26	22	24	19	
Quartile 3	26	17	24	24	
Quartile 4	28	14	16	38	
Hospital Characteristics					
Hospital type (%)					<0.001
Rural	8	3	2	3	
Urban non-teaching	30	19	34	28	
Urban teaching	62	77	64	69	
Region (%)					<0.001
Northeast	26	21	15	23	
Midwest	22	19	7	10	

Variables	White 81,473, 70%	Black 11,247, 10%	Hispanic 13323, 11%	Other 10846, 9%	p-value
South	32	49	33	20	
West	21	11	46	47	
Clinical Characteristics					
Charlson Comorbidity Index (%)					<0.001
Mild	48	49	53	48	
Moderate	36	31	32	35	
Severe	16	21	15	17	
Diabetes (%)	19	20	23	23	<0.001
Hypertension (%)	42	20	23	23	<0.001
Gallstone Disease (%)	44	34	50	47	<0.001
Liver/biliary/pancreatic malignancy (%)	18	21	16	21	<0.001

Table 2.

Clinical Outcomes and Complications in Patients Hospitalized with Cholangitis by Race/Ethnicity

Variables represented as mean (SD) or %	White	Black	Hispanic	Other	p-value
Clinical Outcomes					
Hospital Length of Stay	7.1 (8.5)	9.2 (11.1)	7.9 (9.6)	8.2 (10.0)	<0.001
Died	5	8	5	6	<0.001
ERCP	41	34	46	45	<0.001
Time to ERCP	2.5 (4.0)	3.2 (4.8)	2.8 (4.0)	2.6 (3.9)	<0.001
Percutaneous Drain Placement	5	6	5	6	<0.001
Cholecystectomy	16	12	20	17	<0.001
Complications					
Pancreatitis	12	10	14	13	<0.001
Bacteremia	33	31	33	36	<0.001
Sepsis	21	23	24	26	<0.001

ERCP, endoscopic retrograde cholangiopancreatography

Table 3.

Univariate and Multivariate Logistic Regression Identifying Risk Factors for Inpatient Mortality

Variables	Univariable			Multivariable		
	OR	**95%CI**	**p-value**	**aOR**	**95%CI**	**p-value**
Age ≥ 65	1.62	1.49–1.76	<0.001	1.31	1.17–1.48	<0.001
Race / Ethnicity						
White	--	--	--	--	--	--
Black	1.55	1.36–1.75	<0.001	1.36	1.18–1.58	<0.001
Hispanic	1.04	0.91–1.19	0.593	0.97	0.83–1.13	0.725
Other	1.23	1.07–1.41	0.003	1.03	0.89–1.21	0.674
Female	0.99	0.92–1.07	0.817			
Insurance						
Private	--	--	--	--	--	--
Public	0.60	0.55–0.66	<0.001	0.82	0.72–0.93	0.003
Other	0.69	0.58–0.82	<0.001	1.06	0.8251.33	0.579
Income						
Q1	--	--	--			
Q2	0.78	0.70–0.87	<0.001			
Q3	0.81	0.72–0.90	<0.001			
Q4		0.78–0.96	0.008			
Charlson Severity Index						
Mild	--	--	--	--	--	--
Moderate	2.09	1.88–2.33	<0.001	1.59	1.40–1.81	<0.001
Severe	4.39	3.92–4.91	<0.001	2.90	2.51–3.34	<0.001
Sepsis	12.32	11.36–13.36	<0.001	7.44	6.63–8.34	<0.001
Bacteremia	6.16	5.63–6.74	<0.001	2.01	1.77–2.29	<0.001
Pancreatitis	0.86	0.76–0.96	0.008	0.97	0.85–1.11	0.662

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Variables	Univariable			Multivariable		
	OR	95%CI	p-value	aOR	95%CI	p-value
Gallstone Disease	0.53	0.49–0.58	<0.001	0.49	0.44–0.54	<0.001
Liver/biliary/pancreatic malignancy	1.64	1.48–1.81	<0.001	0.86	0.76–0.97	0.017
Hospital type						
Rural	--	--	--	--	--	--
Urban non-teaching	1.10	0.93–1.28	0.249	0.84	0.69–1.01	0.066
Urban teaching	1.28	1.10–1.49	0.001	0.94	0.78–1.13	0.525
Region						
Northeast	--	--	--	--	--	--
Midwest	0.75	0.67–0.84	<0.001	0.86	0.74–1.00	0.049
South	0.95	0.86–1.06	0.356	1.02	0.91–1.16	0.647
West	0.99	0.89–1.10	0.836	0.99	0.87–1.12	0.840
Early ERCP	0.63	0.51–0.78	<0.001	0.58	0.47–0.72	<0.001