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Research Article



# A Prospective Study and Analysis of the Pattern of Antimicrobial Utilization for Urinary Tract Infection in Tertiary Care Hospital

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**Abstract:** Monitoring utilization pattern of antimicrobial drugs for the treatment of UTIs can provide an important vision into a rational prescription of antimicrobials and prevent inappropriate therapeutic outcomes. This study aimed to focus on the study and analysis pattern of antimicrobial utilization in the management of UTI among patients admitted to a tertiary care hospital. A prospective study was conducted over six months in the Medicine Department of Bangalore Baptist Hospital, Bangalore, India. A total of 150 patients with UTI aged ≥ 18 years were included in the study, of which the majority of patients were female. A comorbidity analysis showed that forty-one (27.3%) patients had diabetes mellitus followed by hypertension (39, 26%), renal failure (23, 15.4%), renal calculi (17, 11.3%), and malaria (8, 5.3%). *E. coli* (23, 54.76%) was the most common isolated organism. Analysis of the utilization pattern of antimicrobial drug classes in patients with urinary tract infection revealed that cephalosporin (90, 60%) was the most-common prescribed class of antimicrobial drugs for management of UTI. Cefotaxime (47, 31.33%) was the most commonly prescribed cephalosporins. Fluoroquinolones (42, 28%) were the second most common pharmacologic class of antimicrobial drugs prescribed for the treatment of UTI of which ciprofloxacin (18, 12%) was the most commonly used fluoroquinolone. Overall, we identified 41 (Drug-Drug Interactions) DDIs between prescribed antimicrobial drugs and other medications. Interaction between ceftriaxone and calcium salts (13, 31.71%) was found to be the most commonly identified DDI. A periodic review of antimicrobial utilization patterns should be performed to enhance the empirical treatment of UTIs according to patients` urine culture reports. Our study findings provide feedback to prescribers to stimulate thinking about their practice and look for ways to improve rational antimicrobials prescription, and patient safety.

**Keywords:** Antimicrobial utilization, Prescription pattern, Urinary tract infection, Antimicrobial drugs, Drug-drug interactions.

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## 1. INTRODUCTION

Drug utilization is defined as marketing, distribution, prescription, and use of drugs in society with special emphasis on the resulting medical and social consequences. Drug utilization studies play a major role in the detection of inappropriate drug therapy and also to find solutions to resolve therapy-related issues. Therefore, monitoring prescription patterns and drug utilization could identify the associated problems and provide feedback to prescribers to create awareness about irrational drug use.[1] Urinary tract infection (UTI) is defined as the presence of bacteria in urine along with symptoms of infection that occur in both males and females of all ages. The prevalence and incidence of UTI are higher in women than in men due to several clinical factors including anatomic differences, hormonal effects, and behavioral patterns. UTI is mostly caused by gram-negative aerobic bacilli found in the gastrointestinal tract like *E. coli.* In most cases, UTIs are treated with antimicrobial drugs. The choice of antimicrobial drug depends on the antimicrobial sensitivity of pathogens in urinary cultures, the severity of the symptoms, and potential comorbidities of the individual.[2] Prescription pattern study of antimicrobial utilization in UTI aids in commenting about unnecessary and irrational prescribing, which increases the burden of the cost of therapy, and also causes loss of working hours either due to hospitalization or morbidity. Certainly, these are not affordable for a developing country like India.[3] Antibiotics are one of the most common drugs prescribed in hospitals today. It is estimated that up to a third of all patients receive at least one antibiotic during hospitalization. The cost involved is therefore correspondingly high and up to 40% of hospital's drug expenditure may be devoted to the purchase of antibiotics.[4] In addition, inappropriate use of antimicrobial drugs for UTIs increases chances of bacterial resistance as well as increases the duration of morbidity. In the past decade, there has been an alarming trend towards increasing antimicrobial resistance in many human pathogens around the world. Of the many possible factors responsible for these developments, the overuse and inappropriate prescribing of broad-spectrum antibiotics have been implicated.[5] Hospital inpatient prescription of antimicrobial drugs has been major concern in the last few decades. For the purchasers of healthcare services and administrators, antibiotic drugs account for a major proportion of the escalating drug budget, especially in hospitals. The overuse and misuse of antibiotic drugs are considered to be one of the reasons for increasing resistance among various pathogens. These worries have led to the implementation of strict antibiotic policies in hospitals in many countries, with different strategies and different outcomes. Therefore, prescription pattern analysis is essential to follow the effects of therapy and medication adherence to the hospital's antimicrobial use policies. Moreover, the ultimate goal of antimicrobial utilization research must be to assess whether drug therapy is rational or not. For the individual patient, the rational use of a drug implies the prescription of a well-documented medication at an optimal dose, together with the correct information, at an affordable price.[1] However, many of these studies have been conducted in developed countries. Data from developing countries are scarce. Drug utilization among outpatients is commonly monitored in many countries, but studies of antimicrobial utilization in UTI among patients admitted to hospital (inpatients) are few. Hence, the current study aimed to focus on the study and analysis pattern of antimicrobial utilization in the management of UTI among patients admitted to a tertiary care hospital.

## 2. MATERIALS AND METHODS

### *2.1 Study Design, Site, and Duration*

A prospective study was conducted over six months in the Medicine Department of Bangalore Baptist Hospital, Bangalore, India.

### *2.2 Inclusion Criteria*

Patients (aged 18 years and above, any gender) who were diagnosed with UTI according to their clinical presentations and laboratory reports and they were admitted to the Medicine Department of Bangalore Baptist Hospital, Bangalore, India.

### *2.3 Exclusion Criteria*

Pregnant and breastfeeding women were excluded. Patients who required hemodialysis also were excluded from the study.

### *2.4 Study Process*

The study received ethical approval from the Institutional Human Ethics Committee of the Department of Pharmacy Practice, Karnataka College of Pharmaceutical Science, Bangalore, India (Reference No: IHEC/14/2017).

#### *2.4.1 Study Materials*

The patients case sheets, prescription charts, nurses` notes were reviewed daily and checked for antimicrobial utilization in patients with UTI. The required data were collected from patients` profile form, which contained;

1. History of current illness and past medication utilization
2. Clinical presentations and physical examination at the time of admission
3. Laboratory investigation charts
4. Medication charts
5. Physician's orders and nurse's notes

#### *2.4.2 Study Procedure*

Throughout the study procedure, all patient and medication related data were documented in a suitably designed data collection form. Data was collected with respect to demographic details (name, age, and sex of patients), diagnosis, admission, and discharge date. Patients` case sheets and prescription charts were reviewed daily to analyze antimicrobial utilization patterns prescribed for the management of UTIs. The prescribed drug data including brand and generic name of all antimicrobial drugs, dose, dose frequency and route of administration were recorded. The study patients were monitored daily until hospital discharge, and any change in prescription orders of antimicrobial medications was noted for further analysis. The LEXICOMP drug information database, textbooks, and national international guidelines were used to review the collected data. In addition, all the prescribed antimicrobial medications along with other medications and relevant information were noted in a suitably designed data collection form to identify

the occurrence of any drug-drug interactions (DDIs). DDIs were identified by using the LEXICOMP interaction database.[6]

## 3. STATISTICAL ANALYSIS

The information obtained from the data collection form was transferred to a Microsoft Excel sheet and subjected to further analysis as required. Descriptive statistics were applied for the calculation of mean, standard deviation, frequencies, and percentages of patients' demographic/clinical characteristics and medication-related data. The Statistical Package for Social Sciences for Windows, version 22.0 was used for data analysis.[7]

## 4. RESULTS

A total of 150 patients with UTI were included during the study period, of which 61.3% and 38.7% were female and male, respectively. The mean (± standard deviation) of patients 'age was 49.1±11.7 years. Analysis of comorbidity conditions showed that the highest number of comorbidities were diabetes mellitus (41, 27.3), followed by hypertension (39, 26), renal failure (23, 15.4), renal calculi (17, 11.3), and malaria (8, 5.3). Clinical presentations of patients diagnosed with UTI are presented in Table 1.

**Table 1. Demographic and clinical characteristics of study patients**

| **Total number of study patients** | **N = 150, n (%)** |
|---|---|
| Age in years (mean ± standard deviation) | 49.1 ± 11.7 |
| Female | 92 (61.3) |
| Male | 58 (38.7) |
| **Number of comorbidities** | **N = 150, n (%)** |
| Diabetes Mellitus | 41 (27.3) |
| Hypertension | 39 (26) |
| Renal Failure | 23 (15.4) |
| Renal Calculi | 17 (11.3) |
| Malaria | 8 (5.3) |
| Others | 22 (14.7) |
| **UTI specific symptoms** | **N (%)** |
| Dysuria | 67 (64.4) |
| Flank pain/back pain | 58 (55.8) |
| Urinary frequency | 47 (45.2) |
| Suprapubic pain | 19 (18.3) |
| Urinary urgency | 15 (14.4) |
| Burning | 13 (12.5) |
| **UTI non-specific symptoms** | **N (%)** |
| Abdominal pain | 39 (37.5) |
| Nausea | 27 (26.0) |
| Subjective fevers/chills | 26 (25.0) |
| Vomiting | 13 (12.5) |
| Malaise | 3 (2.9) |
| **UTI diagnosis** | **N (%)** |
| Complicated UTI including pyelonephritis | 93 (62) |
| Uncomplicated UTI | 57 (38) |

***UTI, urinary tract infection.***

Overall, 150 patients` prescriptions were analyzed for antimicrobial utilization patterns, of which 69 (46%) prescriptions had 6 to 11 drugs in their medication chart. The average of prescribed drugs per patient was 7 drugs. Analysis of the utilization pattern of antimicrobial drug classes in patients with urinary tract infection revealed that cephalosporin (90, 60%) was the most-common prescribed class of antimicrobial drugs for management of UTI. Among cephalosporins pharmacologic class of antibacterials, cefotaxime (47, 31.33%), ceftriaxone (36, 24%), cefixime (3, 2%), and cephalexin (4, 2.67%) were used most commonly among our study patients. Fluoroquinolones (42, 28%) were the second most common pharmacologic class of antimicrobial drugs prescribed for the treatment of UTI. Ciprofloxacin (18, 12%) was the most commonly used fluoroquinolone (Table 2).

| Table 2. Utilization pattern of antimicrobial drug classes in patients with urinary tract infection | | |
|---|---|---|
| **Prescription pattern** | **N** | **%** |
| 0-5 | 27 | 18.00 |
| 6-11 | 69 | 46.00 |
| 12-17 | 47 | 31.3 |
| > 17 | 7 | 4.7 |
| **Antimicrobial drug classes** | | |
| ***Cephalosporins*** | | |
| Cefotaxime | 47 | 31.33 |
| Ceftriaxone | 36 | 24.00 |
| Cefixime | 3 | 2.00 |
| Cephalexin | 4 | 2.67 |
| ***Fluoroquinolones*** | | |
| Ciprofloxacin | 18 | 12.00 |
| Norfloxacin | 12 | 8.00 |
| Ofloxacin | 9 | 6.00 |
| Levofloxacin | 3 | 2.00 |
| ***Others*** | | |
| Nitrofurantoin | 10 | 6.67 |
| Amikacin | 5 | 3.33 |
| Azithromycin | 3 | 2.00 |

Urine culture was performed for 64 (59.26%) patients, of which 42 (65.63%) patients had positive culture, sterile in 17 (26.56%) patients, and no significant growth in 5 (7.81%) patients. *E. coli* (23, 54.76%) was the most common isolated organism (Fig. 1). The three most common organisms isolated from patients` urine grown on plate culture are shown in Fig. 2.

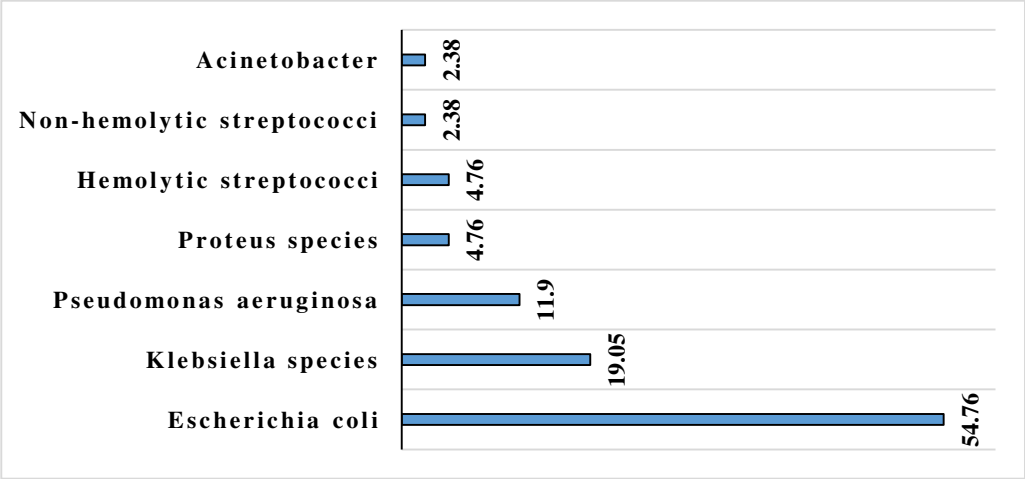


**Fig 1. Isolated organisms from urine culture**

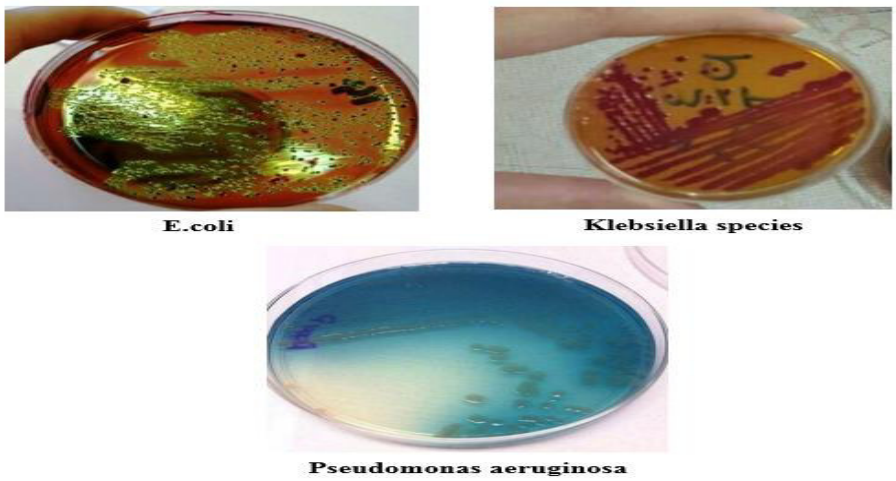


**Fig 2. Isolated organisms from patients urine samples grown on plate culture**

Overall, we identified 41 DDIs between prescribed antimicrobial drugs and other medications. Interaction between ceftriaxone and calcium salts was found to be the most commonly identified DDI. Detected DDIs with their severity rating are presented in table 3.

**Table 3. Identified drug–drug interactions with their severity rating among study patients**

| DDIs | N (%) | Potential outcome | Risk rating | Severity rating |
|---|---|---|---|---|
| Ceftriaxone-Calcium Salts (Intravenous) | 13 (31.71) | It may enhance the adverse/toxic effect of Ceftriaxone. Ceftriaxone binds to calcium forming an insoluble precipitate | D, Consider therapy modification | Major |
| Ceftriaxone-Ringer's Injection (Lactated) | 7 (17.07) | It may enhance the adverse/toxic effect of Ceftriaxone. Ceftriaxone binds to calcium in the Lactated Ringer's forming an insoluble precipitate. | D, Consider therapy modification | Major |
| Cefixime-Warfarin | 1 (2.44) | It may enhance the anticoagulant effect of Warfarin | C, Monitor therapy | Moderate |
| Ciprofloxacin-Sevelamer | 6 (14.63) | It may decrease the absorption of Ciprofloxacin | D, Consider therapy modification | Major |
| Ciprofloxacin-Antacid | 8 (19.51) | It may decrease the absorption of Ciprofloxacin | D, Consider therapy modification | Moderate |
| Levofloxacin-Amiodarone | 1 (2.44) | It may enhance the QTc-prolonging effect of Amiodarone | X, Avoid combination | Major |
| Nitrofurantoin-Spironolactone | 3 (7.32) | It may enhance the hyperkalemic effect of Spironolactone | C, Monitor therapy | Moderate |
| Amikacin-Mannitol (Systemic) | 2 (4.88) | It may enhance the nephrotoxic effect of Amikacin | X, Avoid combination | Major |

***DDI, drug-drug interaction.***

## 5. DISCUSSION

A study and analysis of the pattern of antimicrobial utilization are the tools that help healthcare providers to enhance rational use of medications, including antimicrobial drugs, and enable clinicians to improve the appropriateness of their prescriptions. The practice of evidence-based medicine entails judicious use of medicines so as to maximize the benefits to the patients. Ascertaining rationality of the antimicrobial prescriptions prove to decrease the chances of treatment failure and reduce the financial burden on patients. Analyses of prescription patterns build an important connection between rational drug utilization, pharmacovigilance, evidence-based medicine, and pharmacoeconomics. As UTI is a very common disease, its diagnosis and treatment have important implications for patients' health, development of antibiotic resistance, and health care costs. 8-11 The objective of the study was to analyze the pattern of antimicrobial utilization among patients who were diagnosed with UTI and admitted to the medicine ward of a tertiary care hospital located in Bangalore, India. A total of 150 patients` medication charts were reviewed. All the patient records had the complete documentation of information, including patient's demographic characteristics, diagnosis, urine culture (if available), drug names, dose route, and frequency of administration. A total of 150 patients with UTI were included during the study period, of which 61.3% and 38.7% were female and male, respectively. In this study, UTI was most commonly observed in female patients which is concordant with earlier studies. A UTI is twice more likely to happen in women than men without regard to age groups.12 Also, UTI accounts for 1.2% of all clinician's office visits by women. 13 Up to 70% of women will suffer from a UTI during their lifetime, and of those, 30% will have recurrent UTIs. 14 The relationship between sexual activity and UTI is well established in younger women. During intercourse, vaginal bacteria gain access to the urinary tract by colonizing the periurethral mucosa and ascending to the bladder through the urethra.15 In our analysis, diabetes mellitus was the most common comorbid condition among patients diagnosed with UTI, followed by hypertension and renal calculi. Patients with type 2 diabetes mellitus are at increased risk of infections like UTI. 16 Various impairments in the immune system, in addition to poor metabolic control of diabetes, 17 and incomplete bladder emptying due to autonomic neuropathy 18 may all contribute to the pathogenesis of UTI in diabetic patients. Factors that were found to enhance the risk for UTI in diabetics include age, metabolic control, and long-term complications, primarily diabetic nephropathy and cystopathy. 19 In addition, several findings do indicate a possible association between urinary stones and bacteria, including the high rate of UTI in urinary stone patients. 20 Urine culture analysis revealed E. coli (23, 54.76%) was the most common isolated organism. This finding is consistent with other studies. It has been well studied that, Escherichia coli is heavily associated with UTI. Furthermore, these pathogenic fimbriae are associated with persistent colonization of the urothelium and eliciting an inflammatory response. 21 It has been also theorized that these bacteria can mature into biofilms in the urothelial barrier to cause recurrence of infections and elude the host immune system. 22 Overall 150 prescription charts were reviewed to identify patterns of antimicrobial drugs utilization in patients with UTI. Sixty-nine (46%) prescriptions had 6 to 11 drugs in the medication charts. The average number of drugs per prescription encountered was 7. This value was slightly higher than similar research conducted from seven government health facilities in the Wassa West district of Ghana, which was 4.8. A higher average was reported in Nigeria (6.11). But this was higher than the values obtained in the majority of previous studies from developing countries: Yemen 1.5, Uganda 1.9, Sudan 1.4, Tanzania 2.3, and 1.44 in Bangladesh. 23,24 The higher average number of medicines for prescription in this study is a pointer to the high level of polypharmacy, which in turn may have serious adverse effects on the therapeutic outcome of patients. Patients with UTIs are hospitalized due to the severe nature of the disease, comorbid illnesses, and associated complications. Such patients usually are prescribed antipyretics and antibiotics, including cephalosporins, aminoglycosides, and quinolones. Apart from the use of these drugs, a large number of other drugs are also prescribed to treat the associated symptoms

and comorbid illnesses. 25 The present study showed that cephalosporins pharmacologic class of antimicrobial drugs were the most-common prescribed antibiotic. This is in agreement with a previous study conducted by other authors 26-28 whereas it is contrary to the result of a study performed by Mohan et al., 29 where amikacin was found to be the most-common prescribed antibiotic in the treatment of UTI. We applied LEXICOMP DDI checker and detected 41 DDIs between prescribed antimicrobial drugs and other medications. Interaction between ceftriaxone and calcium salts was found to be the most commonly identified DDI. Calcium salts may enhance the adverse/toxic effect of Ceftriaxone. In addition, ceftriaxone binds to calcium forming an insoluble precipitate. This interaction is a major type of DDI and prescribers need to consider therapy modification to diminish medication-related harm. 30 In general practice, the therapeutic approach for UTI is primarily empirical and as possible. The present study indicates the general trends of use of antimicrobials in urinary tract infection. Drug utilization studies have the potential to make objective evaluation and analysis of health professionals' work. Antibiotic resistance is an emerging problem and has become a major threat to the medical field. Excessive and inappropriate use of antibiotics has been a major contributor to this ever growing problem. 31-33 This study is not intended to speak about the decision of appropriateness in the treatment with antimicrobials against any known guidelines. Rather the purpose is to notice the antimicrobial prescription practices in a tertiary care hospital with the known incidence of urine culture sensitivity to microorganisms. Therefore, the present study throws light on the development of national guidelines for the treatment of UTI among hospitalized patients.

## 6. CONCLUSION

In general practice, the therapeutic approach for UTI is primarily empirical. The present study identified prescribing patterns of antimicrobials utilization for the management of UTI among hospitalized patients. E. coli was the most commonly isolated organism in patients` urine culture and cephalosporins pharmacologic class of antibiotics was the most commonly prescribed antimicrobial drug. A periodic review of antimicrobial utilization patterns should be performed to change the empirical treatment of UTIs. Excessive and inappropriate use of antibiotics is a major contributor to resistance. Therefore, our study findings can provide feedback to prescribers to stimulate thinking about their practice and look for ways to improve rational antimicrobials prescription, and patient safety.

## 7. AUTHORS CONTRIBUTION STATEMENT

Parastoo Abdolmalaki and Raju Koneri developed the study concept, objectives, and design. Parastoo Abdolmalaki performed a major contribution to the acquisition of patient-related data, and data analysis. Raju Koneri supervised the study process. All authors discussed the results and contributed to the writing of the manuscript.

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## 9. CONFLICT OF INTEREST

Conflict of interest declared none.

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