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Hospital Costs and Reimbursement in Patients with Resistant Enterobacteriaceae (ENT) Urinary Tract Infection (UTI) in the United States (US): A Multicenter Analysis

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ABSTRACT

Background: Rates of fluoroquinolone resistance (FQ-R) and third-generation cephalosporin resistance/extended-spectrum beta-lactamases (ESBL+) are rising. These pathogens generally retain susceptibility to intravenous (IV) carbapenems; however, the loss of susceptibility to commonly used oral (PO) antibiotics limits the opportunity to transition these patients home, leading to increased length of stay (LOS) and higher costs. Here, we evaluate the hospital LOS, costs and reimbursement for UTI hospitalizations.

Methods: We analyzed the first positive enterobacteriaceae (ENT) urine culture ≤ 3 days from hospital admission in patients with a primary or secondary UTI ICD10 discharge diagnosis from 68 US hospitals admitted October 1, 2015-2017. Patient characteristics and outcomes were categorized by ESBL+ and FQ-R status. IV to PO was identified as PO therapy after 24 hours of IV. Outcomes were stratified by resistance and PO conversion status.

Results: 16,022 patients were eligible for analysis; 5,017 (31.3%) were FQ-R, 1,763 (11.0%) were ESBL+, and 1,433 (8.9%) were both FQ-R and ESBL+; 2,367 (14.8%) were converted to PO antibiotics during their hospitalization. Overall, mean LOS, costs, and reimbursement were 5.2 days, $9,303 and $8,501 (mean difference between cost and reimbursement: -$878). Mean LOS was shorter and mean difference between cost and reimbursement was lower overall for patients converted to PO therapy vs. those who did not (4.7 vs. 5.3 days, -$532 vs. -$938). Drug resistance was associated with higher LOS and a larger difference between cost and reimbursement; patients who were FQ-R and ESBL+ and did not convert to PO had a mean LOS of 6.0 days, costs of $11,482, and reimbursement of $9,243 (difference: -$2,446). Mean LOS, costs, and reimbursement for patients who were neither FQ-R nor ESBL+ and who did convert to PO therapy were 4.6 days, $7,904, and $7,496 (difference: $527), respectively.

Conclusion: Reduced LOS and substantial cost savings could be recognized by efficiently converting patients receiving IV antimicrobials to PO and discharging them from the hospital. Lack of PO therapies with activity against resistant pathogens has made this challenging; new PO options may help reduce hospital costs and resources required to treat these UTI patients.

INTRODUCTION

- **Fluoroquinolone-non-susceptible (FQ NS) and ESBL-producing (ESBL+) Enterobacteriaceae (ENT) are increasing in frequency as a cause of urinary tract infections in the US and globally.[1,2]**
- **These strains are generally susceptible to intravenous (IV) carbapenems; however there are a lack of oral alternatives.**
- **The loss of susceptibility to the commonly used oral antibiotic treatment alternatives such as quinolones, cephalosporins, trimethoprim/sulfamethoxazole, and nitrofurantoin limits the opportunity to transition these patients home, leading to increased length of stay (LOS) and higher costs.**
- **Here, we evaluate the hospital LOS, costs and reimbursement for UTI hospitalizations.**

METHODS

- **Adult patients were included for analysis if they had a primary or secondary discharge diagnosis of UTI (ICD10 codes) who also had a positive urine culture for the following Enterobacteriaceae (ENT) within 3 days of admission: *Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Enterobacter cloacae, Enterobacter aerogenes*.[3]**
- **Admissions were excluded that underwent surgical procedures or had another cause of infection during index admission using the following ICD10 code categories: any surgical procedure, concomitant skin and skin structure infection, pneumonia or intra-abdominal infection.**
- **Patients from 68 US acute care hospitals in the period between 2015-2017 were included (BD Insights Research Database, Franklin Lakes, NJ USA; [formerly CareFusion Research Database]).**
- **Resistant phenotypes were identified for the following pathogens, where applicable:**
  - Extended spectrum beta-lactamases (ESBLs): confirmed as ESBL+ per commercial panels or intermediate/resistant to extended spectrum cephalosporins (either ceftriaxone, cefotaxime, ceftazidime or cefepime).
  - Fluoroquinolone (FQ) non-susceptible (NS): intermediate or resistant to ciprofloxacin, levofloxacin or moxifloxacin.
- **PO eligibility was identified if, after at least 24 hours of IV therapy, the patient was tolerating PO (identified by pharmacy order for PO medications other than antibiotics) and were clinically stable (white blood cell count of either (a) 2.0-11.0 if baseline was >11 or (b) 2.0-10.0 if baseline was <10.9 24 hours after starting IV antibiotics).**
- **IV to PO was identified as conversion to a PO antibiotic that had a duration of at least 24 hours where PO conversion occurred after at least 24 hours of IV antibiotic therapy.**
- **Patient characteristics and outcomes were categorized by ESBL and FQ resistance status (ESBL- & FQ S, Other [ESBL+ & FQ S OR ESBL- & FQ NS], and ESBL + & FQ NS) in patients that received IV antimicrobials only and/or IV with step-down PO antimicrobial therapy during their hospitalization.**
- **Patient demographics were identified using Agency for Healthcare Research and Quality Clinical Classifications Software (AHRQ CS/CCS) to assess for specific risk factors.[4]**
- **Healthcare-associated (HCA) episodes were defined as admitted from another acute care facility (e.g., skilled nursing facility, long-term acute care hospital, rehabilitation hospital, hospice), admission in the prior 30 days, dialysis ICD10 code Z99.2 (dependence on renal dialysis), or cancer comorbidity as identified in the AHRQ CCS classification.**
- **Unadjusted hospital mortality, cost and length of stay were determined from financial, outcomes and billing data as calculated by each facility.**
- **The Fisher's exact test was used to test for significance.**

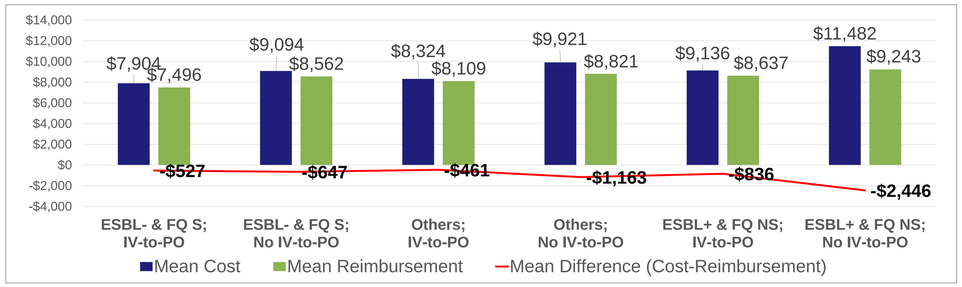
RESULTS

Table 1: Patient Demographics

Measure (mean ± SD, median)	Overall	ESBL- & FQ S		Others (ESBL+ & FQ S OR ESBL- & FQ NS)		ESBL+ & FQ NS	
		IV-to-PO	No IV-to-PO	IV-to-PO	No IV-to-PO	IV-to-PO	No IV-to-PO
N (%)	16,022 (100%)	1,676 (15.5%)	9,108 (84.5%)	535 (14.1%)	3,270 (85.9%)	156 (10.9%)	1,277 (89.1%)
Age	69.5 ± 18.1, 73.0	70.2 ± 18.2, 74.0	68.3 ± 18.9, 72.0	71.9 ± 16.8, 75.0	71.5 ± 16.8, 75.0	70.6 ± 14.3, 72.0	70.7 ± 16.4, 74.0
% Male	22.3%	24.0%	20.3%	23.6%	24.3%	27.6%	28.0%
% Pos. Blood Culture	13.7%	14.3%	14.8%	5.2%	10.8%	5.1%	17.6%
% In ICU	17.2%	15.5%	17.1%	12.3%	19.0%	14.7%	17.1%
% HCA	26.7%	23.3%	25.5%	25.4%	28.7%	34.0%	34.1%
ALaRMS (aggregated severity score)	47.6 ± 19.8, 46.0	47.0 ± 18.0, 46.0	46.8 ± 20.3, 46.0	46.3 ± 17.1, 46.0	49.2 ± 19.5, 47.0	45.9 ± 15.9, 44.0	50.4 ± 20.4, 48.0
% Carbapenem NS	0.6%	0.2%	0.2%	1.1%	0.7%	2.6%	2.7%
% Urinary Catheter/Device	0.8%	1.1%	0.6%	2.4%	1.0%	0.6%	1.2%
% Neurogenic Bladder	3.5%	4.1%	2.7%	5.6%	4.0%	5.1%	6.1%

SD; Standard Deviation. ESBL; Extended Spectrum Beta-Lactamase. FQ; Fluoroquinolone. S; Susceptible. NS; Non-Susceptible. IV; Intravenous. PO; Oral. ICU; Intensive Care Unit. HCA; Health Care-Associated.

Figure 1: Mean Cost and Reimbursement by Resistance Profile



ESBL; Extended Spectrum Beta-Lactamase. FQ; Fluoroquinolone. S; Susceptible. IV; Intravenous. PO; Oral. NS; Non-Susceptible.

Figure 2: Pathogen and Resistance Profile Distribution (N=16,022)

ESBL; Extended Spectrum Beta-Lactamase. FQ; Fluoroquinolone. S; Susceptible. IV; Intravenous. PO; Oral. NS; Non-Susceptible.

CONCLUSIONS

- **Reduced LOS and substantial cost savings could be recognized by efficiently converting patients receiving IV antimicrobials to PO and discharging them from the hospital.**
- **Lack of PO therapies with activity against resistant pathogens has made this challenging; new PO options may help reduce hospital costs and resources required to treat these UTI patients.**

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