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Risk Factors for Infection with *Escherichia coli* in Nursing Home Residents Colonized with Fluoroquinolone-Resistant *E. coli*

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Abstract

A case-control study to determine risk factors for clinical infection with *Escherichia coli* was conducted among nursing home residents colonized with fluoroquinolone-resistant *E. coli*. Among 94 subjects, 11 (12%) developed infections with *E. coli*. Risk factors included the presence of a urinary catheter or tracheostomy, diabetes mellitus, and trimethoprim-sulfamethoxazole exposure.

Resistance to fluoroquinolone (FQ) antibiotics has increased sharply in the long-term care setting, and FQ-resistant *Escherichia coli* are now among the most common antibiotic-resistant organisms in nursing homes.^{1,2} A recent study demonstrated that among nursing home residents colonized with FQ-susceptible *E. coli*, nearly 50% acquired FQ-resistant *E. coli* within 1 year.³ Given that infection due to FQ-resistant *E. coli* is likely preceded by gastrointestinal colonization, the potential morbidity and mortality due to FQ-resistant *E. coli* infections in this population is high. Therefore, we performed this case-control study to identify risk factors for the development of clinical *E. coli* infections in nursing home residents with FQ-resistant *E. coli* colonization.

METHODS

A case-control study was performed in which the primary outcome was clinical infection with *E. coli*. The initial source population included all residents from 3 major nursing homes in the Academic Long-Term Care Network of the University of Pennsylvania: (1) facility

#1, a 124-bed facility; (2) facility #2, a 240-bed facility; and (3) facility #3, a 200-bed facility.

As described previously, nursing home residents, or their legally authorized representatives, were approached for informed consent during the study period from March 8, 2006, to October 2, 2008.³ Rectal swabs (with stool visually present on the swab) were obtained and submitted to the study laboratory at the Philadelphia Veterans Affairs Medical Center for processing. Identification of *E. coli* from rectal swabs was performed as previously described, with FQ resistance defined as a levofloxacin minimum inhibitory concentration (MIC) $\geq 8 \mu\text{g/mL}$.³ Therefore, the source population for the present study consisted of all patients who were colonized with FQ-resistant *E. coli*.

Data on baseline demographic information, comorbidities, and receipt of antibiotics or corticosteroids during the study period or within 30 days prior to enrollment were collected from medical records using standardized forms. History of a urinary catheter, tracheostomy, enteral feeding tube, diarrhea, fecal incontinence, and confinement to a bed or wheelchair within 30 days of fecal sampling were documented. The study was approved by the institutional review board of the University of Pennsylvania.

Cases were defined as residents who developed a clinical *E. coli* infection within 1 year of the rectal swab, or until discharge or death. Control patients were residents who did not develop an infection with *E. coli* within the same period. Infection was determined via medical record review by an infectious disease-trained physician (JHH) using the modified McGeer Criteria.⁴

Descriptive statistics were conducted to characterize the overall study population. Bivariate analyses of potential risk factors were then performed. Categorical variables were compared using Fisher's exact test and continuous variables were compared using the Wilcoxon rank-sum test. An odds ratio (OR) and 95% confidence interval (CI) were calculated to evaluate the strength of each association. A two-tailed *P* value of <0.05 was considered significant. All statistical calculations were performed using commercially available software (STATA v13.0; StataCorp LP, College Station, Texas).

RESULTS

A total of 94 patients were colonized with FQ-resistant *E. coli* during the study period. The median age of the study population was 77 years (interquartile range [IQR], 64–85 years), 62 (66%) were male, and 66 (70%) self-identified as non-white. The distribution of patients among sites was 40 (42%), 46 (49%), and 8 (9%) residents for sites 1, 2, and 3, respectively. The median length of stay in the nursing home prior to the rectal swab was 137 days (IQR, 28–738 days).

A total of 11 residents (12%) developed subsequent clinical infections with *E. coli* within 1 year of the rectal swab. Of these, 10 (91%) had positive urine cultures, while 1 (9%) had a positive blood culture. The majority of infections ($n=10$; 91%) were due to FQ-resistant *E. coli*; however, 1 patient had a urinary tract infection due to fluoroquinolone-susceptible *E.*

coli. The median time to development of a clinical infection was 131 days (IQR, 57–299 days).

Results of bivariate analyses are shown in Table 1. The presence of a urinary catheter (OR, 10.4; 95% CI, 1.85–54.9; $P=.003$) or tracheostomy (OR, 30.4; 95% CI, 2.00–1612; $P=.005$) significantly increased the risk of developing a clinical *E. coli* infection. Trimethoprim-sulfamethoxazole (TMP-SMX) exposure within 30 days prior to enrollment, or at any time during the study period, was associated with development of an *E. coli* infection (OR, 10.7; 95% CI, 1.90–56.3; $P=.003$), as was the presence of diabetes mellitus (OR, 7.80; 95% CI, 1.45–77.2; $P=.007$).

DISCUSSION

In this multisite, case-control study, 12% of nursing home residents who were colonized with FQ-resistant *E. coli* developed clinical infections with *E. coli* during the study period. The majority of these were urinary tract infections, and all cases except 1 were due to FQ-resistant *E. coli*. Significant risk factors for a clinical infection with *E. coli* included exposure to TMP-SMX during the study period or within 30 days prior to enrollment, the presence of a urinary catheter or tracheostomy, and comorbid diabetes mellitus.

A novel finding of our study was that treatment with TMP-SMX was a risk factor for subsequent infection with *E. coli*. Although a mechanism for such activity is unclear, given that the susceptibility rate of FQ-resistant *E. coli* to TMP-SMX in our population was low (~40%), selective pressure exerted by treatment with TMP-SMX may have predisposed patients to infection with FQ-resistant *E. coli*. This finding underscores the results of a recent study showing high rates of inappropriate antibiotic use in nursing homes.⁵ While further exploration is needed to elucidate the association between TMP-SMX and *E. coli* infections, it is clear that standardized antibiotic stewardship measures are urgently needed in the nursing home setting.

Our study underscores the need for more judicious use of indwelling urinary catheters in nursing home residents. Up to 10% of nursing home residents have indwelling urinary catheters, and numerous studies have shown that the associated burden of colonization and infection, particularly with antibiotic-resistant organisms, is high.^{6–8}

In addition, our study revealed an increased risk in clinical *E. coli* infections in patients with diabetes mellitus. The infection risk burden due to diabetes may be increased in the nursing home setting due to high rates of underlying conditions that predispose patients with diabetes toward infections (eg, hyperglycemia-related impairment of immune response, vascular insufficiency, neurogenic bladder), as well as multimorbidity.⁹

This study has several potential limitations. The relatively small number of infections may have precluded our ability to detect certain significant associations. Misclassification bias is a concern in case-control studies. However, medical record review for clinical infection was performed prior to data collection, and cases and controls were drawn from the same nursing home population and were classified solely based on development of infection. Pulsed-field gel electrophoresis of colonizing and clinical isolates was not performed for the present

study; therefore, we cannot definitively conclude that the observed *E. coli* infections arose from strains colonizing the gastrointestinal tract. Finally, because the study was conducted in a single healthcare system, these results may not be generalizable to other institutions.

In conclusion, our study demonstrated a modest rate of development of clinical *E. coli* infections among nursing home residents colonized with FQ-resistant *E. coli*. Future studies should focus on the development and implementation of guidelines for urinary catheter removal and on determining optimal antibiotic management of infections in nursing home populations.

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References

1. Vromen M, van der Ven AJ, Knols A, Stobberingh EE. Antimicrobial resistance patterns in urinary isolates from nursing home residents. Fifteen years of data reviewed. *J Antimicrob Chemother.* 1999; 44:113–116. [PubMed: 10459818]
2. Viray M, Linkin D, Maslow JN, et al. Longitudinal trends in antimicrobial susceptibilities across long-term-care facilities: emergence of fluoroquinolone resistance. *Infect Control Hosp Epidemiol.* 2005; 26:56–62. [PubMed: 15693409]
3. Han JH, Maslow J, Han X, et al. Risk factors for the development of gastrointestinal colonization with fluoroquinolone-resistant *Escherichia coli* in residents of long-term care facilities. *J Infect Dis.* 2014; 209:420–425. [PubMed: 23986544]
4. Stone ND, Ashraf MS, Calder J, et al. Society for Healthcare Epidemiology Long-Term Care Special Interest Group. Surveillance definitions of infections in long-term care facilities: revisiting the McGeer criteria. *Infect Control Hosp Epidemiol.* 2012; 33:965–977. [PubMed: 22961014]
5. Nicolle LE, Bentley DW, Garibaldi R, Neuhaus EG, Smith PW. Antimicrobial use in long-term-care facilities. *Infect Control Hosp Epidemiol.* 2000; 21:537–545. [PubMed: 10968724]
6. Das R, Perrelli E, Towle V, Van Ness PH, Juthani-Mehta M. Antimicrobial susceptibility of bacteria isolated from urine samples obtained from nursing home residents. *Infect Control Hosp Epidemiol.* 2009; 30:1116–1119. [PubMed: 19785518]
7. Nicolle LE. The chronic indwelling catheter and urinary infection in long-term-care facility residents. *Infect Control Hosp Epidemiol.* 2001; 22:316–321. [PubMed: 11428445]
8. Wang L, Lansing B, Symons K, et al. Infection rate and colonization with antibiotic-resistant organisms in skilled nursing facility residents with indwelling devices. *Eur J Clin Microbiol Infect Dis.* 2012; 31:1797–1804. [PubMed: 22274858]
9. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). *FEMS Immunol Med Microbiol.* 1999; 26:259–266. [PubMed: 10575137]

TABLE 1

Bivariate Analyses of Risk Factors for Clinical Infection with *E. coli* in Patients with Baseline Colonization with Fluoroquinolone-Resistant *E. coli*

Variable	Cases (n =11)	Controls (n =83)	OR (95% CI)	P Value
Age, median years, no. (IQR)	68 (52–85)	76 (64–85)15
Female sex, no. (%)	4 (36)	28 (34)	1.12 (0.22–4.86)	>.99
Length of stay prior to initial swab date, median days (IQR)	150 (28–255)	122 (27–767)67
Site, no. (%)				
Facility #1	38 (46)	2 (18)	...	
Facility #2	38 (46)	8 (73)		.15
Facility #3	7 (8)	1 (9)		
Year of sampling, no. (%)				
2006	56 (67)	8 (73)	...	
2007	14 (17)	1 (9)		>.99
2008	13 (16)	2 (18)		
Receipt of trimethoprim-sulfamethoxazole, no. (%) ^{a,b}	5 (45)	6 (7)	10.7 (1.90–56.3)	.003
Bed-bound, no. (%)	1 (9)	9 (11)	0.82 (0.02–7.19)	.67
Wheelchair bound, no. (%)	6 (5)	40 (49)	1.26 (0.29–5.65)	.76
Skilled nursing needed, no. (%)	4 (36)	36 (44)	0.73 (0.15–3.15)	.75
Feeding tube, no. (%)	0 (0)	11 (13)35
Admitted from an acute care hospital, no. (%)	7 (64)	61 (73)	0.63 (0.14–3.25)	.49
Hospitalization in previous year, no. (%)	7 (70)	67 (83)	0.49 (0.96–3.31)	.39
Diabetes mellitus, no. (%)	9 (82)	30 (37)	7.80 (1.45–77.2)	.007
Cardiovascular disease, no. (%)	3 (27)	14 (17)	1.82 (0.27–8.84)	.42
Respiratory disease, no. (%)	2 (18)	10 (12)	1.60 (0.15–0.89)	.63
Chronic kidney disease, no. (%) ^c	1 (9)	16 (19)	0.42 (0.01–3.38)	.68
Malignancy, no. (%)	2 (18)	19 (23)	0.74 (0.07–4.03)	>.99
Fecal incontinence, no. (%)	8 (73)	42 (51)	2.54 (0.55–15.6)	.21
Decubitus ulcer, no. (%)	2 (18)	19 (23)	0.74 (0.72–4.03)	>.99
Urinary catheter, no. (%)	5 (45)	6 (7)	10.4 (1.80–54.9)	.003
Central venous catheter, no. (%)	1 (9)	5 (6)	1.52 (0.29–15.7)	.54
Tracheostomy, no. (%)	3 (27)	1 (1.2)	30.4 (2.00–1612)	.005

NOTE. OR, odds ratio; CI, confidence interval; IQR, interquartile range.

^a <30 d prior to enrollment up to study follow-up.

^b All other antibiotic exposures had *P* values >.05.

^c Serum creatinine >2 mg/dL or requirement of hemodialysis.