Risk factors for recurrence of community-onset urinary tract infections caused by extended spectrum cephalosporin-resistant Enterobacterales

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Abstract

Background: Extended spectrum cephalosporin-resistant Enterobacterales (ESCR-E) are increasingly implicated in community-onset urinary tract infections (UTIs). In this study, we assessed risk factors for recurrence among patients with community-onset UTI caused by ESCR-E.

Methods: This retrospective cohort study included adult patients evaluated April 2018 – December 2021 in the Duke University Health System with community-onset ESCR-E UTI, defined as (1) ESCR-E in a urine culture obtained in an outpatient clinic, emergency department, or within 48 hours of hospital admission; (2) ≥10 leukocytes per high-power field on urine microscopy or urine dipstick positive for leukocyte esterase; and (3) new antibiotic administration or prescription. ESCR-E UTI recurrence was assessed 14 to 180 days after completion of antibiotic treatment for the index UTI. Patients were right censored at end of follow up period or upon death. Univariate Cox proportional hazards regression was performed to evaluate the relationships between candidate risk factors and time to recurrence.

Results: 1347 patients were included; 202 (15.0%) experienced recurrence. Independent risk factors for recurrence included neurogenic bladder (adjusted HR [aHR] = 1.8, 95% CI = 1.2 to 2.6, p = 0.005), prior history of UTI (aHR = 2.4, 95% CI = 1.7 to 3.3, p<0.001), and fluoroquinolone non-susceptibility (aHR = 1.5, 95% CI = 1.1 to 2.1, p = 0.02). Klebsiella pneumoniae infection was associated with increased hazard of recurrence relative to Escherichia coli in univariate analysis (HR = 1.6, 95% CI = 1.1 to 2.1, p = 0.007) but not in multivariate analysis (aHR = 1.4, 95% CI = 1.0 to 1.9, p = 0.06).

Conclusions: ESCR-E UTI recurrence was common, and several clinical and microbiologic characteristics were associated with recurrence. Patients with these characteristics should receive particular consideration for aggressive UTI risk factor modification and other non-antibiotic prevention strategies. Future studies should evaluate strategies to reduce the risk of recurrence among patients with ESCR-E UTI.

Background

- Extended spectrum cephalosporin-resistant Enterobacterales (ESCR-E) are a leading antimicrobial resistance threat.

- Increasing ESCR-E colonization prevalence and infection incidence in the community; majority of community-associated ESCR-E infections are urinary tract infections (UTIs).

- ESCR-E UTI is associated with increased risk for recurrence compared to extended spectrum cephalosporin-susceptible UTI.

- Risk factors for recurrent ESCR-E UTI have not been previously evaluated.

Methods

- Retrospective cohort study in Duke University Health System, April 2018 – December 2021

- Study cohort: Adults with community-onset ESCR-E UTI* who were alive at 14 days after end of antibiotic therapy

  *Urine culture in outpatient, emergency department, or within 48 hours of hospital admission *with E. coli, K. pneumoniae, K. oxytoca, or P. mirabilis* testing intermediate or resistant to ceftriaxone or ceftazidime + ≥10 white blood cells or positive leukocyte esterase on urinalysis + antibiotic administration/prescription

- UTI recurrence by same species assessed 14-180 days after end of antibiotics for index infection

- Cox proportional hazards regression performed

Results

- Of 1,347 patients with community-onset ESCR-E UTI, 202 (15.0%) experienced recurrence within 6 months.

Table 1. Characteristics of patients with community-onset Extended spectrum cephalosporin-resistant Enterobacterales UTI in Duke University Health System, April 2016 – December 2021 (N=1,347).

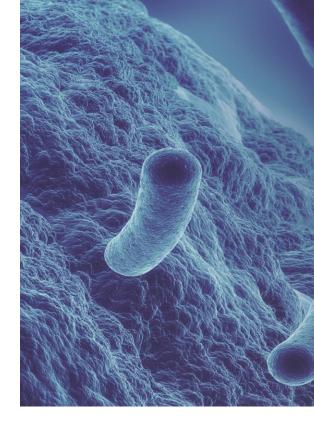| Demographic characteristics	
Age (years), median [IQR]	68 [54-77]
Male sex, n (%)	424 (31.5)
Race, n (%)	
White	733 (54.4)
Black/African American	440 (32.7)
Other/Not reported	174 (12.9)
Ethnicity, n (%)	
Hispanic/Latino	101 (7.5)
Not Hispanic/Latino	1216 (90.3)
Not reported	30 (2.2)
Co-morbidities	
UTI within prior one year, n (%)	728 (54.0)
Diabetes mellitus, n (%)	593 (44.0)
Chronic renal insufficiency, n (%)	478 (35.5)
Renal transplant, n (%)	64 (4.8)
Neurogenic bladder, n (%)	133 (9.9)
Benign prostatic hyperplasia or prostate cancer, n (%)	237 (17.6)
Index UTI characteristics	
Urinary catheter present, n (%)	112 (8.3)
Urologic stone present, n (%)	153 (11.4)
Bacteremia or pyelonephritis, n (%)	241 (17.9)
Pathogen, n (%)	
Escherichia coli	1018 (75.6)
Klebsiella pneumoniae	257 (19.1)
Klebsiella oxytoca	35 (2.6)
Proteus mirabilis	37 (2.8)
Susceptible antibiotics, n (%)	
Ciprofloxacin (1 not tested)	422 (31.3)
Trimethoprim-sulfamethoxazole	509 (37.8)
Nitrofurantoin	970 (72.0)
Piperacillin-tazobactam	1226 (91.0)
Initial antibiotic, n (%)	
Ceftriaxone	389 (28.9)
Piperacillin-tazobactam	199 (14.8)
Nitrofurantoin	190 (14.1)
Ciprofloxacin	115 (8.5)
Other	454 (33.7)
Inappropriate initial therapy, n (%)	653 (48.5)
Definitive antibiotic, n (%)	
Nitrofurantoin	277 (20.6)
Ciprofloxacin	164 (12.2)
Amoxicillin-clavulanate	160 (11.9)
Trimethoprim-sulfamethoxazole	142 (10.5)
Other	604 (44.8)
Inappropriate definitive therapy, n (%)	240 (17.8)
Antibiotic duration (days), median [IQR]	7 [5-10]

Table 2. Univariate and multivariate analyses of risk factors for recurrence of community-onset Extended spectrum cephalosporin-resistant Enterobacterales UTI.

Candidate Risk Factor	Univariate		Multivariate	
	HR (95% CI)	p-value	aHR (95% CI)	p-value
Age (per 1 year increase)	1.01 (1.00 – 1.01)	0.26	1.00 (0.99 – 1.01)	0.64
Male sex	1.09 (0.81 – 1.46)	0.57	0.86 (0.55 – 1.34)	0.51
Pathogen (ref: *E. coli*)				
K. oxytoca	1.07 (0.44 – 2.61)	0.88	0.98 (0.39 – 2.46)	0.97
K. pneumoniae	1.55 (1.13 – 2.13)	0.007	1.37 (0.98 – 1.90)	0.06
P. mirabilis	1.20 (0.53 – 2.73)	0.66	1.18 (0.52 – 2.69)	0.70
Bacteremia or pyelonephritis	1.23 (0.88 – 1.72)	0.24	1.24 (0.88 – 1.76)	0.22
Diabetes mellitus	1.49 (1.13 – 1.97)	0.004	1.26 (0.94 – 1.70)	0.12
Chronic renal insufficiency	1.64 (1.25 – 2.17)	<0.001	1.29 (0.94 – 1.76)	0.11
BPH or prostate cancer	1.08 (0.76 – 1.54)	0.67	1.07 (0.64 – 1.79)	0.80
Neurogenic bladder	2.07 (1.44 – 2.96)	<0.001	1.77 (1.19 – 2.65)	0.005
Renal transplant	1.48 (0.86 – 2.55)	0.16	1.00 (0.55 – 1.79)	0.99
UTI within the prior one year	2.79 (2.03 – 3.85)	<0.001	2.38 (1.70 – 3.31)	<0.001
Inappropriate initial therapy	0.87 (0.66 – 1.15)	0.34	1.02 (0.75 – 1.39)	0.91
Inappropriate definitive therapy	0.83 (0.57 – 1.22)	0.35	0.89 (0.58 – 1.36)	0.59
Quinolone non-susceptible	1.58 (1.14 – 2.19)	0.006	1.50 (1.07 – 2.10)	0.019
TMP-SMX non-susceptible	1.36 (1.01 – 1.82)	0.042	1.12 (0.82 – 1.52)	0.47

Abbreviations: aHR = adjusted hazard ratio; BPH = benign prostatic hyperplasia; HR = hazard ratio; TMP-SMX = trimethoprim-sulfamethoxazole; UTI = urinary tract infection

Contact

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Conclusions

- Recurrence of community-onset ESCR-E UTI was common in this cohort.

- Prior UTI, neurogenic bladder, and fluoroquinolone non-susceptibility were strong risk factors for recurrence.

- Inappropriate antibiotic therapy was not predictive of recurrence.

- Role of pathogen species in ESCR-E UTI recurrence requires further study.