



Appropriateness of antibiotic prescription among hospitalized patients with urinary tract infection in Jordan

Anan Jarab Jarab^{1,2}, Treq Lewis Mukattash¹, Buthaina Nusairat¹, Maher Khmour^{3*}

¹Faculty of Pharmacy, Jordan University of Science and Technology, Irbid, Jordan.

²Department of Clinical Sciences, Faculty of Pharmacy, Al Ain University, Abu Dhabi, United Arab Emirates.

³Faculty of Pharmacy, Al-Quds University, Abu Deis, Palestine.

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ABSTRACT

Lack of adherence to recent antibiotic prescription guidelines leads to antibiotic resistance which causes treatment failure and the development of disease complications in patients with urinary tract infection (UTI). The study aim was to evaluate patterns and appropriateness of antibiotic selection among hospitalized patients with UTI. The computerized medical records of the hospitalized patients in the Urology Department at King Abdullah University Hospital were used for data collection. The American Urological Association and the Infectious Disease Society of America guidelines of UTI management were used as references to determine the appropriateness of antibiotic prescription in different cases of UTI. Statistical analysis using Excel program, 2015 version, was used for data analysis. A total of 168 intravenous (IV) antibiotic prescriptions were prescribed for 148 hospitalized UTI patients. Imipenem/cilastatin was the most common prescribed antibiotic and used in 66.7% of complicated cystitis and 57.1% of complicated pyelonephritis cases, while 75% of the participants received ceftriaxone as the most common prescribed antibiotic in uncomplicated pyelonephritis. Imipenem/cilastatin and ceftriaxone were equally the most prescribed antibiotics among patients with prostatitis. The choice of antibiotics was inappropriate in 32.43% of the studied cases. The most common inappropriate antibiotic choice was prescribing IV ceftriaxone and IV imipenem/cilastatin in cases with uncomplicated pyelonephritis and complicated cystitis and prostatitis. Lack of adherence to antibiotic selection guidelines sheds light on the necessity to improve antibiotics prescription practice and avoid the inappropriate antibiotic selection and hence antibiotic resistance among patients with UTI.

INTRODUCTION

A urinary tract infection (UTI) is the most common bacterial infection in the ambulatory care setting in the USA, accounting for around 8.6 million visits in 2007 (Hooton, 2012; Schappert and Rechtsteiner, 2011). Complications of a UTI include recurrent infections, permanent kidney damage and scarring, premature delivery or low birth weight, urethral strictures, and sepsis (Alpay *et al.*, 2018; Bahadi *et al.*, 2010; Lugg-Widger *et al.*, 2019). Antimicrobial resistance due to the incorrect selection

of antibiotics, incorrect antibiotic dose regimen, and misuse of antibiotics that lead to resistant causative species of UTIs could lead to the development of such complications (Neal, 2008). Antimicrobial resistance is considered a major health problem worldwide; such resistance is caused by the excessive use of antibiotics with a lack of well-constructed programs that guide antibiotic use (Vivas *et al.*, 2019). Around 700,000 patients die every year around the world due to antibiotic resistance (O'Neill, 2016). Earlier reports revealed a 40% prevalence of antibiotics' self-medication (Nusair *et al.*, 2021) and 87.8% of all deaths were due to secondary infections (Tseng *et al.*, 2014) in Jordan. According to a hospital-based survey in the USA, 576 out of 1,941 therapy days with antibiotics were not essential due to the unnecessary prescribing length and using of antibiotics for nonbacterial causes (Hecker *et al.*, 2003).

*Corresponding Author

Maher Khmour, Faculty of Pharmacy, Al-Quds University,
Abu Deis, Palestine.

E-mail: maher.khmour@gmail.com

Several guidelines, such as those of the American Urological Association (AUA) and Infectious Diseases Society of America (IDSA), have been developed to optimize antibiotic use to minimize antibiotic resistance in UTI management. However, little is known about the extent of adherence to these guidelines for the management of hospitalized patients with UTIs in Jordan. Therefore, the current study is the first one that evaluated antibiotic prescription patterns among hospitalized patients with UTIs in Jordan.

AIM OF THE STUDY

The study's aim was to evaluate the patterns and appropriateness of antibiotic selection among hospitalized patients with UTIs in Jordan.

METHOD

Study site and subjects

The largest hospital in the north of Jordan, King Abdullah University Hospital (KAUH), where this study was conducted, serves nearly a million people from the Irbid, Mafraq, Ajloun, and Jerash districts and represents a clinical training site for medical students at Jordan University of Science and Technology (JUST) (KAUH, 2018).

Data collection

Data were retrospectively collected by reviewing the electronic medical records of patients admitted between April and July 2019 to the Urology Department. The collected data included age, gender, height, weight, vital signs, white blood cell count, serum creatinine, the prescribed antibiotics and their dose regimens, microbiology reports, and sites of infection. Patients who were less than 18 years old, those who were hemodynamically unstable (e.g., ICU, cancer), and patients who were immunocompromised, had major illnesses, or had life-threatening infections were not included in the study. Antibiotics were classified according to the type of UTI. The AUA and the IDSA guidelines (AUA, 2021; IDSA, 2021) of UTI management were utilized to determine the appropriateness of antibiotic selection with regard to indication, dose, route of administration, and duration of therapy in UTI patients. In case of reporting inappropriate antibiotic use, the reason for the inappropriateness was reported and the suitable alternative therapy and its regimen were determined after referral to the AUA and IDSA guidelines. Both guidelines are complementary to each other. The IDSA guidelines are used to combat antibacterial resistance, and the AUA guidelines are used to assess the quality of urologic healthcare.

The study was ethically approved by the Institutional Review Board Committee at KAUH/JUST in April 2019 and received Ethical Approval Number 22/104/2019.

Statistical analysis

Analytical and descriptive statistics and tables with summary data were created using percentage and mean to quantify and describe the demographics of the patients, the antibiotic prescription patterns according to the type of UTI, and the adherence to guidelines regarding appropriate antibiotic selection using the Excel program, 2015 version.

RESULTS

Table 1 shows some sociodemographics and the prevalence and distribution of UTI cases among the study participants. A total of 148 UTI patients were recruited for this study. The mean age of the participants was $M = 55.29$ years ($SD = 9.94$). More than half of the participants were female (54.1%) and under 65 years old (56.8%). Most of the participants (64.86%) were found to have complicated cystitis. A total of 68 patients had extended-spectrum β -lactamase (ESBL) +ve UTIs and 8 cases had multi-drug resistant (MDR) UTIs. For patients who had ESBL +ve UTIs, 4 cases were ESBL +ve complicated pyelonephritis and 64 cases were ESBL +ve complicated cystitis. For patients who had MDR UTIs, four cases were MDR complicated cystitis and the other four cases were MDR complicated pyelonephritis. Table 2 presents antibiotics prescribed for ESBL +ve and MDR UTI cases.

A total of 168 intravenous (IV) antibiotic prescriptions were prescribed for 148 hospitalized UTI patients. As shown in Table 3, imipenem/cilastatin was the most commonly prescribed antibiotic, which was prescribed for 54.8% of the current study participants, followed by ceftriaxone, which was prescribed for 26.2% of the study participants. Other prescribed antibiotics included ertapenem, piperacillin/tazobactam, meropenem, metronidazole, amikacin, and lastly colistin. On the other hand, 10.8% of the patients received a combination therapy, such as colistimethate sodium and amikacin for MDR complicated cystitis; piperacillin/tazobactam, metronidazole, and meropenem for MDR complicated pyelonephritis; ceftriaxone and imipenem/cilastatin for patients with ESBL+ complicated cystitis; and imipenem/cilastatin and ceftriaxone for patients with uncomplicated pyelonephritis. With regard to the most commonly prescribed antibiotics (Table 4), imipenem/cilastatin was prescribed for 66.7% of the complicated cystitis cases and 57.1% of the complicated pyelonephritis cases. On the other hand, ceftriaxone was prescribed for 75% of the uncomplicated pyelonephritis cases. Imipenem/cilastatin and ceftriaxone were prescribed for 50% of the prostatitis cases.

Table 1. Demographics and UTI cases among the study participants ($n = 148$).

Demographics	Number of patients (%)
Gender	
Female	80 (54.1%)
Male	68 (45.9%)
Age, mean (55.29) (SD = 9.94)	
<65 years	84 (56.8%)
≥ 65 years	64 (43.2%)
Type of UTI	
Complicated cystitis	96 (64.86%)
Complicated pyelonephritis	28 (18.92%)
Uncomplicated pyelonephritis	16 (10.81%)
Prostatitis	8 (5.41%)
Uncomplicated cystitis	0

Table 2. Cases of ESBL* +ve and MDR** UTIs and the prescribed antibiotics.

Case (n)	Type of UTI (n)	Prescribed antibiotics
ESBL +ve UTIs (68)	Complicated cystitis (64)	Ertapenem, imipenem/cilastatin, and ceftriaxone
	Complicated pyelonephritis (4)	Imipenem/cilastatin
MDR UTIs (8)	Complicated cystitis (4)	Colistin sodium and amikacin
	Complicated pyelonephritis (4)	Piperacillin/tazobactam, metronidazole, and meropenem

*ESBL: extended-spectrum β -lactamase.

**MDR: multidrug resistant.

Table 3. Patterns of antibiotic prescription among the study participants (n = 168).

Antibiotic class	Number of antibiotic prescriptions (%)
Carbapenems	
Imipenem/cilastatin	92 (54.8%)
Ertapenem	8 (4.8%)
Meropenem	4 (2.4%)
Cephalosporines	
Ceftriaxone	44 (26.2%)
Extended-spectrum penicillin/ β -lactamase inhibitor	
Piperacillin/tazobactam	8 (4.8%)
Nitroimidazoles	
Metronidazole	4 (2.4%)
Aminoglycosides	
Amikacin	4 (2.4%)
Polymyxin E	
Colistin	4 (2.4%)

The choice of antibiotics was inappropriate in 32.43% of the study participants.

The most common inappropriate antibiotic choice was prescribing IV ceftriaxone and IV imipenem/cilastatin in cases of uncomplicated pyelonephritis, complicated cystitis, and prostatitis, where guidelines recommend the administration of oral antibiotics such as ciprofloxacin or trimethoprim/sulfamethoxazole. Table 5 shows other examples of inappropriate antibiotic choice for the current study participants.

DISCUSSION

The current study is the first one that investigates the appropriateness of antibiotic prescription among patients with UTIs in Jordan. Considering the effects of improper antibiotic prescription procedures on raising antimicrobial resistance and poor health outcomes, it is crucial that medical professionals choose the right course of action for the treatment of UTIs.

According to the Centers for Disease Control and Prevention estimates, hospitals provide antibiotics in about 30% of the cases inappropriately or needlessly. This puts patients at risk of having negative outcomes and infections with antibiotic resistance (Bartlett *et al.*, 2011). Antibiotic usage in cases when they are not necessary or protracted courses of therapy when shorter durations would be just as effective are two factors that contribute

to antimicrobial resistance, which is seen as a major health issue globally (Dryden *et al.*, 2011; Trémolières, 2002; Volluz *et al.*, 2010). Therefore, for the prescription based on the patient's history, antibiotics should be sensible, reasonable, and tailored to them, considering the prevalence of resistance, local practice patterns, and medication cost (Gupta *et al.*, 2011). Utilizing the updated treatment guidelines for selecting the appropriate antibiotic and dosage regimen and avoiding unnecessary antibiotics could help improve clinical outcomes and decrease the potential toxicity and resistance (Abbo and Hooton, 2014).

The current study showed high prevalence of inappropriate antibiotic selection among hospitalized patients with UTIs. Clinical pharmacists in Jordan need to follow the updated UTI management guidelines of appropriate antibiotic selection in order to reduce the emergence of antibiotic resistance, reduce the cost of treatment, decrease the risk of hospitalization, and improve health outcomes.

The current study revealed that imipenem/cilastatin was the most commonly prescribed antibiotic for complicated UTI cases. In a prospective observational study conducted in Mumbai on patients with complicated UTIs, quinolones followed by β -lactamase inhibitors were the most commonly prescribed antibiotics (Dhodi *et al.*, 2014). In a study conducted at the Institute of Nephrology at a tertiary care hospital for inpatients

Table 4. Patterns of antibiotic prescription according to the type of UTI.

Antibiotic class	Complicated cystitis (n = 96) n (%)	Complicated pyelonephritis (n = 28) n (%)	Uncomplicated pyelonephritis (n = 16) n (%)	Prostatitis (n = 8) n (%)
Carbapenems				
Imipenem/cilastatin	64 (66.7%)	16 (57.1%)	8 (50%)	4 (50%)
Ertapenem	4 (4.2%)	4 (14.3%)	0	0
Meropenem	0	4 (14.3%)	0	0
Cephalosporines				
Ceftriaxone	24 (25%)	4 (14.3%)	12 (75%)	4 (50%)
Extended-spectrum penicillin/ β -lactamase inhibitor				
Piperacillin/tazobactam	4 (4.2%)	4 (14.3%)	0	0
Nitroimidazoles				
Metronidazole	0	4 (14.3%)	0	0
Aminoglycosides				
Amikacin	4 (4.2%)	0	0	0
Polymyxin E				
Colistin	4 (4.2%)	0	0	0
Carbapenems				
Imipenem/cilastatin	64 (66.7%)	16 (57.1%)	8 (50%)	4 (50%)
Ertapenem	4 (4.2%)	4 (14.3%)	0	0
Meropenem	0	4 (14.3%)	0	0
Cephalosporines				
Ceftriaxone	24 (25%)	4 (14.3%)	12 (75%)	4 (50%)
Extended-spectrum penicillin/ β -lactamase inhibitor				
Piperacillin/tazobactam	4 (4.2%)	4 (14.3%)	0	0
Nitroimidazoles				
Metronidazole	0	4 (14.3%)	0	0
Aminoglycosides				
Amikacin	4 (4.2%)	0	0	0
Polymyxin E				
Colistin	4 (4.2%)	0	0	0

with complicated UTIs, the most commonly prescribed antibiotics were cephalosporins, followed by quinolones and penicillins (Muraraiah *et al.*, 2012). An earlier prospective study showed that quinolones, including ofloxacin, ciprofloxacin, and levofloxacin, followed by ceftriaxone \pm sulbactam and piperacillin + tazobactam, were the most commonly prescribed antibiotics for inpatients with complicated UTIs in India (Pallavi *et al.*, 2015).

The current study showed that ceftriaxone was the most commonly prescribed antibiotic in cases of uncomplicated UTIs. An earlier study showed that amoxicillin and after that nitrofurantoin were the most commonly prescribed antibiotics for females with uncomplicated UTIs in Hong Kong (Wong *et al.*, 2017). Another study showed that fluoroquinolones were the most commonly prescribed antibiotics for female outpatients with uncomplicated UTIs in the USA (Kobayashi *et al.*, 2016). With regard to combination therapy, the current study participants received imipenem/cilastatin in combination with ceftriaxone, colistimethate sodium in combination with amikacin, and piperacillin/tazobactam in combination with metronidazole and meropenem. In comparison with a study conducted in a pediatric

teaching hospital in Nepal, ceftriaxone with amikacin was the most common antibiotic combination prescribed (Panayappan *et al.*, 2017). Variables including physicians' experience, school of graduation, participation in training programs, and the impact of medical representatives could have influenced the antibiotic prescription patterns in different research studies.

The most commonly reported inappropriate antibiotic prescription was prescribing IV antibiotics such as ceftriaxone and imipenem/cilastatin in cases of mild to moderate infection for afebrile patients without or with slight elevation in WBC, who could be treated as outpatients with an oral antibiotic such as ciprofloxacin or trimethoprim/sulfamethoxazole. In a study conducted on patients with UTIs attending an academic emergency department, β -lactams were the most inappropriate antibiotic prescribed for adult patients (Chardavoynne and Kasmire, 2020).

The percentage of inappropriate antibiotic selection in the present study represents an average of the findings of earlier studies. Earlier research studies reported a significant variation regarding the extent of adherence to treatment guidelines of antibiotic prescription in patients with UTIs. A cross-sectional

Table 5. Selected cases of inappropriate antibiotic prescribing.

Case	Antibiotic given	Antibiotic recommended	Justification
Suspected uncomplicated pyelonephritis	Ceftriaxone 2 g IV q 24 hours for 9 days	Trimethoprim/sulfamethoxazole for 14 days or a short course of ceftriaxone, then converted to oral ABX	Stable vitals without nausea or vomiting, afebrile, had history of ciprofloxacin intake 4 days prior. According to guidelines can be treated with trimethoprim/sulfamethoxazole
Suspected uncomplicated pyelonephritis	Ceftriaxone 2 g IV q 24 hours for 1 day	Ciprofloxacin or trimethoprim/sulfamethoxazole orally	Stable vitals, afebrile, no pyuria in UA
Complicated cystitis	Imipenem-cilastatin 500 mg IV q 8 hours for 4 days	Ciprofloxacin orally	Clinically well, afebrile, with no previous ABX or admissions
Complicated cystitis	Ceftriaxone 2 g IV q 24 hours for 2 days	Trimethoprim/sulfamethoxazole orally	UA showed WBC (0–2), no bacterial growth, had previous ABX intake before 20 days of ciprofloxacin. Patient can be treated with oral trimethoprim/sulfamethoxazole
Complicated cystitis	Imipenem/cilastatin 500 mg IV q 6 hours for 4 days.	Ciprofloxacin orally	Patient admitted due to positive UC without sensitivity, afebrile and stable, no previous ABX given at home
ESBL-negative <i>E. coli</i> , uncomplicated pyelonephritis	Imipenem/cilastatin 250 mg IV q 6 hours for 7 days	Trimethoprim/sulfamethoxazole	UC sensitive to trimethoprim; however, patient afebrile and vitally stable. Can be treated with ciprofloxacin
Uncomplicated pyelonephritis	Imipenem/cilastatin 500 mg IV q 6 hours for 2 days, ceftriaxone 2 g IV q 24 hours for 7 days	Ciprofloxacin orally	UC showed heavy bacteria without sensitivity, afebrile, ciprofloxacin orally. Can tolerate oral intake
ESBL-negative <i>E. coli</i> , complicated cystitis	Ceftriaxone 2 g IV q 24 hours for 4 days.	Ciprofloxacin orally	Patient was clinically stable and afebrile, no nausea or vomiting
Complicated cystitis	Ceftriaxone 2 g IV q 24 hours for 17 days.	Ciprofloxacin orally	UA showed Heavy Bacteria with urinary symptoms, afebrile; after week of admission, UC showed no growth
Complicated cystitis	Piperacillin-tazobactam 2.25 g IV q 6 hours for 5 days.	Ciprofloxacin orally	Patient had no fever during and at admission, UA showed abundant bacteria, UC on third day showed no growth, WBC normal, no previous admissions
Prostatitis	Ceftriaxone 2 g IV q 24 hours for 3 days.	Ciprofloxacin or trimethoprim/sulfamethoxazole orally	Patient was vitally stable, WBC normal, UA at admission free of WBC and bacteria, UC free. Can be converted at admission to ciprofloxacin or trimethoprim/sulfamethoxazole
Prostatitis	Imipenem/cilastatin 500 mg IV q 6 hours for 4 days.	Ciprofloxacin orally	Patient was afebrile, stable vitals, UA normal

IV: intravenous, UC: urine culture, UA: urine analysis, and WBC: white blood cell count.

study conducted in the emergency departments of 10 hospitals in Spain found that 13.6% of the antibiotic prescriptions were inappropriate (Martinez *et al.*, 2007). In a study conducted in a Swiss primary care center for the treatment of uncomplicated UTIs, fluoroquinolones were inappropriately prescribed for about 13.8% of the patients (Plate *et al.*, 2020). Another retrospective study showed that antibiotic prescription was inappropriate in 12% of children and 32% of adults with cystitis and 19% of children and 54% of adults with pyelonephritis (Chardavoyne and Kasmire, 2020). A higher percentage of inappropriate antibiotic selection was reported in a study conducted on patients with UTIs, where 59% of the patients received inappropriate antibiotic treatment for UTI management at the emergency department and 68% of them received inappropriate antibiotics after hospital admission (Kiyatkin *et al.*, 2016).

CONCLUSION

According to the results of the recent research, imipenem/cilastatin is the antibiotic combination that is administered most often to treat problematic UTI patients; ceftriaxone is the antibiotic that is prescribed to patients most often for treating UTIs that are

not complicated; and the most often reported incorrect antibiotic prescription was IV antibiotics such as ceftriaxone and imipenem/cilastatin given to patients with mild to severe infections.

Inappropriate antibiotic prescription for patients with UTIs in this study sheds light on the necessity to improve physicians and pharmacists' antibiotic prescription patterns by adhering to the updated UTI management guidelines, with the aim of avoiding or minimizing antibiotic resistance and improving health outcomes among patients with UTIs.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the international committee of medical journal editors (ICMJE) requirements/guidelines.

ETHICAL APPROVALS

The study was ethically approved by the Institutional Review Board Committee at KAUH/JUST in April 2019 and received Ethical Approval Number 22/104/2019.

DATA AVAILABILITY

All data generated and analyzed are included within this research article.

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