



Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Risk factors for early return visits to the emergency department in patients with urinary tract infection☆

Sarah Jorgensen, Pharm. D.^{a,b}, Mira Zurayk, Pharm. D.^a, Samantha Yeung, MSc, Pharm. D.^b, Jill Terry, Pharm. D.^a, Maureen Dunn, MD^c, Paul Nieberg, MD^d, Annie Wong-Beringer, Pharm. D.^{a,b,*}

^a Department of Pharmacy, Huntington Hospital, 100 W California Blvd, Pasadena, CA 91105, United States

^b University of Southern California, School of Pharmacy, 1985 Zonal Ave, Los Angeles, CA 90089, United States

^c Division of Emergency Medicine, Department of Medicine, Huntington Hospital, 100 W California Blvd, Pasadena, CA 91105, United States

^d Division of Infectious Diseases, Department of Medicine, Huntington Hospital, 100 W California Blvd, Pasadena, CA 91105, United States

ARTICLE INFO

Article history:

Received 5 April 2017

Received in revised form 15 June 2017

Accepted 21 June 2017

Available online xxxx

Keywords:

Urinary tract infection

Return visits

Emergency department

ABSTRACT

Background: Optimal management of urinary tract infections (UTIs) in the emergency department (ED) is challenging due to high patient turnover, decreased continuity of care, and treatment decisions made in the absence of microbiologic data. We sought to identify risk factors for return visits in ED patients treated for UTI.

Methods: A random sample of 350 adult ED patients with UTI by ICD 9/10 codes was selected for review. Relevant data was extracted from medical charts and compared between patients with and without ED return visits within 30 days (ERVs).

Results: We identified 51 patients (15%) with 59 ERVs, of whom 6% returned within 72 h. Nearly half of ERVs (47%) were UTI-related and 33% of ERV patients required hospitalization. ERVs were significantly more likely ($P < 0.05$) in patients with the following: age ≥ 65 years; pregnancy; skilled nursing facility residence; dementia; psychiatric disorder; obstructive uropathy; healthcare exposure; temperature ≥ 38 °C heart rate > 100 ; and bacteremia. *Escherichia coli* was the most common uropathogen (70%) and susceptibility rates to most oral antibiotics were below 80% in both groups except nitrofurantoin (99% susceptible).

Cephalexin was the most frequently prescribed antibiotic (51% vs. 44%; $P = 0.32$). Cephalexin bug-drug mismatches were more common in ERV patients (41% vs. 15%; $P = 0.02$). Culture follow-up occurred less frequently in ERV patients (75% vs. 100%; $P < 0.05$).

Conclusions: ERV in UTI patients may be minimized by using ED-source specific antibiogram data to guide empiric treatment decisions and by targeting at-risk patients for post-discharge follow-up.

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1. Introduction

Urinary tract infection (UTI) is a leading cause of infection among patients presenting to the emergency department (ED), accounting for nearly 2 million visits in females of all ages and 160,000 visits in males age 65 and older in the US in 2013 [1]. Relapse or recurrent infection occurs in up to 44% of women with community-acquired cystitis [2]. The likelihood of treatment failure increases with age and in those with complicated infection [3]. Several investigators have also identified UTI to be among the most common diagnosis in patients with return visits to the ED [4–6]. Revisits to the ED are expensive and add strain to already overburdened EDs [6]. The evolving structure of healthcare reimbursement places increasing emphasis on value driven care. Thus,

accurate identification of patients at risk for return visits is critical to inform the development of interventions aimed at improving outcomes and healthcare resource utilization.

Optimal management of UTIs in the ED setting is particularly challenging due to high patient turnover, decreased continuity of care, and therapeutic decisions made in the absence of microbiologic data. Furthermore, the increasing emergence of antimicrobial resistance among uropathogens in the community and inpatient settings [7,8] presents a significant challenge for ED clinicians to balance prompt initiation of effective empiric antibiotic therapy without overprescribing broad spectrum agents. ED return visits within 30 days (ERVs) in patients with UTI may be related to a number of factors including resistance to antimicrobial therapy, uncorrected functional or structural urinary tract abnormalities, recurrent infection or unrelated issues. Previous studies have sought to identify risk factors for ERVs in the general ED population [5,9–11]. Several revisit prediction models have also been developed for the elderly, for patients within specific payor groups and/or within specific disease groups [12–16] but none, to our knowledge,

☆ Investigator initiated grant support from Merck Inc. to AWB

* Corresponding author at: University of Southern California, School of Pharmacy, United States.

E-mail address: anniew@usc.edu (A. Wong-Beringer).

have investigated the risk factors for ERVs in ED patients treated for UTI. Thus, we sought to examine host factors, antimicrobial resistance and treatment decisions in ED patients with UTI to identify at risk groups for ERVs.

2. Methods

This was a retrospective cohort study conducted at a 636-bed, non-profit, community teaching hospital in Pasadena, CA. The 50-bed Level II Trauma Center and ED have an annual census of >70,000 patient visits. The study protocol was approved by the Huntington Hospital and the University of Southern California Institutional Review Boards with waivers for informed consent.

Patients presented to the ED with a primary or secondary UTI diagnosis by ICD codes (ICD-9595.9, 599.0; ICD-10 N30.00, N30.01, N39.0) and discharged directly from the ED between July 2015 and June 2016 were identified. A total of 350 patients were randomly selected to represent approximately 10% of the population of interest. Exclusion criteria were: 1) age < 18 years, 2) refusal of evaluation and/or treatment, and 3) incomplete medical record. Only the first visit was counted as the index visit for patients with multiple ED visits during the study period. Time to ERV was recorded as within 72 h or beyond 72 h of the index visit. Relevant patient demographic, laboratory and clinical data were extracted from the electronic medical record using a structured data collection form and entered into REDCap (Research Electronic Data Capture, Vanderbilt University), an electronic data capture tool hosted at the University of Southern California.

Urinalysis and urine cultures were collected from ED patients in the course of routine medical care. For the purposes of this study, a positive urinalysis was defined as one or more of the following: leukocytes \geq trace and/or nitrite positive on urine dipstick; leukocyte esterase \geq trace and/or nitrite positive on macroscopic urinalysis; and/or WBC \geq 10/HPF and/or bacteria \geq small on microscopic urinalysis. Uropathogen colony counts $\geq 10^3$ cfu/mL in a voided or catheter specimen were reported as positive. Urine cultures showing three or more organisms were reported as probable contamination. Automated bacterial identification and susceptibility testing was conducted on positive urine cultures using the BD Phoenix Automated Microbiology System (BD Diagnostic Systems, Sparks, MD). Antibiotic susceptibility was interpreted using the CLSI 2015 breakpoint criteria [17]. An *E. coli* cefazolin breakpoint of ≤ 16 mcg/mL was used as a surrogate for cephalixin susceptibility in patients with uncomplicated cystitis while a breakpoint of ≤ 2 mcg/mL was used for complicated UTI [17]. Intermediate susceptibility was considered non-susceptible. ESBL phenotype was detected via the Phoenix BDXpert system (BD Diagnostic Systems, Sparks, MD). Phenotypic ESBL confirmation testing, using *disk-diffusion* with both cefotaxime and ceftazidime alone and in combination with clavulanic acid, was performed on isolates demonstrating indeterminate susceptibility patterns by the BDXpert system.

Symptomatic presentation was classified as UTI-specific (dysuria, urinary urgency, urinary frequency, flank/back pain) or non-specific (nausea/vomiting, abdominal pain, subjective fevers/chills, acutely altered mental status, fall, anorexia, malaise, lethargy, dizziness, and new or worsening incontinence). Patients without UTI-specific or non-specific symptoms were classified as asymptomatic. We observed that, irrespective of the reason prompting the ERV, UTI was often listed as an active diagnosis in patients returning within a week of their index visit and coded as such. Thus we considered ERVs to be UTI-related based on both ICD codes and documentation of UTI signs or symptoms in the medical record. Symptomatic patients were considered to have a complicated UTI if any of the following characteristics were present: age ≥ 65 years; male gender; pregnancy; history of structural or functional urinary tract abnormality (history of kidney stones, prostate pathology, urinary catheter within 30 days, genitourinary procedure within 60 days, neurogenic urinary retention, ureteral stricture, renal or bladder cancer, renal transplant, single kidney, and nephrostomy

tubes); immunocompromising condition (diabetes with A1c > 8.5% and/or random glucose >200 mg/dL, active cancer, chemotherapy or biological agent within 30 days, prednisone or equivalent ≥ 20 mg/day ≥ 2 weeks, dialysis and HIV infection); failure of outpatient management for index UTI; history of recurrent UTI (≥ 2 UTI/6 months or ≥ 3 UTI/12 months) or presence of signs or symptoms of upper tract/systemic infection (subjective fever/chills, flank/back pain, acutely altered mental status, temperature ≥ 38 °C, WBC > $12 \times 10^3/\mu\text{L}$, bands >5%, systolic blood pressure < 100 mm Hg). All other symptomatic patients were considered to have an uncomplicated UTI.

A pharmacist-managed culture follow-up program has been operational in our ED since 2014. Clinical pharmacists with specialized post-graduate emergency medicine training are present in the ED between 0700 h and 2300 h daily during which time computerized decision software alerts them to positive cultures for patients discharged from the ED. For patients with discordant therapy, the ED pharmacist and physician determine a follow-up plan which may include a change in therapy or patient re-evaluation. The pharmacist is responsible for contacting the patient by telephone to communicate the plan.

3. Data analysis

Comparisons between categorical variables in patients with and without ERVs were performed using Chi-square or Fisher's exact tests as appropriate. Differences among continuous variables were evaluated using Mann Whitney *U* test. All statistical tests were performed using Prism version 7.0 (GraphPad Software, San Diego, CA). A 2-tailed *P* value of <0.05 was considered to be statistically significant.

4. Results

We identified 51/350 patients (15%) with 59 ERVs during the study period, of whom 6% (20/350) returned within 72 h of their index visit and 2% (8/350) returned twice within 30 days. Nearly half (47%, 28/59) of ERVs were UTI-related. The proportions of patients with a UTI-related reason for return did not differ between those returning within 72 h and those returning beyond 72 h (55% vs. 44%; *P* = 0.41). Overall one-third of ERV patients (17/51) were subsequently hospitalized, biasing towards those returning within 72 h compared to those returning later (40% vs. 29%; *P* = 0.14) and those returning for a non-UTI-related reason (39% vs. 18%; *P* = 0.09).

Patient characteristics are shown in Table 1. Patients with ERVs were significantly older than those who did not return to the ED (mean age 57 years vs. 49 years; *P* = 0.03). Specifically, nearly half of ERV patients were 65 years or older (45% vs. 27%; *P* = 0.008) and had Medicare insurance (31% vs. 17%; *P* = 0.01). In contrast, the proportions of patients with Medicaid, private insurance or no insurance were similar between groups. ERVs were more likely in patients with the following characteristics in descending order of odds ratio: pregnancy (odds ratio [OR], 6.3; 95% confidence interval [CI], 1.8–22.0; *P* = 0.02); residence in a SNF (OR, 5.6; 95% CI, 1.4–15.7; *P* = 0.001); obstructive uropathy (OR, 5.3; 95% CI 1.7–19.0; *P* = 0.03); comorbid dementia (OR, 4.5; 95% CI, 1.7–11.1; *P* = 0.0009); healthcare exposure within 6 months of the index ED visit (OR, 2.3; 95% CI 1.2–4.1; *P* = 0.01) and psychiatric disorder (OR, 2.2; 95% CI, 1.1–4.5; *P* = 0.03).

A comparison of the clinical presentation in those with and without ERVs is shown in Table 2. The majority of patients in both groups presented with a complicated UTI (73% vs. 67%; *P* = 0.67) and less than half reported UTI-specific symptoms (45% vs. 46%; *P* = 0.96). Approximately 15% of patients in both groups were asymptomatic (16% vs. 14%; *P* = 0.81). ERVs were significantly more likely in patients with fever (*T* ≥ 38 C; OR 5.3; 95% CI, 1.7–19.0; *P* = 0.01) and tachycardia (HR > 100; OR 3.6; 95% CI, 1.6–8.4; *P* = 0.002).

Microbiological characteristics are shown in Table 3. Urinalysis was performed in all study patients and the results were positive in >99% (347/350). Among the patients with a negative urinalysis result (*n* =

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