



Escherichia coli Resistance to Ciprofloxacin in Acute Uncomplicated Pyelonephritis

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Abstract

Background: Severe acute uncomplicated pyelonephritis is an infection of the kidneys that usually have an ascending route and occur in presumably healthy urinary tract. The most common pathogen involved is *E. coli*. The Infectious Diseases Society of America (IDSA) has issued an updated guideline in 2010 suggesting IV quinolones to be considered in the initial empiric antimicrobial therapy giving known resistance of less than 10%. However, *E. coli* resistance to quinolones has been increasing, the recent data of *E. coli*, causing pyelonephritis, resistance is not known in the Midwest. Local hospital antibiogram for two years showed up to 22% resistance to ciprofloxacin among *E. coli* isolates. **Methods:** We conduct a retrospective non-concurrent cohort study in one teaching hospital in the Midwest, females who were admitted with severe acute uncomplicated pyelonephritis in a three years period were included. Patients with urinary tract obstruction, pregnancy, immuno-suppression, males, and indwelling Foley's catheters were excluded. Data collected include causative pathogens and resistance to antibiotics were collected. Percentages, frequencies, and measures of central tendency and dispersion were calculated to describe the study sample **Results:** 73 patients were included in the final analysis. *E. coli* was the most common isolated pathogen (81%), followed by other enteric gram negative. *E. coli* resistance to ciprofloxacin was 13.5%, 37% to trimethoprim-sulfamethoxazole, and 5% to ceftriaxone. **Conclusion:** Ciprofloxacin should be avoided initially in treating severe acute uncomplicated pyelonephritis until culture results and sensitivity is available.

Subject Areas

Pharmacology

Keywords

E. coli, Pyelonephritis, Ciprofloxacin

1. Introduction

Acute pyelonephritis is a severe infection of the kidney, usually have an ascending route of infection, that carries an annual incidence of 15 - 17 cases per 10,000 population among females [1]. It is classified into complicated and uncomplicated pyelonephritis, where complicated urinary tract infection (UTI) occurs in patients with abnormal urinary tract. UTI and pyelonephritis are considered uncomplicated when it occurs in non-pregnant females and presumed healthy urinary tract [2] [3]. *E. coli* is the most common cause of uncomplicated pyelonephritis accounting for almost 80%, followed by other enteric gram negative bacteria [1] [3].

The Infectious Diseases Society of America (IDSA) has issued in 2010 a clinical practice guideline for the treatment of uncomplicated cystitis and pyelonephritis in women. It recommends the use of intravenous antimicrobial, such as fluoroquinolones; an aminoglycoside; an extended-spectrum cephalosporin or extended-spectrum penicillin; or carbapenem [2]. They also suggest considering the local *E. coli* antimicrobial resistance when selecting the initial intravenous antimicrobial, resistance prevalence threshold above which the fluoroquinolones is not recommended is 10% [3]. Rates of quinolones resistance among *E. coli* have shown an upward trend [4]. Consequently, IDSA has suggested continuing monitoring local *E. coli* resistance and evaluating its rate over time to sustain optimum empiric therapy [2].

According to our knowledge, local data for *E. coli* resistance is missing in the Midwest, it has been reported that United State medical centers have higher rates of resistance than Canadian centers. This study was performed at a community hospital in the Midwest, the hospital's microbiology antibiogram for 2016 has shown 20% *in vitro* ciprofloxacin resistance among *E. coli* isolates (in 2015 it was 22%). Ceftriaxone resistance was only 5%; this antibiogram reported all *E. coli* isolates from all sources (blood, urine, skin, etc.) and doesn't differentiate between clinical infection or colonization.

The aim of this study is to follow the *E. coli* resistance trend in the Midwest following the IDSA recommendation.

2. Methods

Setting: A 443-bed public teaching hospital located in the Midwest.

Subjects: This study included all female patients who were admitted to the hospital between January 2013 and December 2016 with acute uncomplicated pyelonephritis. Patients were identified from the electronic medical records using the international classification of diseases-9 (ICD-9) and 10 (ICD-10). Codes

for pyelonephritis, sepsis, and urinary tract infection were used. The study was reviewed and approved by the cognizant Institutional Review Board.

Project Design: This is a non-concurrent cohort study comprised of 362 patients whose charts were reviewed. Patients with complicated pyelonephritis were excluded (pregnant, males, urinary tract obstruction by stones or tumors, immune-compromised, indwelling foleys catheter, urinary incontinence, advanced uncontrolled diabetes mellitus, and patients with ureteral stents); patients with simple cystitis were excluded as well. Only patients with positive urine culture were included. A total 72 patients met the inclusion criteria for this study.

Data-Collection: Sociodemographic, pyelonephritis clinical features, and laboratory and microbiological information were obtained from medical charts using the electronic medical records system. Data gathered included patient's age, race, presence or absence of co-morbidities (e.g. diabetes mellitus, hypertension, chronic kidney disease, and non-obstructing kidney stones), laboratory studies, blood culture results, urine culture results, initial antibiotic used, complications, (e.g. *Clostridium difficile* infection), and health outcomes (e.g. in-hospital death).

Data-Analysis: Before any statistical analysis was done, we determined the presence of data outliers, out of range values, and any need for data cleaning and editing by performing a series of frequencies, proportions, descriptive statistics (e.g. mean, median and standard deviation) and figures (e.g. histograms and box and whisker plots). After this process was completed, any needed data editing and cleaning was conducted. Percentages, frequencies, and measures of central tendency and dispersion were calculated to describe the study sample. All analyses were done using Stata (Stata Corporation, College Station, TX).

3. Results

A total of 72 patients met the criteria for analysis; selected sociodemographic characteristics, laboratory findings, outcomes, and co-morbidities are summarized in **Table 1**. Mean age was 35.2 years, 22% of the patients are diabetic, and these patients have controlled diabetes mellitus and has no genitourinary complications. Patients with neurogenic bladder as a complication from diabetes mellitus were excluded.

Causative bacteria are summarized in **Table 2**. Most common organism was *Escherichia coli*, followed by *Klebsiella pneumonia*. This is consistent with the known causative agents for urinary tract infections in general.

Resistance pattern of *E. coli* is summarized in **Table 3**, 5% of the isolates were ESBL positive. Ceftriaxone was chose as the first empirical antibiotics in 58% of the cases while ciprofloxacin in 30.5%. Among *E. coli* isolates, 13.5% were resistant to Ciprofloxacin.

There was no in-hospital deaths or development of CD colitis.

4. Discussion

Acute uncomplicated pyelonephritis that is severe enough requiring admission

Table 1. Patient characteristics, laboratory finding, and outcome.

Characteristics	
Mean Age (years)	35.2
African American	54%
Diabetes Mellitus	22%
Hypertension	30%
Chronic Kidney Disease	7%
Non-Obstructing kidney stone	13%
White Blood cells > 10 K	57%
Urine Leukocyte esterase	83%
Pyuria	95%
Urine Nitrates	44%
Intensive care unit admission	6%
Septic shock	4%
Acute Kidney Injury	13%

Table 2. Causative bacteria.

Bacteria	(n)
<i>Escherichia coli</i>	82.0% (59)
<i>Klebsiella pneumoniae</i>	14.0% (10)
<i>Citrobacter</i>	2.7% (2)
<i>Pseudomonas aeruginosa</i>	1.3% (1)

Table 3. Antibiotics resistance among *E. coli*.

Antibiotics	Resistance percentage (%)
Ceftriaxone	5.0
Cefazolin	17.0
Ciprofloxacin	13.5
Cefepime	5.0
Piperacillin-tazobactam	1.6
Bactrim	37.0
Imipenem	0.0

to the hospital and intravenous antibiotics can result in significant morbidity and possibly mortality if not treated properly with the right empiric antibiotic. Choosing the best antibiotics should be based on the recent guidelines and guided by the local data of bacterial resistance, it is also important to take into consideration the clinical condition of the patient. Local epidemiological data is not readily available in all settings, and some hospitals depend on microbiology laboratory derived bacterial resistant chart (antibiogram). The antibiogram pro-

vide guidance keeping in mind the accuracy is not optimum as these data represents all isolates and not specific for specific diseases, one study compared one hospital antibiogram with actual cystitis cases and found less *E. coli* resistance in cystitis patients than what was reported in the antibiogram [5].

E. coli is the most common causative pathogen in uncomplicated pyelonephritis as well as UTI (75% - 90%) [1] [6]. Our study showed that *E. coli* is responsible for 81% of the cases. Quinolones and Ciprofloxacin are widely used in treating uncomplicated pyelonephritis and considered to be highly effective for inpatient and outpatient management [7]. In our study, 30 % of patients received Ciprofloxacin as the initial antibiotics. Some *E. coli* strains can develop resistance to ciprofloxacin through either changes in the targeted protein or decreased penetration, and that is acquired through chromosomal mutation [8] [9]. Recent studies has suggested an increasing trend of Cipro resistance among *E. coli* isolates [10]. IDSA and some recent review articles has suggested a threshold of 10% Cipro resistance above which Quinolones should not be used empirically before the sensitivity results [2] [3]. Our study found 13.5% resistance among ciprofloxacin in *E. coli* isolates in female patients admitted with severe acute uncomplicated pyelonephritis, this increasing resistance maybe due to increasing usage of quinolones in general treating the simple cystitis. It was also noted that *E. coli* has high resistance to trimethoprim-sulfamethoxazole (37%). This is higher than the previously reported resistance range from previous studies (up to 22%) [10].

This study suggests using other antibiotics than ciprofloxacin and trimethoprim-sulfamethoxazole that are known to be effective empirically until culture results are back in treating severe uncomplicated pyelonephritis inpatient. Weather these results should be used in treating mild to moderate cases of pyelonephritis is uncertain, additional studies are required to determine valid resistance patterns.

Limitations

Our study included only patients with severe pyelonephritis requiring inpatient treatment. The reported *E. coli* resistance could be different in less severe cases of pyelonephritis.

5. Conclusion

Ciprofloxacin and Trimethoprim-sulfamethaxazole should be avoided as first line empiric antibiotics for severe cases of uncomplicated pyelonephritis in this Midwest teaching hospital.

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