

Patient demographics and comorbidity profiles associated with hospitalized patients admitted with resistant vs. susceptible urinary tract infections (UTI): A multicenter analysis

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ABSTRACT

Background: A significant percentage of patients admitted to the hospital with UTI are infected with ESBL positive and quinolone non-susceptible (FQ NS) enterobacteriaceae (ENT) that can complicate patient outcomes due to potentially inadequate antibiotic therapy. We used a large national multicenter database to identify the demographics associated with susceptible and resistant UTI and the underlying comorbidities.

Methods: We analyzed the first positive ENT urine culture ≤ 3 days from admission in those with a discharge primary or secondary UTI ICD10 code from 68 US hospitals from October 1, 2015-2017 (BD Insights, Franklin Lakes, NJ). Patient demographics were identified using AHRQ classifications to assess for specific risk factors and categorized by ESBL and FQ non-susceptible status. Healthcare-associated (HCA) episodes were defined as admissions from another care facility, admission in the prior 30 days, and presence of dialysis or cancer comorbidity. The Fisher's exact test was used to test for significance.

Results: Of 16,022 adults (mean age 69.5 years; 77.7% female) with culture positive ENT UTI were identified; 11.0% (n=1763) were ESBL +, 31.3% (n=5017) were FQ NS & 8.9% (n=1433) being both ESBL + and FQ NS. Admissions with ESBL + /FQ NS were significantly more likely to be male, admitted with HCA risk factors and with higher important comorbidities, such as diabetes, congestive heart failure and chronic pulmonary disease.

Conclusion: About 1 in 11 admissions with UTI are ESBL + /FQ NS and are more likely to be male, with HCA risk factors and other important comorbidities. Current oral antibiotic therapy is limited in such episodes and oral treatment alternatives are needed

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 carbapenem 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.
- We evaluated the epidemiology of IV to PO transition during hospitalization in ENT ESBL + and/or FQ NS UTI admissions.

METHODS

- We analyzed adult patients with 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
- We excluded admissions 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 intraabdominal 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:
 - ESBLs: confirmed as ESBL-positive per commercial panels or intermediate/resistant to extended spectrum cephalosporins (either ceftriaxone, cefotaxime, ceftazidime or cefepime).
 - Quinolone NS: intermediate or resistant to ciprofloxacin, levofloxacin or moxifloxacin.
- 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 non-susceptible status (ESBL -/FQ S, Other [ESBL + OR 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

- Of 16,022 adults (mean age 69.5 years; 77.7% female) with culture positive ENT UTI were identified; 11.0% (n=1763) were ESBL +, 31.3% (n=5017) were FQ NS & 8.9% (n=1433) being both ESBL + and FQ NS.
- ESBL+/FQ NS UTI admissions are associated with a trend toward higher hospital mortality, LOS & cost with other differences noted compared to ESBL-/FQ S & Other (ESBL + or FQ NS) admissions.
- Admissions with ESBL + /FQ NS were significantly more likely to be male, admitted with HCA risk factors and with higher important comorbidities, such as diabetes, congestive heart failure and chronic pulmonary disease.

TABLE 1. US HOSPITAL CHARACTERISTICS.

Region	BD Sites: n=68	
	n	(%)
Northeast	5	(7.4%)
South	32	(47.1%)
Midwest	26	(38.2%)
West	5	(7.4%)
Urban/Rural		
Urban	62	(91.2%)
Rural	6	(8.8%)
Medical School Affiliation		
Major	4	(5.9%)
Limited	12	(17.6%)
Graduate	2	(2.9%)
No Affiliation	50	(73.5%)
Bed size		
<100	12	(17.6%)
100-300	27	(39.7%)
>300	29	(42.6%)

Short-term acute hospitals: Acute & Critical Access, excludes Children's & Specialty sites

TABLE 2. PATIENT COMORBIDITIES BY ESBL AND FQ RESISTANCE STATUS.

Measure	ESBL +		ESBL -	
	FQ NS, N (%)	FQ S, N (%)	FQ NS, N (%)	FQ S, N (%)
N	1,437 (9.0%)	326 (2.0%)	3,580 (22.3%)	10,679 (66.7%)
% Male	403 (28.04)**	62 (19.02)	879 (24.6)¶	2,230 (20.88)
Age (avg ± sdev, med)	70.7, 16.274**	66.9, 19.1, 72	72.1, 16.4, 75¶	68.5, 18.8, 72
% Positive Blood Culture	233 (16.21)*	45 (13.8)	348 (9.72)¶	1,573 (14.73)
% ICU	243 (16.91)	59 (18.1)	651 (18.8)	1,797 (16.83)
% HCA	492 (34.24)**	93 (28.53)	1,015 (28.4)¶	2,678 (25.08)
% Hospital Mortality	44 (3.1)**	8 (2.5)	88 (2.5)¶	201 (1.9)
Length of stay (avg ± sdev, med)	6.3, 5.0, 5.0**	5.4, 4.6, 4.0	5.3, 4.4, 4.4¶	5.0, 4.4, 4
Comorbidities				
Alcohol abuse	30 (2.09)	8 (2.45)	67 (1.87)¶	376 (3.52)
Deficiency Anemias	509 (35.42)*	94 (28.83)	1,054 (29.44)¶	2,797 (26.19)
Rheumatoid arthritis/collagen vascular disease	62 (4.31)**	13 (3.99)	169 (4.72)	458 (4.29)
Congestive heart failure	294 (20.46)**	42 (12.88)	717 (20.03)¶	1,620 (15.17)
Chronic pulmonary disease	345 (24.01)*	65 (19.94)	846 (23.63)¶	1,988 (18.62)
Depression	280 (19.49)**	54 (16.56)	636 (17.77)	1,808 (16.93)
Diabetes w/o chronic complications	320 (22.27)*	61 (18.71)	775 (21.65)¶	1,931 (18.08)
Diabetes w/ chronic complications	313 (21.78)**	71 (21.78)§	666 (18.6)	1,854 (17.36)
Hypertension	894 (62.21)	207 (63.5)	2,265 (63.27)¶	6,537 (61.21)
Hypothyroidism	304 (21.16)*	77 (23.62)	788 (22.01)¶	2,155 (20.18)
Liver disease	72 (5.01)	24 (7.36)§	154 (4.3)	484 (4.53)
Other neurological disorders	274 (19.07)*	49 (15.03)	756 (21.12)¶	1,622 (15.19)
Paralysis	157 (10.93)	22 (6.75)	334 (9.33)¶	562 (5.26)
Peripheral vascular disease	86 (5.98)	13 (3.99)	274 (7.65)¶	704 (6.59)
Psychoses	74 (5.15)	8 (2.45)	207 (5.78)¶	511 (4.79)
Renal failure	404 (28.11)**	74 (22.7)	823 (22.99)¶	2,176 (20.38)
Peptic ulcer Disease x bleeding	23 (1.6)*	2 (0.61)	42 (1.17)	111 (1.04)
Valvular disease	70 (4.87)*	23 (7.06)	173 (4.83)¶	696 (6.52)
Weight loss	156 (10.86)	23 (7.06)	348 (9.72)¶	983 (9.2)

p < .0332 for ESBL+ FQNS vs ESBL-FQNS; * p < .0487 for ESBL+FQNS vs ESBL+FQS; + p < .0175 for ESBL+FQNS vs ESBL-FQS; † p < .0084 for ESBL-FQNS vs ESBL+FQS; ‡ p < .0244 for ESBL-FQNS vs ESBL-FQS; § p < .0395 for ESBL+FQS vs ESBL-FQS

CONCLUSIONS

- About 1 in 11 admissions with UTI are ESBL +/FQ NS and 1 in 3 are ESBL + and/or FQ NS. These admissions are more likely to be male, with HCA risk factors and other important comorbidities.
- Current oral antibiotic therapy is limited in such episodes and oral treatment alternatives are needed.

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