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Effects of *Clostridium difficile* Infection in Patients with Alcoholic Hepatitis

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Abstract

Background & Aims—Infection increases mortality in patients with alcoholic hepatitis (AH). Little is known about the association between *Clostridium difficile* infection (CDI) and AH. We examined the prevalence and effects of CDI in patients with AH, compared with those of other infections.

Methods—We performed a cross-sectional analysis using data collected from the Nationwide Inpatient Sample, from 2008 through 2011. International Classification of Diseases, Ninth Revision, Clinical Modification codes were used to identify patients with AH. We used multivariable logistic regression to determine risk factors that affect mortality, negative binomial regression to evaluate the effects of CDI on predicted length of stay (LOS), and poisson regression to determine the effects of CDI on predicted hospital charges. χ^2 and Wilcoxon rank-sum analyses

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Author contributions:
Dr. Vinay Sundaram was responsible for study concept and design, acquisition of data, data analysis, writing and revision of the manuscript.
Dr. Folasade May was responsible for study design, data analysis and critical revision of the manuscript.
Dr. Vignan Manne was responsible for writing and critical revision of the manuscript.
Dr. Sammy Saab was responsible for obtaining the dataset, study design, critical revision of the manuscript, and study supervision.

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were used to compare mortality, LOS, and hospital charges associated with CDI to those associated with urinary tract infection (UTI) and spontaneous bacterial peritonitis (SBP).

Results—Of 10,939 patients with AH, 177 had CDI (1.62%). Patients with AH and CDI had increased odds of inpatient mortality (adjusted odds ratio, 1.75; P=.04), longer predicted LOS (10.63 days vs 5.75 days, P<.001) and greater predicted hospital charges ($36,924.30 vs $29,136.58, P<.001), compared to those without CDI. Compared to UTI, CDI was associated with similar mortality but greater LOS (9 vs 6 days, P<.001) and hospital charges ($45,607 vs $32,087, P<.001). SBP was associated with higher mortality than CDI (17.3% vs 10.1%, P=0.045), but similar LOS and hospital charges.

Conclusions—In patients with AH, CDI is associated with greater mortality and healthcare utilization. These effects appear similar to those for UTI and SBP. We propose further studies to determine the cost-effectiveness of screening for CDI among patients with AH.

Keywords

ICD-9-CM; alcoholic liver disease; NIS; database

Introduction

Alcoholic hepatitis (AH) is a condition of acute hepatic inflammation in the setting of recent alcohol abuse. One-month mortality rates for this disease range from less than 10% in non-severe AH, to as high as 30–50% in severe AH.[1–5] Infection is a major cause of mortality in this population, and a prior study from Louvet et al demonstrated that severe AH patients are at particularly high risk of developing infection, with bacteremia, urinary tract infection (UTI), and spontaneous bacterial peritonitis (SBP) among the most prevalent.[6] Based on these findings, guidelines from the European Association for the Study of the Liver have recommended routine screening with blood, urine and ascites fluid cultures prior to corticosteroid administration.[7]

Clostridium difficile infection (CDI) is becoming an increasingly incident and virulent disease in hospitalized patients. In the United States, the incidence of CDI has more than doubled from 31 cases per 100,000 population in 1996 to 85 cases per 100,000 population in 2005.[8] CDI has also been demonstrated to confer higher risk of mortality in patients with an immunocompromised state such as advanced age, inflammatory bowel disease, or solid organ transplantation.[9–11] Given the high rate of hospitalization among those with AH, along with the associated immune system dysfunction, such patients may be at risk for acquisition of CDI and increased mortality related to CDI. The clinical implications of CDI in AH, however, currently remain unexplored.

As there is a paucity of data regarding the impact of CDI in AH, the objectives of this study were to use a national inpatient database to determine the prevalence of CDI in patients hospitalized with AH, to evaluate the impact of CDI on inpatient mortality, length of stay (LOS) and total hospital charges in AH, and to compare the impact of CDI to that of other infections screened for in AH, specifically urinary tract infection (UTI) and spontaneous bacterial peritonitis (SBP).

Methods

Study design and patient database

This study utilized a retrospective, cross-sectional design examining records from the Nationwide Inpatient Sample (NIS), years 2008–2011.[12] The NIS is the largest publicly available inpatient database. The patients are a 20% stratified sample of all the discharges occurring in a given year from approximately 1000 non-federal United States hospitals in 42 to 47 states (depending on the year of the study). Each discharge record from the NIS contains demographic information, such as age, sex, and race, primary and secondary insurance information, source of admission, and patient disposition upon discharge. A primary discharge diagnosis and up to 14 secondary discharge diagnoses are provided for the patients through 2008, and up to 24 secondary diagnosis codes are listed for patients from 2009 and afterwards. Each hospital included in the NIS participates in the Agency for Healthcare Research and Quality Healthcare Cost and Utilization Project. In order to present national population estimates in the present study and to control for bias in the selection of the study participants, survey weights were applied to the patient-level observations in the dataset.

The institutional review board of Cedars-Sinai Medical Center approved the study protocol.

Study population

The study population consisted of patients age 18 or older with a primary diagnosis of AH, using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code 571.1. Use of diagnostic coding is an accepted method of identifying patients with AH, based on previously published literature.[5, 13, 14] We stratified these patients into those with and without CDI, based on the presence of an additional diagnosis code for CDI (ICD-9-CM code 008.45).

Data analysis

We used Chi-square and Fisher's exact testing to compare categorical variables and Wilcoxon Rank-Sum testing to compare continuous variables with non-normal distribution, such as LOS or hospital charges. All analyses were performed with STATA 12.1 software (Stata Corp., College Station, TX) and with the appropriate survey estimation commands and strata weights provided in each NIS file. A p-value < 0.05 on two-tailed testing was considered significant. As less than 5% of data was missing from the variables incorporated into our regression models, we did not impute for missing data.

Impact of CDI on inpatient mortality, LOS and total hospital charges

We determined risk factors for inpatient mortality using multivariable logistic regression analysis. We utilized the Deyo modification of the Charlson index as a proxy for patient comorbidity. The index is a tool that has been validated for use in administrative databases, with a higher score corresponding to a larger burden of co-morbidity.[15] We stratified the Charlson index into three categories: Charlson category 1 (score =0), Charlson category 2 (score 1–3), and category 3 (score > 3) to represent degree of comorbidity.

We additionally created a variable called any infection, to adjust for patients who may have acquired CDI due to antibiotic treatment for other concurrent infections. For this variable, we included all ICD-9-CM codes used for infections (other than CDI and viral illnesses) that can potentially be treated with antibiotics. Ali et al. employed similar methodology for their study regarding CDI in liver transplant recipients.[16] The ICD-9-CM codes utilized for this variable are listed in the supporting information text.

As length of stay was a count variable with evidence of overdispersion, we used negative binomial regression to predict average length of stay for patients with AH alone and average length of stay for patients with AH and CDI. Given the non-normal distribution of hospital charges, we used poisson regression to assess total hospital charges in the two groups, which is equivalent to performing a least squares linear regression on the logarithmic transformation of the cost variable. The cost estimates were adjusted for length of stay.

Both the logistic regression model for mortality and count models were adjusted for those demographic and health-related predictors that were significant ($p<0.05$) in single variable regression models.

Comparison to UTI and SBP

We also compared prevalence, inpatient mortality, LOS, and hospital charges between patients with AH and CDI to those with AH and UTI or SBP. These infections were chosen for comparison because routine screening for UTI and SBP prior to corticosteroid administration is suggested in professional society guidelines and has been incorporated into clinical trial protocols studying AH.[6, 7, 17] Furthermore, patients with UTI or SBP can be readily identified using ICD-9-CM codes.[18–20] To identify patients with UTI, we utilized the following codes: 599.0, 111.2, 590.10, 590.11, 590.2, 590.3, 590.80, 590.81, 595.0, and 597.0. Patients with SBP were ascertained using ICD-9-CM code 567.23. Prevalence of UTI and SBP and associated inpatient mortality was compared to that of CDI using Chi-square testing. LOS and hospital charges were compared using Wilcoxon rank-sum testing. When evaluating inpatient mortality, LOS, and hospital charges, patients with CDI and concurrent UTI or SBP were excluded.

Results

Prevalence of CDI

There were a total of 26,793,757 discharge records available for inpatients age 18 or older from 2008–2011, of which 10,939 were associated with AH. Among patients with AH, the prevalence of CDI was 1.62% (177/10,939), while the prevalence of CDI was 1.04% (279,344/26,782,818) among those without AH. Chi-square analysis demonstrated that the prevalence of CDI was significantly higher among AH patients ($p<0.001$).

Alcoholic hepatitis patients

Table 1 depicts the characteristics of the study population with AH, with and without CDI. Patients with CDI had significantly higher Charlson index scores ($p <0.001$) and were more likely admitted from outside facilities (2.8% vs 0.8%; $p = 0.004$), when compared to patients

without CDI. Furthermore, those with CDI had significantly more deaths during hospitalization (10.8% vs 4.2%; p <0.001) and were more likely to be discharged home with aid (7.6% vs 4.7%; p=0.04). CDI was also associated with longer median length of stay (10 vs 4 days; p <0.001) and greater median total hospital charges ($52,304 vs $22,151; p <0.001). The two groups were similar in distribution of age, gender, race, socioeconomic status, and payer source.

Predictors of inpatient mortality

Significant predictors of in-hospital mortality among AH inpatients are provided in Table 2. The presence of CDI in patients with alcoholic was associated with higher odds of inpatient mortality. This association remained significant after adjusting for confounders (adj. OR 1.75; 95%CI=1.01–3.03; p=0.04). Risk of mortality was also higher for individuals over age 65 (adj. OR 1.96; 95%CI=1.18–3.27; p=0.01), males (adj. OR 1.49; 95%CI=1.20–1.85; p<0.001), individuals with another infection (OR 4.09; 95%CI=3.33–5.02; p<0.001), and those with modest and high Charlson co-morbidity scores (adj. OR 4.24; 95%CI=2.95–6.11; p<0.001 and adj. OR 10.30; 95%CI=7.15–14.87; p<0.001, respectively). Black race was associated with lower odds of inpatient mortality when compared to white race (adj. OR=0.53; 95%CI=0.35–0.82; p=0.004).

Length of Stay and Hospital Charges

Table 3 provides post-estimate predicted values for length of stay and hospital charges in AH patients with and without CDI. Holding all model covariates at the observed values, the average predicted length of stay was 5.75 days (95% CI: 5.64–5.86; p<0.001) for those with AH alone and 10.63 days (95% CI: 9.53–11.72; p<0.001) for those with both AH and CDI. In the poisson regression model for total hospital charges, the average cost of hospitalization for patients with AH alone was $29,136 (95% CI: $28,532 – $29,741; p<0.001) when all other variables in the model were held at observed values. For patients with AH and CDI, the average cost was $36,924 (95% CI: $31,542 – $42,306; p<0.001).

Comparison to UTI and SBP

A total of 1,502 of 10,939 patients were identified as having UTI, yielding a significantly higher prevalence estimate than that of CDI (13.7 vs 1.62%; p<0.001). Additionally, 177 of 10,939 patients with AH had SBP, giving an estimated prevalence of 1.62%, which was identical to that of CDI.

Table 4 depicts inpatient mortality, LOS and hospital charges among patients with CDI, UTI, and SBP. Both LOS and hospital charges are expressed as median and interquartile range (IQR). For this analysis, 36 patients were excluded due to concurrent CDI and UTI, while 2 patients were eliminated for having both CDI and SBP. As compared to UTI, CDI conferred a similar mortality but significantly higher median LOS (9 vs 6 days; p<0.001) and hospital charges ($45,607 vs $32,087; p<0.001). When compared to SBP, CDI had lower associated inpatient mortality (10.3 vs 17.3%; p=0.045) but similar associated LOS and hospital charges.

Discussion

Our cross-sectional study utilizing data from the NIS for 2008–2011 demonstrated that CDI is more prevalent in inpatients with AH compared to those without AH, and that CDI is associated with increased mortality in AH. Our findings also indicated that CDI in the setting of AH was associated with greater LOS and hospital charges. Furthermore, in our study population the LOS and hospital costs associated with CDI were greater than those of UTI and similar to those of SBP.

Though it is well known that AH patients are susceptible to infection, the impact of specific infections on mortality and healthcare utilization is unknown. CDI is becoming an increasingly incident disease, with the greatest risk of infection occurring in hospitalized patients and with a particularly high mortality in immunosuppressed patients.[21, 22] Treatment of AH often requires hospitalization, placing these patients at risk for CDI acquisition. Furthermore, severe hepatic inflammation in AH leads to an immunocompromised state, which may be further compounded by corticosteroid administration.[6] The rationale for this study, therefore, was to investigate the impact of CDI in AH, utilizing a nationwide database of hospitalized patients.

There are several novel findings demonstrated in our study. First, we determined the prevalence of CDI in AH (1.62%) was significantly greater than in patients without AH (1.04%). To our knowledge, there have been no prior prevalence estimates of CDI in this population. In addition, we demonstrated that CDI was associated with more than a two-fold increase in mortality in our population of AH patients (10.8 vs 4.2%) and independently predicted risk of inpatient death (adj OR=1.75). This finding is of particular importance and emphasizes the need for a high index of suspicion for CDI when managing AH patients.

Our estimate of 10.8% inpatient deaths in inpatients with CDI and AH suggests that CDI confers greater mortality in AH compared to other groups. For instance, studies have shown mortality to range from 4.2–7.0% in inflammatory bowel disease with CDI and 5.5–7.4% in solid organ transplant recipients with CDI.[16, 23–25] We believe the higher mortality from CDI in AH is because AH patients have a greater degree of immunosuppression compared to other patient groups, due to severe hepatic inflammation leading to liver dysfunction.[26] AH is associated with a massive inflammatory infiltrate in the liver, leading to Kupfer cell activation and release of pro-inflammatory cytokines.[27] Consequently, there is a depletion of antioxidants and release of reactive oxygen species, causing disruption of hepatic innate immunity.[28, 29] Additionally AH patients often are malnourished, have underlying liver cirrhosis, and may receive corticosteroids, all of which can worsen immunosuppression and increase mortality risk from infection.[30, 31]

CDI is a significant burden in the health care system, with total associated costs estimated to be approximately a billion dollars a year.[32] The results of our study also demonstrate a significant increase in health care utilization with CDI in AH patients. The adjusted mean length of stay almost doubled when CDI was present, which is consistent with prior observations. Pakyz et al demonstrated the adjusted length of stay to double with CDI using administrative claims from 45 academic medical centers in the United States.[33] In a

systematic review of the burden of CDI in Europe, Wiegand et al showed that infection was associated with increased incremental hospital length of stay which ranged from 2.7 in Finland to 18 days in the Netherlands.[34]

The increase in costs associated with CDI was another principal finding in our analysis. The adjusted costs in patients with alcohol hepatitis and CDI were significantly higher than those of patients without CDI. Studies have consistently shown greater incremental costs associated with CDI, which may be related to increased resource utilization and need for intensive care.[35]

In a previous study, Bajaj et al utilized the NIS to evaluate the impact of CDI on outcomes in hospitalized patients with alcohol-induced and non-alcoholic liver cirrhosis. Their findings similarly demonstrated a significant increase in mortality, length of stay and hospital charges.[36] However, there are several important distinctions between their study population and ours. First, although patients with AH may have underlying cirrhosis, AH is a distinct disease entity associated with acute hepatic inflammation, which may warrant treatment with corticosteroids. This is not the case with decompensated alcoholic or non-alcoholic liver cirrhosis. Additionally, testing for infection without presence of symptoms is not currently recommended in the management of decompensated liver cirrhosis. However, guidelines from the European Association for the Study of the Liver do recommend routine screening of certain infections in patients with severe AH prior to corticosteroid administration, even without manifestation of symptoms associated with these infections. Therefore, given the distinctions between patients with AH versus liver cirrhosis, we believe our study contributes novel information.

Whereas prior studies have focused on the costs associated with infections, there are limited studies assessing whether routine screening for CDI would be cost-effective and in which patients it should be considered. Current guidelines by the Infectious Diseases Society of America and the American College of Gastroenterology and recommend testing for CDI only in patients who exhibit symptoms of diarrhea.[37, 38] From our study alone, recommendations cannot be made regarding screening for CDI in AH. However, what is notable is the prevalence, mortality, and healthcare burden associated with CDI relative to two other infections for which routine screening is recommended in this population. The prevalence of CDI and SBP in AH was identical, and despite greater associated mortality with SBP, the impact of these infections on LOS and hospital charges was otherwise similar. Furthermore, although prevalence of UTI was significantly higher than CDI, our results indicated that CDI had a larger impact on healthcare utilization. Given these findings, it may be beneficial to conduct additional studies to confirm the prevalence of CDI in AH and evaluate the cost-effectiveness of screening for CDI prior to corticosteroid use. Additionally, we suggest awareness of the presence and impact of CDI in AH, particularly since diarrhea, which is the primary symptom of CDI, may be unrecognized in AH patients concurrently receiving lactulose.

Our study had several limitations. The NIS dataset does not include patient identifiers, thus limiting our ability to account for repeat admissions by the same patient. Given that CDI is most often a hospital-acquired condition and that readmissions account for only a small

portion of admissions overall, we feel that potential bias from this limitation is minimal. Second, as the dataset does not provide laboratory data, we could not calculate discriminant function to characterize patients with severe AH. Our findings do, however, reflect degree of comorbidity and presence of other infections. Another limitation was that timing of infection could not be accounted for, as the NIS only provides final discharge diagnoses, thereby precluding us from determining the percentage of patients infected on admission. Additionally, given the lack of data regarding medications, we could not account for corticosteroid therapy or proton pump inhibitor use. However, there is no evidence that proton pump inhibitor use would vary significantly between patients with and without AH. Finally, as our study is a retrospective observational study based on secondary data, coding errors in the dataset, missing data, and the inability to conclude causation may influence the outcomes. Despite these limitations, however, we believe our study presents novel information utilizing a large patient volume representative of the United States. Such findings may form the basis for future research.

In conclusion, our analysis identified a higher prevalence of CDI in AH than non-AH inpatients. Additionally, CDI was associated with increased mortality, length of stay and hospital charges in AH. The impact of CDI on healthcare burden in this population appears to be greater than that of UTI and similar to that of SBP. We suggest vigilance for suspecting CDI in hospitalized patients with AH. Further research confirming the prevalence of CDI in AH and the cost-effectiveness of screening for CDI prior to corticosteroid administration is recommended.

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List of Abbreviations

AH	Alcoholic hepatitis
CDI	*Clostridium difficile* infection
LOS	Length of stay
NIS	Nationwide inpatient sample
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
IQR	Interquartile range
SBP	Spontaneous bacterial peritonitis
UTI	Urinary tract infection

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TABLE 1

Descriptive characteristics of all patients in the sample[a,b]

	Alcoholic Hepatitis without CDI Unweighted *n*=10,762 Weighted *N*=53,173	Alcoholic Hepatitis with CDI Unweighted *n*=177 Weighted *N*=868	P-value
	Unweighted n (Weighted %) or Median (IQR)	Unweighted n (Weighted %) or Median (IQR)	
Age			
18 – 35	1,782 (16.5)	32 (17.9)	0.59
36 – 49	4,468 (41.5)	68 (38.7)	0.41
50 – 64	3,890 (36.2)	66 (37.2)	0.75
≥ 65	622 (5.8)	11 (6.2)	0.81
Gender			
Male	6,699 (62.3)	99 (56.3)	0.09
Female	4,063 (37.7)	78 (43.7)	
Race			
White	6,700 (62.1)	102 (57.3)	0.21
Black	1,048 (9.8)	17 (9.5)	0.95
Hispanic	1,010 (9.4)	16 (9.3)	0.88
Other	503 (4.7)	8 (4.7)	0.92
Socioeconomic status			
Very Low	2,911 (27.2)	49 (27.8)	0.85
Low	2,752 (25.6)	44 (24.5)	0.83
Medium	2,564 (23.8)	40 (22.5)	0.70
High	2,167 (20.1)	36 (20.6)	0.95
Payer			
Medicaid	2,421 (22.6)	34 (19.6)	0.30
Medicare	1,489 (13.9)	19 (10.7)	0.24
Private	3,227 (30.0)	58 (32.7)	0.42
Self-pay	2,569 (23.8)	44 (24.5)	0.76
Other	1,008 (9.3)	22 (12.6)	0.17
Deaths	451 (4.2)	19 (10.8)	<0.001
Admission Source			
Emergency room	2,037 (18.7)	36 (20.8)	0.64
Outside hospital	88 (0.8)	5 (2.8)	0.004
Other facility	20 (0.2)	0 (0)	0.57
Other source	656 (6.1)	19 (10.9)	0.01
Length of Stay (days)	4 (3 – 8)	10 (6 – 17)	<0.001
Total hospital Charges (dollars)	$22,151 ($13,043 – $38.938)	$52,304.50 ($26,899 – $105,900)	<0.001
Disposition			
Home	7,291 (67.9)	93 (52.2)	<0.001

	Alcoholic Hepatitis without CDI Unweighted *n*=10,762 Weighted *N*=53,173	Alcoholic Hepatitis with CDI Unweighted *n*=177 Weighted *N*=868	P-value
	Unweighted n (Weighted %) or Median (IQR)	Unweighted n (Weighted %) or Median (IQR)	
Home with aid	500 (4.7)	14 (7.6)	0.04
Other inpatient facility	96 (0.9)	0 (0)	0.21
Long term facility	1,099 (10.3)	25 (14.4)	0.09
Other	407 (3.8)	16 (9.0)	<0.001
Charlson Index			
Category 1	4,437 (41.3)	50 (27.8)	<0.001
Category 2	4,056 (37.7)	70 (40.0)	0.61
Category 3	2,269 (21.0)	57 (32.1)	<0.001
Any infection	2,482 (23.0)	66 (36.8)	<0.001
Hospital Type			
Teaching	5,063 (46.9)	107 (39.4)	<0.001
Nonteaching	5,699 (53.1)	70 (60.6)	
Hospital Location			
Northeast	2,272 (21.6)	28 (16.3)	0.09
Midwest	2,234 (20.9)	40 (22.3)	0.55
South	3,886 (35.8)	58 (32.0)	0.36
West	2,370 (21.7)	51 (29.5)	0.03

[a]Table includes total study sample as unweighted n as well as weight national estimates as weighted N. Frequency data is presented as an unweighted n and weighted %.

[b]Numbers may not sum to group totals and percentages do not add to 100% in categories with missing values.

TABLE 2

Multivariable logistic regression for factors associated with mortality in hospitalized alcoholic hepatitis patients (2008–2011); n=10,939

Variable	Reference Group	Odds Ratio	95% Confidence Interval	*P* Value
CDI		1.75	1.01 – 3.03	0.04
Age 36–49	Age 18 – 35	1.02	0.73 – 1.42	0.91
Age 50–64		1.32	0.95 – 1.84	0.10
Age ≥65		1.96	1.18 – 3.27	0.01
Male	Female	1.49	1.20 – 1.85	<0.001
Black	White	0.53	0.35 – 0.82	0.004
Hispanic		0.93	0.66 – 1.32	0.69
Other Race		1.15	0.74 – 1.78	0.53
Any Infection		4.09	3.33 – 5.02	<0.001
Charlson Category 2	Charlson Category 1	4.24	2.95 – 6.11	<0.001
Charlson Index 3		10.30	7.15 – 14.87	<0.001
Non-Teaching Hospital	Teaching Hospital	1.11	0.91 – 1.35	0.32
Midwest Region	Northeast Region	0.95	0.70 – 1.28	0.73
South Region		1.04	0.79 – 1.36	0.79
West Region		1.00	0.74 – 1.36	0.99
Medicare		0.84	0.60 – 1.17	0.30
Medicaid		1.02	0.79 – 1.33	0.86
Selfpay		1.01	0.76 – 1.34	0.96
Other Payment		0.69	0.45 – 1.05	0.08

TABLE 3

Adjusted predicted values for average length of stay and total hospital charges for patients with alcoholic hepatitis with and without CDI

	Alcoholic hepatitis without CDI Unweighted n=10,762 Weighted N=53,173	**Alcoholic hepatitis with CDI Unweighted n=177 Weighted N=868**	**P-Value**
Average length of stay (95% CI), days*	5.75 (5.64 – 5.86)	10.63 (9.53 – 11.72)	< 0.001
Average total hospital charges (95% CI), $**	$29,136.58 ($28,531.76 – $29,741.39)	$36,924.30 ($31,542.27 – $42,306.33)	< 0.001

* Adjusted for age, race, gender, any infection, Charlson index, payer, hospital teaching status, and hospital location by region

** Adjusted for age, race, gender, any infection, Charlson index, payer, hospital teaching status, hospital location by region and length of stay

Table 4

Comparison of inpatient mortality, LOS and hospital charges between CDI, UTI, and SBP

	CDI (n=151)[a] (n=175)[b]	**UTI [a] (n=1516)**	**SBP [b] (n=175)**	**P-value[c]**	**P-value[d]**
Inpatient mortality (%)	10.7%[a] 10.1%[b]	6.9%	17.3%	0.08	0.045
Length of stay, days median (IQR)	9 (6–15)[a] 10 (6–17)[b]	6 (4–12)	9 (5–15)	<0.001	0.38
Hospital charges, dollars median (IQR)	$45,607 ($24,998 – $85,388)[a] $47,473.50 ($26,641 – $102,480)[b]	$32,087 ($19,310 – $69,923)	$48,164 ($26,376 – $89,729)	<0.001	0.54

[a] Estimates are with exclusion of patients with concurrent CDI and UTI

[b] Estimates are with exclusion of patients with concurrent CDI and SBP

[c] P-value comparing CDI to UTI

[d] P-value comparing CDI to SBP