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Outcomes of ESBL status among UTI admissions: a retrospective analysis of the Nationwide Inpatient Sample from 2016 to 2022

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Abstract

Background

Extended-spectrum beta-lactamase (ESBL) producing organisms are an increasing cause of urinary tract infections (UTIs) and pose significant challenges to inpatient management due to antimicrobial resistance and limited treatment options. Prior studies focus on prevalence and resistance patterns, but nationally representative inpatient outcome data are lacking. This study assesses the association between ESBL status and clinical outcomes among hospitalized adults with UTIs in the United States.

Methods

A retrospective cohort study was conducted using the Nationwide Inpatient Sample (NIS) from 2016–2022. Adult patients aged ≥ 18 years hospitalized with a primary diagnosis of UTI were included. ESBL status was identified using ICD-10-CM code Z16.12, with non-ESBL UTIs serving as the comparison group. The primary outcome was in-hospital mortality, while secondary outcomes included hospital length of stay (LOS) and total inflation-adjusted hospital costs. Propensity score matching and multivariable regression adjusted for demographic, clinical, and hospital confounders.

Results

Among 1,844,239 UTI hospitalizations from 2016 to 2022, 63,190 (3.4%) involved ESBL-producing organisms. ESBL status was not associated with increased in-hospital mortality compared with non-ESBL UTIs. However, ESBL infections were associated with longer hospital stays (mean difference 1.0 days; 95% CI 0.93 to 1.10; $p < 0.001$) and higher total hospital charges (mean difference $9,179; 95% CI $8,101 to $10,257; $p < 0.001$).

Conclusions

In this nationally representative analysis, ESBL-producing UTIs were associated with increased healthcare utilization but not higher in-hospital mortality. These findings highlight the clinical and economic burden of ESBL infections and the importance of targeted prevention and optimized inpatient management strategies.

INTRODUCTION

Urinary tract infections (UTIs) are among the most common bacterial infections encountered in healthcare settings and significantly contribute to inpatient morbidity, healthcare costs, and antibiotic utilization in the United States[1]. Some bacteria, most frequently Escherichia coli and Klebsiella pneumoniae, produce extended-spectrum beta-lactamases (ESBLs), enzymes that confer resistance to

penicillins, cephalosporins, and aztreonam. The global prevalence of ESBL-producing organisms has risen sharply, with rates in North American E. coli UTIs increasing from 7.8% to 18.3% between 2010 and 2014, particularly in hospitalized patients, males, and older adults[2]. The spread of ESBL-producing bacteria poses a significant public health challenge, affecting both hospitalized and community patients, with roughly 50% of infections occurring in non-hospitalized individuals[3]. While previous literature has reported specific characteristics and prevalence of UTIs, many of these studies are limited to a smaller population. Our study aims to characterize the effects of ESBL UTIs using the National Inpatient Sample (NIS) database, which provides a large-scale perspective on this disease.

Escherichia coli bacteria are responsible for 80% of acute community-acquired uncomplicated UTIs, followed by Staphylococcus saprophyticus, which causes 10–15% of cases. In non-catheterized older adults, UTIs are typically caused by a single bacterial species. However, when structural urinary tract abnormalities or catheterization are present, urine cultures often reveal multiple bacterial species[1]. First-line therapy for acute, uncomplicated UTIs includes nitrofurantoin, trimethoprim-sulfamethoxazole (TMP-SMX), and fosfomycin, which are highly effective, have favorable resistance profiles, and cause minimal collateral damage.

Across the literature, the most consistently reported risk factor for ESBL-producing UTIs is prior antibiotic exposure, particularly with penicillins, cephalosporins, fluoroquinolones, or recent outpatient antibiotic use[3–9]. Hospitalization and healthcare exposure, including recent admissions and prolonged length of stay, are also major risk factors[2, 3, 5–7, 10–13]. Recurrent UTIs[3, 4, 10] and urinary catheterization[4, 10, 14] are also frequently implicated. While previous studies have focused on ESBL prevalence, resistance patterns, or antibiotic therapy comparisons, few large-scale analyses have directly assessed the impact of ESBL status on inpatient outcomes such as length of stay, mortality, readmissions, and healthcare costs. Existing data are limited to a handful of large-scale cohort studies. Esteve-Palau et al. (2015) demonstrated that hospitalized patients with ESBL E. coli UTIs experienced worse clinical outcomes defined by the increased need for outpatient parenteral therapy, longer hospitalizations, and greater healthcare costs compared to non-ESBL cases[9]. Similarly, Gamble et al. (2022) reported that patients with ESBL status typically had a longer length of hospital stay, higher rates of treatment failure, and increased readmissions than those with non-ESBL UTIs[15]. More narrowly, Yagel et al. (2018) examined ESBL UTIs in pregnancy and found worse maternal outcomes and increased neonatal intensive care admissions compared to non-ESBL infections[16]. Collectively, these studies suggest that ESBL-producing organisms are linked to poorer inpatient outcomes, but the evidence remains limited in scope and largely restricted to specific populations or single-center cohorts. This highlights the need for broader, nationally representative analyses to define the burden of ESBL-associated UTIs more clearly in hospitalized patients.

METHODS

Data Source and Ethics Statement

Hospital data were abstracted from years 2016–2022 in the National Inpatient Sample (NIS) database. The NIS is part of a family of databases and software tools developed for the Healthcare Cost and Utilization Project (HCUP) and is the largest publicly available all-payer inpatient healthcare database in the United States; when weighted, the NIS represents approximately 35 million annual hospitalizations nationally[17]. This research is exempt from institutional review board approval, as it used publicly available, de-identified data adherent to 45 CFR § 46.

Patients

All admissions with a primary diagnosis of urinary tract infections in patients ≥ 18 years old were included. These hospitalizations were identified using International Classification of Diseases-10 Clinical Modification (ICD-10-CM) code N390 as the primary diagnosis. Admissions were excluded if they had the following: ICD-10-CM codes: urinary infections in pregnancy (O23), immunocompromised (D84.9), other postprocedural complications and disorders of the genitourinary system (N99.89), ESRD on dialysis (Z99.2), other specified sepsis (A41.89), various other bacterial diseases (A30, A31, A32, A33, A34, A35, A36, A37, A38, A39, A40, A42, A43, A44, A45, A46), congenital hydronephrosis (Q62.0), atresia or stricture of ureter (Q62.1), primary megaureter (Q62.11), vesicoureteral reflux unilateral (Q62.31), vesicoureteral reflux bilateral (Q62.32), congenital posterior urethral valves (Q64.2), congenital malformation of urinary system, unspecified (Q64.9), vesicoureteral reflux, acquired (N13.7). The NIS combines “race” and “ethnicity” into one data element “race”. If both “race” and “ethnicity” were available, HCUP preferred ethnicity over race in assigning a value for the “race” variable[18, 19]. The race groups included White, Black, Hispanic, Asian or Pacific Islander, Native American and Other. “White” group refers to non-Hispanic White patients, “Black” group refers to non-Hispanic Black patients, similarly “Asian or Pacific Islander” and “Native American” groups refer to non-Hispanic patients in these ethnic groups, and “Hispanic” group refers to Hispanic patients of all races and origins. “Other” refer to patients who are not the aforementioned ethnic groups.

Exposure

Extended-spectrum beta lactamase resistance status (ESBL status) was defined as having any of the following ICD-10-CM codes: Z16.12.

Outcomes

The primary study outcome was in-hospital mortality. Secondary outcomes included hospital length of stay (LOS), and total hospital charges. Total hospital charges were inflation-adjusted to mid-year 2025 US dollars[20].

Statistical Analysis

Continuous variables are presented as means with standard errors, compared using Kruskal-Wallis test, whereas categorical variables are presented as percent, compared using the Pearson's X^2 with Rao-Scott adjustment. Associations between ESBL status and in all-cause in-hospital mortality were evaluated using generalized linear models. Hospital length of stay and inflation-adjusted total hospital charges were evaluated using linear regression models[21].

To minimize selection bias, we used propensity score stratification.[22] Propensity scores were estimated by a logistic regression model using ESBL status as the outcome and age, biological sex, race, insurance status, hospital teaching status, hospital region, median household income in zip code, hospital bed size, weekend admission, elective admission, Elixhauser sum, uncomplicated diabetes, complicated diabetes, renal failure and disease, metastatic cancer, solid tumor without metastasis, coagulopathy, weight loss, acquired immune deficiency syndrome, fluid and electrolyte disorders, drug abuse, COVID19, ESRD, lower urinary tract calculi, congenital malformations, personal history of UTI, personal history of other urinary system disease, benign prostatic hyperplasia (BPH), Infection following procedure, nursing home, dialysis dependence, beta-lactam resistance, other antimicrobial resistance, single antibiotic resistance, penicillin resistance, quinolones and fluoroquinolones resistance, current long term antibiotic use, nosocomial infection, urogenital implants, kidney transplant, type 2 diabetes mellitus, immunosuppression, bladder drainage device, Klebsiella pneumoniae, Proteus, other bacteria, Heart transplant, Lung transplant, Bone marrow transplant, Stem cell transplant. The propensity score was subclassified into six groups using the MatchIt package in R[20, 23]. The quality of the match was evaluated by comparing distributions of the propensity scores (histograms, cumulative distribution functions) as well as standardized differences for individual covariates used to estimate the propensity score. The decision to retain nonlinear forms was determined using likelihood ratio test[24]. All analyses were conducted using R version 4.4.2, accounted for the NIS sampling design, and were weighted to estimate national-level effects. Two-tailed $p < 0.05$ was defined to indicate statistical significance.

RESULTS

Demographic Information

All percentages regarding patient demographics are summarized in Table 1. A total of 1,844,239 patients with urinary tract infections were included in the analysis, of whom 63,190 had infections due to ESBL–producing organisms. The mean age was 74.9 years overall, with patients in the ESBL group being slightly younger than those in the non-ESBL group (72.9 vs 74.9 years, $p < 0.001$). Biological sex distribution was similar between groups ($p = 0.056$), with females comprising the majority overall and in both subgroups. Racial distribution differed significantly between patients with and without ESBL infection ($p < 0.001$). White patients represented the largest racial group overall but made up a smaller proportion within the ESBL group.

Hospital teaching status differed significantly between patients with and without ESBL infection ($p < 0.001$). Most patients in both groups were admitted to urban teaching hospitals, which accounted for

60% of all hospitalizations. Hospital region differed significantly between patients with and without ESBL infection ($p < 0.001$). In both groups, the region with the most patients was the South, followed by the West in patients with ESBL, and the Midwest/North Central in patients without ESBL.

Table 1
Baseline Demographic information

Variable	Overall N = 1,844,239[1]	Non-ESBL N = 1,781,049[1]	ESBL N = 63,190[1]	p-value[2]
Age, years	74.9 ± 0.0	74.9 ± 0.0	72.9 ± 0.1	< 0.001
Biological sex				0.056
Male	534,870 (29%)	517,030 (29%)	17,840 (28%)	
Female	1,309,064 (71%)	1,263,719 (71%)	45,345 (72%)	
Race				< 0.001
White	1,339,469 (76%)	1,297,684 (76%)	41,785 (69%)	
Black	218,045 (12%)	211,225 (12%)	6,820 (11%)	
Hispanic	158,830 (9.0%)	149,300 (8.7%)	9,530 (16%)	
Asian or Pacific Islander	33,295 (1.9%)	31,500 (1.8%)	1,795 (3.0%)	
Native American	8,240 (0.5%)	7,980 (0.5%)	260 (0.4%)	
Other	12,090 (0.7%)	11,585 (0.7%)	505 (0.8%)	
Insurance status				< 0.001
Medicare	1,495,669 (84%)	1,446,874 (84%)	48,795 (80%)	
Medicaid	128,000 (7.2%)	121,935 (7.1%)	6,065 (9.9%)	
Private Insurance	162,410 (9.1%)	156,245 (9.1%)	6,165 (10%)	
Hospital teaching status				< 0.001
Urban Teaching	1,100,405 (60%)	1,061,720 (60%)	38,685 (61%)	
Rural	281,929 (15%)	273,859 (15%)	8,070 (13%)	
Urban Nonteaching	461,904 (25%)	445,469 (25%)	16,435 (26%)	
Hospital region				< 0.001
Northeast	361,890 (20%)	350,725 (20%)	11,165 (18%)	
Midwest or North Central	394,325 (21%)	384,945 (22%)	9,380 (15%)	
South	808,890 (44%)	777,645 (44%)	31,245 (49%)	
West	279,134 (15%)	267,735 (15%)	11,400 (18%)	

[2]Design-based Kruskal Wallis test; Pearson's X^2: Rao & Scott adjustment

Variable	Overall N = 1,844,239[1]	Non-ESBL N = 1,781,049[1]	ESBL N = 63,190[1]	p-value[2]
Median household income in zip code				0.179
0-25th percentile	563,884 (31%)	544,534 (31%)	19,350 (31%)	
26th to 50th percentile	478,500 (26%)	462,005 (26%)	16,495 (27%)	
51st to 75th percentile	412,320 (23%)	398,740 (23%)	13,580 (22%)	
76th to 100th percentile	363,910 (20%)	351,135 (20%)	12,775 (21%)	
Hospital bed size				0.346
Small	500,004 (27%)	483,314 (27%)	16,690 (26%)	
Medium	569,169 (31%)	549,334 (31%)	19,835 (31%)	
Large	775,065 (42%)	748,400 (42%)	26,665 (42%)	
Weekend admission				< 0.001
Weekday	1,376,249 (75%)	1,327,854 (75%)	48,395 (77%)	
Weekend	467,975 (25%)	453,180 (25%)	14,795 (23%)	
Elective admission				< 0.001
Non-elective	1,763,659 (96%)	1,703,884 (96%)	59,775 (95%)	
Elective	78,345 (4.3%)	75,030 (4.2%)	3,315 (5.3%)	

[1]Mean ± SE; n (%)

[2]Design-based Kruskal Wallis test; Pearson's X^2: Rao & Scott adjustment

Mortality of UTI admissions

Mortality outcomes for UTI admissions are summarized in Table 2. There was no significant difference in mortality among male or female patients that were positive for ESBL infection compared to those with non-ESBL UTI infection (p = 0.40 and 0.13, respectively). There was a significant interaction between ESBL status and sex for in-hospital mortality (p = 0.030). Additionally, when compared to admissions of White patients, admissions of Hispanic patients had lower overall in-hospital mortality (OR: 0.78, 95% CI: 0.62 to 0.97, p = 0.028).

Medicaid patients had increased mortality compared to Medicare patients (OR: 1.46, 95% CI: 1.09 to 1.96, p = 0.010). Similarly, patients with private insurance also had increased mortality compared to Medicare patients (OR: 1.43, 95% CI: 1.17 to 1.75, p < 0.001). Patients at rural hospitals had a higher

likelihood of mortality when compared to urban teaching centers (OR: 1.50, 95% CI: 1.29 to 1.75, p < 0.001), as opposed to urban nonteaching hospitals which showed no statistically significant difference (p = 0.23). Mortality by region was significantly lower in the Midwest/North Central region (OR 0.77, 95% CI 0.64 to 0.91, p = 0.002) and in the South (OR 0.76, 95% CI 0.65 to 0.88, p < 0.001) when compared to the Northeast.

When comparing the median household income using the patient's ZIP code, patients in the 76th -100th percentile had lower odds of mortality (OR: 0.79, 95% CI: 0.67 to 0.93, p = 0.006) compared to patients in the 0-25th percentile. There was no significant difference between the mortality odds ratios of patients admitted during the week, or weekend (p = 0.22; Table 2). However, elective admissions had greater odds of mortality when compared to non-elective admissions (OR: 1.57, 95% CI: 1.25 to 1.98, p < 0.001).

Comparisons of medical comorbidities among UTI admissions revealed several significant associations with mortality. In the overall population, UTI admissions with comorbid renal failure were associated with increased mortality compared to those without (OR: 1.41, 95% CI: 1.10 to 1.81, p = 0.006). However, when stratified by sex, male patients did not exhibit this difference (p = 0.35) while female patients did (OR = 1.50, 95% CI: 1.11 to 2.02, p = 0.008). For the overall population, admissions with fluid and electrolyte disorders were associated with increased odds of mortality (OR: 2.28, 95% CI: 1.84 to 2.83, p < 0.001). Admissions with comorbid COVID-19 infection among the overall population demonstrated an increased odds of mortality (OR: 2.11, 95% CI: 1.53 to 2.91, p < 0.001). In the overall population, admissions with for UTI that had comorbid end-stage renal disease also demonstrated increased odds of mortality (OR: 2.60, 95% CI: 1.70 to 3.98, p < 0.001). Admissions with nosocomial infection demonstrated increased odds of mortality in the overall population (OR: 3.82, 95% CI: 2.17 to 6.73, p < 0.001). Bladder drainage device such as a Foley catheter demonstrated higher mortality in the overall population (OR: 1.88, 95% CI: 1.30 to 2.72, p < 0.001). This difference was preserved among female patients (OR: 2.25, 95% CI: 1.40 to 3.63, p < 0.001) but not among male patients (p = 0.39).

Certain conditions were associated with lower odds of mortality among UTI admissions. In the overall population, personal history of urinary tract infection was associated with lower mortality (OR: 0.59, 95% CI: 0.47 to 0.74, p < 0.001). When stratified by sex, this relationship remained true for females (OR: 0.52, 95% CI: 0.40 to 0.68, p < 0.001), however it was not true for males (p = 0.31). In the overall population, a diagnosis of Klebsiella pneumoniae was associated with lower mortality (OR: 0.68, 95% CI: 0.55 to 0.85, p < 0.001). Admissions of male patients with BPH also had lower in-hospital mortality (OR: 0.70, 95% CI: 0.57 to 0.87, p = 0.001).

Table 2
Overall mortality in all patients

Variable	OR[1]	95% CI[1]	p-value
Intervention			
Non-ESBL	—	—	
ESBL	0.78	0.59, 1.03	0.074
Age, years	1.05	1.04, 1.05	< 0.001
Race			
White	—	—	
Black	0.90	0.74, 1.10	0.30
Hispanic	0.78	0.62, 0.97	0.028
Asian or Pacific Islander	0.70	0.46, 1.06	0.089
Native American	1.18	0.59, 2.36	0.64
Other	1.31	0.68, 2.52	0.41
CHF	2.01	1.59, 2.54	< 0.001
Renal failure and disease	1.41	1.10, 1.81	0.006
Metastatic cancer	3.10	2.28, 4.23	< 0.001
Solid tumor without metastasis	1.70	1.27, 2.26	< 0.001
Coagulopathy	2.02	1.60, 2.56	< 0.001
Weight loss	2.82	2.28, 3.49	< 0.001
Fluid and electrolyte disorders	2.28	1.84, 2.83	< 0.001
COVID19	2.11	1.53, 2.91	< 0.001
ESRD	2.60	1.70, 3.98	< 0.001
Personal history of UTI	0.59	0.47, 0.74	< 0.001
BPH	0.70	0.57, 0.87	0.001
Nosocomial infection	3.82	2.17, 6.73	< 0.001
Immunosuppression	0.61	0.52, 0.72	< 0.001
Bladder drainage device	1.88	1.30, 2.72	< 0.001

[1]OR = Odds Ratio, CI = Confidence Interval

Variable	OR[1]	95% CI[1]	p-value
Intervention			
Klebsiella pneumoniae	0.68	0.55, 0.85	< 0.001
[1]OR = Odds Ratio, CI = Confidence Interval			

Total charges of UTI admissions

Total charges for UTI admissions are summarized in Table 3. Admissions with ESBL UTIs had higher charges compared to those with non-ESBL UTIs (mean difference: $9,179, 95% CI: $8,101 to $10,257, p < 0.001). There was no significant interaction between ESBL status and sex for total charges (interaction p = 0.41). Black patients were charged $3,756 more than White patients on average (95% CI: $2,884 to $4,628, p < 0.001). Similarly, Hispanic patients were charged on average $9,004 more than White patients (95% CI: $7,887 to $10,121, p < 0.001). Asian/Pacific Islander patients were charged $7,749 more on average than White patients (95% CI: $5,615 to $9,884, p < 0.001). Finally, patients who identified as “Other” experienced $10,267 greater charges compared to White patients on average (95% CI: $5,610 to $14,923, p < 0.001).

Compared to urban teaching hospitals, patients in rural hospitals were charged $15,722 less for hospitalizations (95% CI: -$16,572 to -$14,871, p < 0.001), and those admitted to urban nonteaching hospitals were charged $1,683 less on average (95% CI: -$2,651 to -$715, p < 0.001). Medium bed sized hospitals had significantly higher hospital charges compared to small bed size hospitals (mean difference: $4,496, 95% CI: $3,454 to $5,538, p < 0.001), as did large bed size hospitals (mean difference: $6,692, 95% CI: $5,690 to $7,695, p < 0.001).

Several notable comorbidities were associated with higher total charges. Admissions in the overall population with comorbid COVID-19 infection had an additional $11,261 charges on average compared to those without (95% CI: $12,775 to $21,760, p < 0.001). Those with end-stage renal disease had an additional $17,267 on average when compared to those without ($17,267, 95% CI: $8,606 to $13,915, p < 0.001). Admissions with nosocomial infections spent an additional $41,898 on average (CI: $27,752 to $56,044, p < 0.001) compared to those without. Admissions for patients with bladder drainage devices experienced an additional $8,620 on average (95% CI: $6,124 to $11,117, p < 0.001). Admissions of patients with lower urinary tract calculi had $11,200 greater charges overall (95% CI: $7,712 to $14,699, p < 0.001). Additionally, patients with Klebsiella pneumoniae were charged an additional $1,833 overall (95% CI: $1,118 to $2,548, p < 0.001). Proteus infection was associated with $2,716 (Mean difference: $2,761, 95% CI: $1,555 to $3,966, p < 0.001) had significantly higher charges.

Several pertinent comorbidities were associated with lower charges. Admissions with comorbid renal failure experienced $4,153 less in charges on average as compared to those without (95% CI: -$5,173 to -$3,314, p < 0.001). Admissions for patients with kidney transplants experienced $7,047 less in charges

as compared to those without (Mean difference: -$7,047 to -$3,507, $p < 0.001$) Penicillin resistance was associated with $3,061 lower charges overall (95% CI: −$5,546 to −$577, $p < 0.016$). Patients who had infection following a procedure also did not show statistically significant differences in overall charges ($p = 0.85$).

Table 3
Overall charge of hospital stay

Variable	Mean difference	95% CI[1]	p-value
Intervention			
Non-ESBL	—	—	
ESBL	9,179	8,101, 10,257	< 0.001
Age, years	-25	-46, -4.8	0.015
Race			
White	—	—	
Black	3,756	2,884, 4,628	< 0.001
Hispanic	9,004	7,887, 10,121	< 0.001
Asian or Pacific Islander	7,749	5,615, 9,884	< 0.001
Native American	-5,383	-7,758, -3,008	< 0.001
Other	10,267	5,610, 14,923	< 0.001
Renal failure and disease	-4,153	-5,173, -3,134	< 0.001
Coagulopathy	2,550	1,054, 4,045	< 0.001
Weight loss	12,054	10,735, 13,374	< 0.001
Fluid and electrolyte disorders	2,694	1,952, 3,437	< 0.001
Drug abuse	-2,657	-4,176, -1,138	< 0.001
COVID19	11,261	8,606, 13,915	< 0.001
ESRD	17,267	12,775, 21,760	< 0.001
Lower urinary tract calculi	11,200	7,712, 14,688	< 0.001
Personal history of UTI	-1,976	-2,572, -1,379	< 0.001
Personal history of other urinary system disease	-5,690	-11,339, -42	0.048
Nursing home	5,208	1,750, 8,666	0.003
Dialysis dependence	-6,879	-11,525, -2,233	0.004
Penicillin resistance	-3,061	-5,546, -577	0.016
Current long term antibiotic use	3,956	1,912, 6,000	< 0.001

[1]CI = Confidence Interval

Variable	Mean difference	95% CI[1]	p-value
Intervention			
Nosocomial infection	41,898	27,752, 56,044	< 0.001
Urogenital implants	-2,992	-4,858, -1,125	0.002
Kidney transplant	-5,277	-7,047, -3,507	< 0.001
T2DM	-2,770	-5,218, -322	0.027
Immunosuppression	-3,105	-3,749, -2,461	< 0.001
Bladder drainage device	8,620	6,124, 11,117	< 0.001
Klebsiella pneumoniae	1,833	1,118, 2,548	< 0.001
Proteus	2,761	1,555, 3,966	< 0.001
Heart transplant	15,401	4,187, 26,616	0.007
Stem cell transplant	17,705	3,704, 31,707	0.013

[1]CI = Confidence Interval

Length of stay of UTI admissions

All values regarding the length of a patient's hospital stay are recorded in Table 4. Overall, patients diagnosed with ESBL UTI stayed hospitalized for 1.0 days longer compared to patients with non-ESBL UTI (95% CI: 0.93 to 1.1, p < 0.001). This difference was comparable among both female patients (mean difference = 1.0 days, 95% CI: 0.93 to 1.1 days, p < 0.001) and male patients (mean difference = 0.96 days, 95% CI: 0.79 to 1.1 days, p < 0.001). There was a significant interaction between ESBL status and sex for LOS (p < 0.001).

Compared to White patients, Black patients had a significantly longer length of stay (mean difference: 0.38 days, 95% CI: 0.29 to 0.47, p < 0.001), while Hispanic patients had a significant shorter length of stay (mean difference = -0.19 days, 95% CI: -0.27 to − 0.12, p < 0.001). Asian/Pacific Islander, Native American, and Other patients did not have significant differences in the length of stay compared to White patients (p = 0.69, 0.82, and 0.20 respectively).

Various comorbidities were associated with statistically significant changes in length of stay. Admissions with comorbid COVID-19 were associated with an additional 2.1 days per stay on average (95% CI: 1.8 to 2.4 days, p < 0.001). Admissions for patients with end-stage renal disease were associated with an additional 1.1 days on average (95% CI: 0.71 to 1.4 days, p < 0.001). Admissions with nosocomial infections were associated with an increase in length of stay by 3.5 days on average (95% CI: 2.6 to 4.4 days, p < 0.001). Admissions for patients with bladder drainage devices were associated with increases of 0.88 days on average (95% CI: 0.47 to 1.3 days, p < 0.001). Admissions in the overall

population for UTIs with beta-lactam resistance were associated with an increase of 0.76 hospitalization days (95% CI: 0.29 to 1.2 days, p = 0.002). This difference was maintained among females (mean difference = 0.47 days, 95% CI: 0.21 to 0.74 days, p < 0.001) but not males (p = 0.054). Additionally, admissions with Klebsiella pneumoniae infections were associated with an increase of 0.50 days on average (95% CI: 0.41 to 0.59 days, p < 0.001), while admissions with proteus infections were associated with an increase of 0.66 days on average (95% CI: 0.51 to 0.80 days, p < 0.001). Patients who had infection following a procedure also did not show statistically significant differences in length of hospital stay (p = 0.69).

Table 4
Overall length of hospital stay

Variable	Mean difference	95% CI[1]	p-value
Intervention			
Non-ESBL	—	—	
ESBL	1.0	0.93, 1.1	< 0.001
Age, years	0.01	0.01, 0.01	< 0.001
Race			
White	—	—	
Black	0.38	0.29, 0.47	< 0.001
Hispanic	-0.19	-0.27, -0.12	< 0.001
Asian or Pacific Islander	0.03	-0.13, 0.19	0.69
Native American	0.03	-0.25, 0.32	0.82
Other	0.17	-0.09, 0.43	0.20
Renal failure and disease	-0.18	-0.29, -0.08	< 0.001
Solid tumor without metastasis	-0.26	-0.38, -0.15	< 0.001
Coagulopathy	0.20	0.08, 0.33	0.002
Weight loss	1.5	1.4, 1.6	< 0.001
Fluid and electrolyte disorders	0.25	0.17, 0.33	< 0.001
Drug abuse	-0.42	-0.58, -0.26	< 0.001
COVID19	2.1	1.8, 2.4	< 0.001
ESRD	1.1	0.71, 1.4	< 0.001
Lower urinary tract calculi	0.37	0.11, 0.63	0.006
Personal history of UTI	-0.17	-0.24, -0.11	< 0.001
Personal history of other urinary system disease	-0.50	-0.91, -0.09	0.018
BPH	-0.11	-0.20, -0.02	0.012
Dialysis dependence	-0.90	-1.2, -0.54	< 0.001
Beta lactam resistance	0.76	0.29, 1.2	0.002

[1]CI = Confidence Interval

Variable	Mean difference	95% CI[1]	p-value
Intervention			
Other antimicrobial resistance	0.42	0.22, 0.62	< 0.001
Quinolones and fluoroquinolones resistance	0.29	0.07, 0.51	0.010
Nosocomial infection	3.5	2.6, 4.4	< 0.001
Immunosuppression	-0.28	-0.33, -0.23	< 0.001
Bladder drainage device	0.88	0.47, 1.3	< 0.001
Klebsiella pneumoniae	0.50	0.41, 0.59	< 0.001
Proteus	0.66	0.51, 0.80	< 0.001
Other bacteria	0.28	0.19, 0.37	< 0.001

[1]CI = Confidence Interval

DISCUSSION

In this study of over 1.8 million patients hospitalized with urinary tract infections, 3.4% were infected with ESBL-producing organisms. Our findings highlight important demographic, socioeconomic, and hospital-level differences between patients with ESBL UTIs and those with non-ESBL UTIs. Overall, ESBL patients were slightly younger than non-ESBL UTI patients (72.9 vs. 74.9 years), with similar sex distribution and exhibited notable disparities by race, insurance type, and hospital characteristics. Hispanic patients had lower mortality compared to white patients, but race was otherwise not a significant contributor to mortality. Although overall mortality did not differ significantly by ESBL status, notable variations in outcomes were found for specific demographics, socioeconomic characteristics, hospital factors, and clinical comorbidities.

Hospital teaching status:

Hospital teaching status impacted a patient's outcomes of mortality, length of stay, and cost. Patients at a rural hospital experienced higher mortality, shorter stays, and lower costs compared to an urban, teaching hospital. The data follow the historic pattern of shorter stays and lower costs for rural hospitals[25]. This pattern in rural hospitals is likely attributed to smaller bed sizes, lower socioeconomic patient population, and the tendency to send more complicated and resource-intensive cases to urban hospitals[26].

Hospital Region

The uneven distribution of ESBL patients across U.S. regions observed in this study mirrors some findings from prior research. Patients in the Midwest/North Central and South incurred lower hospital charges, while patients in the West experienced higher charges compared with the Northeast. These findings align with prior studies that found that the West had the highest average cost of stay compared to all the other regions[27], which reflects the overall higher cost of living in the West.

Hospitals in the South had the lowest mortality rate, and while there were no prior studies on ESBL mortality outcomes stratified by region, regional disparities in infection-related outcomes are well documented, with the South experiencing higher mortality[28]. The South has the highest prevalence of ESBL yet significantly lower mortality, shorter hospital stays, and lower costs, highlighting the need to examine how this region manages ESBL infections, with the goal of applying similar strategies in other regions.

Median Household Income

While all groups were equally experiencing ESBL hospitalization rates, the highest income group experienced lower odds of mortality, a shorter length of stay, and higher hospital charges compared to all other groups. These findings align with prior literature showing that patients in higher-income areas have lower overall all-cause hospitalization length of stay but higher costs per stay whereas lower income groups had longer stay[27]. The association between higher income and reduced mortality parallels existing literature linking greater socioeconomic resources with improved access to health care, health literacy, and chronic disease management[28], highlighting a clear socioeconomic disparity in ESBL outcomes that warrants further investigation, with strategies focused on improving early care for lower-income populations.

Elective or non-elective admission:

In ESBL patients, elective admissions were linked to increased mortality, longer stays, and lower charges compared to non-elective admissions, suggesting a unique clinical profile for ESBL patients. This inverse pattern reflects the distinct clinical circumstances under which ESBL infections occur. ESBL patients are often already hospitalized for other conditions, medically complex, or undergoing elective interventions that increase exposure to invasive devices and healthcare environments, placing them at higher risk for hospital-acquired ESBL infection[29]. As a result, the “elective admission” designation does not necessarily signal lower acuity but instead may identify patients with substantial underlying illness and unintentionally prolonged healthcare contact.

Medical Comorbidities:

Among ESBL patients, higher odds of mortality were observed in male patients and patients with history of renal failure and disease, metastatic cancer, solid tumors without metastasis, fluid and electrolyte disorders, COVID-19, end-stage renal disease, nosocomial infections, and bladder drainage devices. These findings are broadly consistent with previous studies of ESBL infections, which also identify male

sex and comorbidity burden as important risk factors, and demonstrate that ESBL infections are associated with longer hospital stays[3].

Conditions associated with longer LOS and higher costs included nosocomial infections, weight loss, COVID-19, end-stage renal disease, bladder drainage devices, paralysis, fluid and electrolyte disorders, and lower urinary tract calculi. These findings align with a prior study showing that ESBL-producing infections are associated with higher all-cause mortality and longer hospital stays[30]. Patient-level data from prior studies indicate that COVID-19 exacerbates the severity and clinical burden of ESBL infections[31].

Similarly, co-infection with Klebsiella pneumoniae or Proteus was associated with both longer hospital stays and higher costs compared with ESBL infection alone. While ESBL-positive infections are already known to increase length of stay and resource utilization, these findings suggest that the presence of additional pathogen-specific infections further amplifies this effect[32]. Other comorbidities were associated with longer LOS without higher costs, including organisms with antibiotic resistances which may indicate that strict infection control and monitoring high-risk patients may help mitigate LOS and costs.

Limitations:

This study has several limitations. First, the NIS relies on administrative coding, which may lead to misclassification. ESBL infections and comorbidities were identified solely using ICD-10-CM codes, which may not perfectly reflect microbial or other recorded data, and coding practices may vary across hospitals. Second, the NIS captures hospitalizations rather than unique patients, meaning that repeat admissions for the same individual appear as separate observations. Third, the NIS only includes inpatient encounters, meaning that previous outpatient antibiotic exposures, outpatient management of UTIs, or post-discharge outcomes limit the ability to fully assess risk factors and downstream healthcare utilization. Fourth, residual confounding cannot be completely excluded, however multivariate analysis using demographic, clinical, and hospital-level factors was used to mitigate this effect. Finally, missing data was excluded from the analysis, which may have limited the available sample size, however we believe the existing sample size is sufficient to have a 95% confidence level with 5% margin of error.

CONCLUSION

ESBL UTIs are associated with greater healthcare utilization, including longer hospital stays and higher costs, but not with increased in-hospital mortality. These findings suggest that while ESBL infections impose a significant economic and resource burden on the healthcare system, timely recognition and effective inpatient management may mitigate their impact on short-term survival. Understanding the burden of ESBL status among UTI admissions will help healthcare providers and hospital systems optimize resources and establish better outcomes.

Declarations

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AUTHOR CONTRIBUTIONS

S.G. and R.Y. conceived the project. E.B. and S.Z. acquired the data and performed statistical analysis. S.G., R.Y., E.B., S.Z., and J.R. interpreted the data. S.G. and R.Y. wrote the manuscript. E.B., S.Z., J.R., A.T., and M.M. reviewed and edited the manuscript. All authors read and approved the final manuscript.

STATEMENTS AND DECLARATIONS

Ethical considerations

The study was not submitted for research ethics approval as the activities described were conducted as part of the National Inpatient Sample, which is part of the family of databases and software tools developed for the Healthcare Cost and Utilization Project. The study was exempt from our institution's institutional review board since NIS only contains de-identified data collected from hospitalized patients.

Consent to participate

Not applicable.

Consent for publication

Not applicable.

Declaration of conflicting interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article

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Data availability

The National Inpatient Sample is publicly accessible and provided online through the Healthcare Cost and Utilization Project, https://hcup-us.ahrq.gov/nisoverview.jsp.

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