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Original Research Article

Drug therapy and cost analysis of urinary tract infections in a tertiary care teaching hospital in Nepal

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ABSTRACT

Background: Urinary tract infection (UTI) is the most common infection caused by the presence and growth of pathogenic microorganisms within the human urinary system into the lower and upper genito-urinary tract. UTI continues to be major health problems in developing countries like Nepal.
Methods: A prospective observational study was conducted from June 2019 to November 2019 in the outpatient and inpatient department of Manipal teaching hospital. The face-to-face interview was adopted in 137 UTI patients with the census sampling technique.
Results: A total of 137 patients (121 out-patients and 16 in-patients), 82 (59.85%) female, and 55 (40.15%) males were enrolled in which UTI was observed in more than half of the sample in the aged group of 25-54. *Escherichia coli* was the most common uropathogens isolated whereas dysuria was the most common presenting symptom among the patients. Cefixime 200 mg followed by nitrofurantoin 100 mg was the most commonly prescribed medicine for UTI. Disodium hydrogen 1.40 g oral liquid, pantoprazole 40 mg tablet, and multivitamins were commonly prescribed supportive medications. The empirically prescribed average cost was Nepalese rupee (NRs.) 820.44 whereas the total definitive average cost was NRs. 305.54. The average cost of medical management for in-patients was NRs. 2316.55 including registration, urine analysis, investigation bed charge, and other consumable charges as well as discharge medicine cost.
Conclusions: With lower cost, higher sensitivity, and high prescription, cefixime, and nitrofurantoin could be better drugs for the management of UTI among outpatient department (OPD) patients while ceftriaxone could be better for in-patients.

Keywords: Urinary tract infections, Drug therapy, Cost analysis, Antimicrobial susceptibility pattern

INTRODUCTION

Urinary tract infection (UTI) is the most frequently occurring infectious disease, due to the presence of pathogenic microorganisms in the genio-urinary tract system.[1] The most common causative agents are *E.coli*, *Pseudomonas spp.*, *Staphylococcus spp.*, *Neisseria gonorrhea*, *Chlamydia trachomatis*, *Candida spp.*, Mycoplasma whereas *E.coli* which accounts for >80% of all UTI cases.[2] UTIs with no prior instrumentation is considered uncomplicated, whereas complicated UTIs (cUTI) is associated with structural or functional abnormalities of the genitourinary tract, which is the most frequent causes of hospitalization, prevalence of antimicrobial resistance is higher than uncomplicated UTI.[3] The predisposing factor responsible for UTI risk are extremes of age, female gender, pregnancy, infants, urinary tract abnormalities and dysfunction, catheterized

patients with spinal cord injury, renal disease, diabetes mellitus, and immune suppressant patients.[4] The therapeutic management of UTI depends on the affected part of the urinary tract which includes cystitis (bladder infection), pyelonephritis (kidney infection), and urethritis (urethra infection).[5] Depending on type and symptoms, therapy may vary, patients with fever or systemic symptoms of infection should be treated with parenteral antibiotics, while local susceptibility pattern of E. coli and other uropathogens were treated with empirical therapy.[6] The duration of therapy and choice of antibiotics may vary depending on the type of UTI.[6,7] Antibiotic-resistant is a major worldwide issue, which is due to improper and irrational selection and use of antibiotics.[8,9]

UTI is the most common disease in the world, Likewise, UTI patients are also growing in Nepal. Hence, this study compares both empirical therapy and definitive therapy. Similar types of researches had also conducted in Gandaki Province but there is no research to compare empirical therapy or definitive therapy-related economic burden during medical management of UTI. Therefore, this study helps to compare therapy and contribute to regular monitoring, modifying prescription, and cost-effective therapy of UTI.

METHODS

Study design

A prospective observational study was conducted in the outpatient and inpatient department of Manipal teaching hospital, Pokhara, Nepal from June 2019 to November 2019. Ethical approval of this study was obtained from the Institutional Review Committee (IRC), Pokhara University Research Centre (PURC), Kaski, Nepal.

Study population

The UTI patients visiting the OPD and admitted IPD, who meet inclusion criteria was taken into consideration for the study.

Data collection

The data were collected from the patient chart, which includes the patient's history and laboratory investigation report and therapy data taken from the outpatient pharmacy with a direct questionnaire method. The purpose of the study and procedure were explained to all the patients concerned. The researcher visited the medicine and surgery ward during the study period and asked the patients whether their urine culture had been performed or not. The patients whose urine culture had been performed in the microbiology lab of hospitals and were found culture positive were taken for the study. Semi-structured questionnaire was used as a tool for the collection of information. Questionnaires were filled by the principal investigator. The data needed about the routine urine test and sensitivity report were collected by the principal investigator from the microbiology lab of Manipal teaching hospital.

Data analysis

The data from the study were entered in Microsoft (MS) excel and analyzed using statistical package for social sciences (SPSS) version 16. Both inferential test and non-inferential test method was applied. For the presentation of data, several graphical tools like table, charts were used. The variables were presented as the frequency and their respective percentage.

RESULTS

Among a total of 137 cases, UTI was seen more in females 82 (62.45%) in comparison to male 55 (37.55%). The prevalence was higher in the age group of 25-54 years in both sex males (23.35%) and females (48.10%) respectively. Similarly, in the case of ethnicity, as the population ratio of upper caste is higher, the prevalence of UTI seems higher in the upper caste as shown in Table 1.

Table 1: UTI in gender of various age groups and ethnicity.

Variables	Gender (n=137)	
	Male (n=55) Frequency (%)	Female (n=82) Frequency (%)
Age group (in years)		
18-24	7 (5.10)	16 (11.67)
25-54	32 (23.35)	48 (35.10)
55-64	15 (10.94)	17 (12.40)
65	1 (0.72)	1 (0.72)
Ethnic groups		
Upper caste	32 (23.35)	38 (27.73)
Janajatis (Adv)	10 (7.29)	26 (18.97)
Dalits	10 (7.29)	13 (9.48)
Non-dalit Terai	2 (1.45)	2 (1.45)
Janajatis (Dis.)	1 (0.72)	2 (1.45)
Minorities	0 (0)	1 (0.72)

Symptomatologically, dysuria 50 (36.5%), fever 30 (21.9%), lower abdomen pain 22 (16.1%) are the most common symptom followed by burning micturition, flank pain as presented in Table 2.

As depicted in Table 3, out of the 137 isolate samples, gram-negative bacteria had a higher frequency of occurrence than gram-positive. Most common isolated uropathogens in gram-negative. Bacilli and gram-positive bacteria were *E. coli* (58.39%) and *Staphylococcus* (13.86%) respectively. *E. coli*, the most common uropathogens isolated more commonly from the female (63.75%) patients compared to the male (36.25%) patients

and isolation of *E. coli* among female patients is statistically insignificant (p<0.854), whereas isolation of *Staphylococcus sps.* among male patients is statistically significant (p<0.05).

Table 2: Symptoms suspected with UTI.

Symptoms	Frequency (n=137)	Percentage (%)
Dysuria	50	36.5
Low abdominal pain	22	16.1
Hematuria	6	4.4
Fever	30	21.9
Cloudy urine	1	0.7
Flank pain	12	8.8
Burning micturition	16	11.7

A similar pattern in prescription was observed for empiric and definitive therapy. Similarly, In definitive therapy, the three most prescribed antibiotics were nitrofurantoin 100 mg (35.53 %) >cefixime 200 mg (34.71%) >ciprofloxacin 500 mg (17.35%), while the least prescribed were azithromycin 500 mg and amoxicillin-clavulanic acid 625 mg as shown in Figure 1.

As presented in Figure 2, the prescription order was as follows: 1 cefixime >2 nitrofurantoin >3 ciprofloxacin > 4 norfloxacin. In definitive therapy, nitrofurantoin was highly prescribed for it had higher sensitivity to most uropathogens. Even though norfloxacin was the least prescribed, but it seems to be the most potent against *E.coli*. Correlation of medication cost of oral therapy, with sensitivity pattern and prescription frequency, shows that with lower cost, high sensitivity, and high prescription cefixime and nitrofurantoin had higher cost-efficacy for outpatients as given in Figure 3. Supportive therapy in UTI consists mainly of agents that reduce burning micturition like disodium hydrogen citrate, proton pump inhibitors (PPI) like pantoprazole 40 mg, and non-steroidal anti-inflammatory drugs (NSAIDs) like paracetamol. In a few cases, multivitamins and Ayurveda preparation have also been prescribed as presented in Figure 4.

Table 4 demonstrates that in most of the cases, both empirical and definitive therapy was prescribed for 5-7 days each. Sometimes the treatment is longer than one week. Mostly definitive cases took a long time. Among 121 prescriptions, 80 (48.20%) have the same therapy as per susceptibility reports suggest for choice of antimicrobials. It indicates that the prescriber knows the susceptibility pattern of antimicrobials in the study site. Among the antibiotics prescribed for 16 complicated cases, amikacin and ceftriaxone antibiotics are prescribed highly. Ceftriazone 1 g (50%) >amikacin 500 mg (31.25%) and PIT (1.25+1 gm) (25%) while the least prescribed were gentamycin 80 mg as shown in Table 5.

On the cost of therapy; the average cost for empirical therapy (465.44) was higher than the definitive therapy cost (255.54). The total direct cost of 150 empirically prescribed cases was NRs. 125016, average NRs. 820.44 and 121 culture-positive definitive therapy cost was NRs. 45, 832, average NRs. 305.54 calculated as per cost rate of study site at the study period.

The total direct cost of medical management for 16 inpatients was NRs. 199765, average NRs. 2316.55 including registration, urine analysis, investigation bed charge, and other consumable charges as well as discharge medicine cost as presented in Table 6.

Table 3: Distribution of uropathogens with gender of patients (n=137).

Isolate bacteria	Gender		Total bacteria isolate N (%)	P value
	Male (%)	Female (%)		
Gram-negative bacteria				
Escherichia coli	29 (21.16)	51 (37.22)	80 (58.39)	0.854
Klebsiella spp.	3 (2.18)	5 (3.64)	8 (5.83)	0.906
Proteus spp.	6 (4.37)	10 (7.29)	16 (11.67)	0.863
Acinetobacter spp.	2 (1.45)	0 (0)	2 (1.45)	0.055
Gram-positive bacteria				
Enterococcus spp.	3 (2.18)	9 (6.56)	12 (8.75)	0.428
Staphyloococcus spp.	12 (8.75)	7 (5.10)	19 (13.86)	0.008*

*Represents p value is statistically significant

Table 4: Antibiotic prescribed duration for empiric and definitive therapy (n=121).

Medication duration	Empirical therapy	Definitive therapy
0	5	5
3	1	23
5	39	15
7	74	44
10	2	28
≥14	0	6

Table 5: Injection antibiotic prescribed (n=16 IPD).

Intravenous antibiotics prescribed (gm)	Frequency (n)	Percentage (%)
Amikacin (500)	5	31.25
Ceftriaxone (1)	8	50
Doxycycline (1)	2	12.5
Gentamycin (80)	1	6.25
PIT (1.25+1)	4	25

Table 6: Total cost form medical management for outpatients and inpatients.

Cost category	Inpatients		Outpatients			
	Total	Average	Empirical total	Average	Definitive total	Average
Registration	800	50	7500	50	7500	50
Urine analysis	2340	130	19500	130	--	--
Bacterial culture	2800	175	26250	175	--	--
Investigation	15715	982.18	1950	--	--	--
Bed	6800	425	--	--	--	--
Medication cost	162440	10152.5	69816	465.44	38332	255.54
Others consumable	8870	554.37	--	--	--	--
Total NRs.	199765	2316.55	125016	820.44	45832	305.54

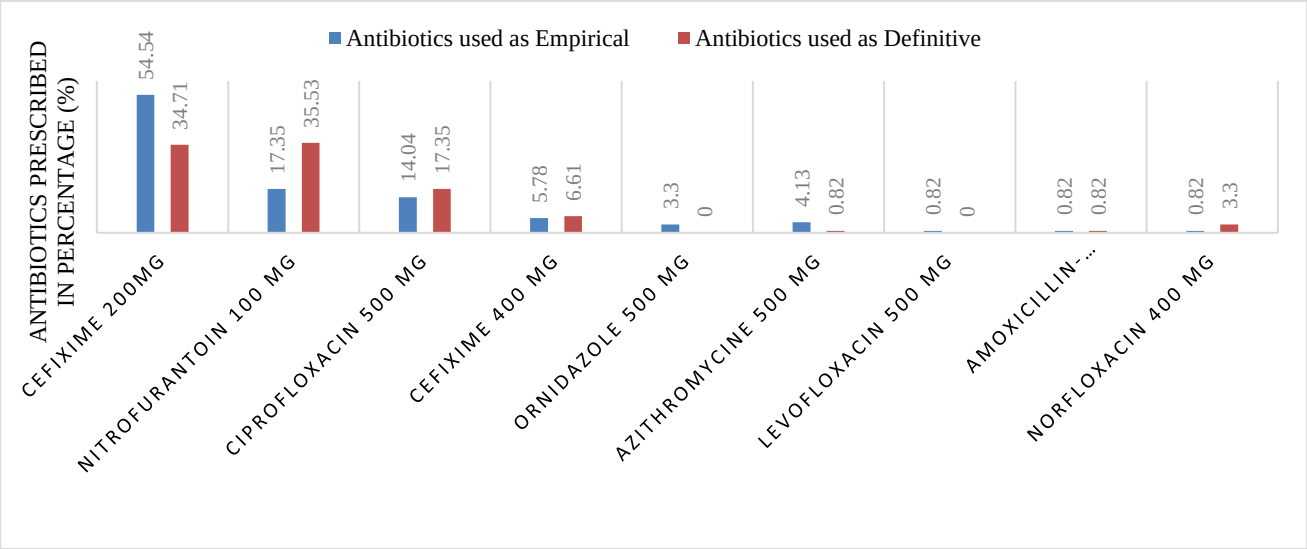

Figure 1: Antibiotics prescribed for empiric and definitive therapy.

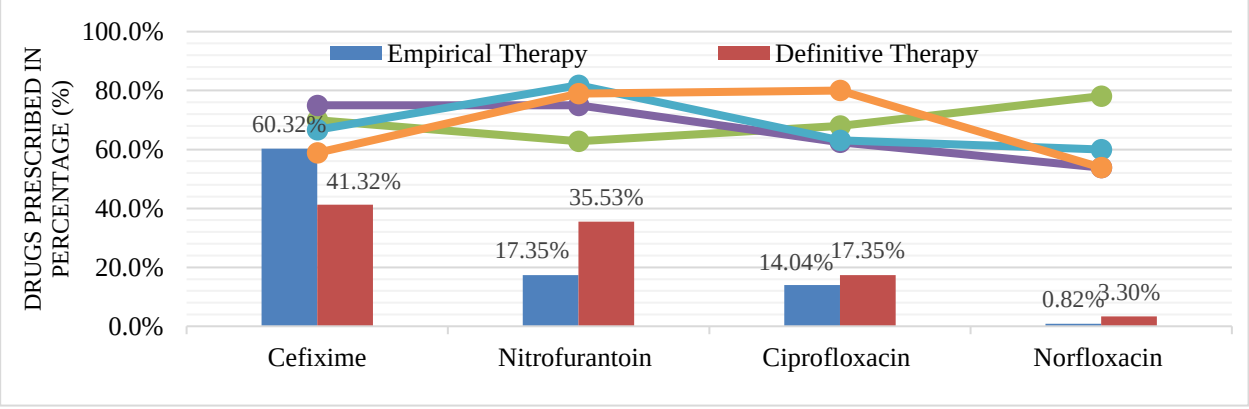

Figure 2: Correlation between antibiotic prescribed and antibiotic sensitivity.

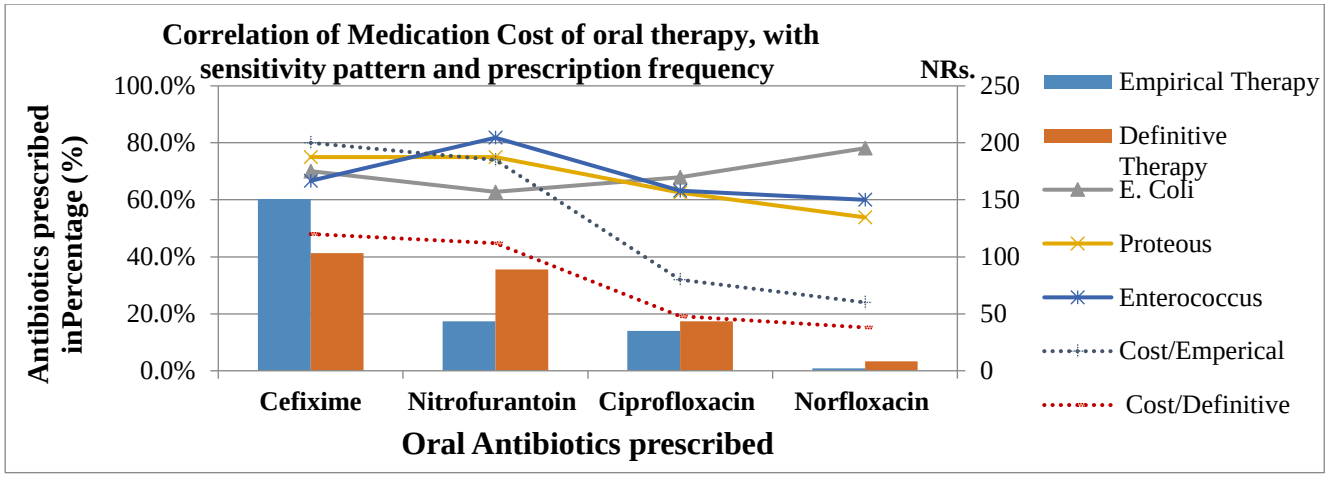

Figure 3: Medication cost of oral therapy with sensitivity pattern and prescription frequency.

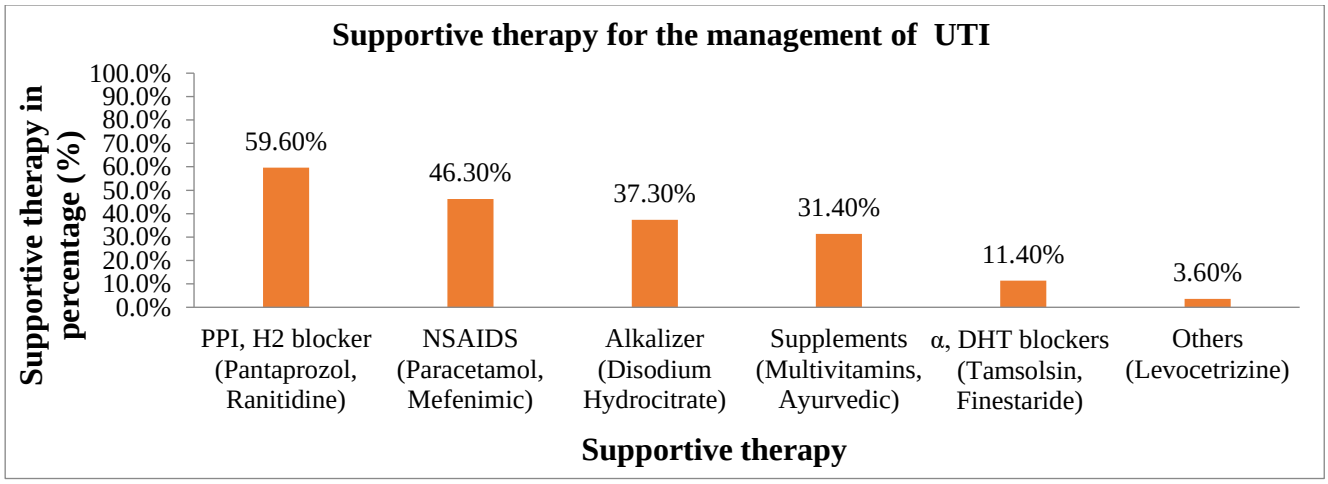

Figure 4: Supportive therapy for the management of UTI.

DISCUSSION

This study determines the drug therapy and its related costs among patients attending hospitals for the treatment of UTI. Out of a total of 137 patients (121 from outpatients and 16 from inpatients), the prevalence of UTI was observed higher in the case of female 82 (59.85%) than male 55 (40.15%). These findings are in agreement with the study done in Iran which reported that 74% are girls and 26% are boys.[10] The anatomical and physical factors like proximity of female urethral meatus to anus, shorter urethra, sexual intercourse are the major factors for the occurrence of higher incidence rates in women. In terms of the age group, the more prone to the UTI was highest in the 25-54 age group among them 35.03% and 23.55% were female and male respectively. The data were similar to a study conducted by Jha et al in Kathmandu where the age group of 21-30 was found to be higher.[11]

Our study showed that the predominant uropathogens to be reported was *E. coli* (58.39%) in gram-negative and *Staphylococcus spp.* (13.86%) in gram-positive respectively. Other common uropathogenic organisms were *Proteus spp.* (11.67%), *Enterococcus spp.* (8.75%), *Klebsiella spp.* (5.83%), and *Acinetobacter spp.* (1.45%). This result is consistent with the study conducted in Tribhuwan University Teaching Hospital (TUTH) of Nepal where *E. coli* was observed in 56.7% cases and *Staphylococcus aureus* in 27.7% cases.[12]

The findings of our study also showed that both empirical and definitive therapy were concurrently prescribed for the treatment of UTI. In about half of the cases 80 (48.24%), empirical therapy was the same as definitive therapy. While in 1/4th cases, 41 (24.7%) prescription was changed in definitive therapy after a sensitivity test. Most of the prescriptions included a single antibiotic with rare cases of multiple antibiotics depending on the symptoms of the patient. The most commonly prescribed antibiotics were: cefixime 200 mg, 66 (48.17%) in empirical and 52 (37.9%) in definitive followed by nitrofurantoin 100 mg, 21 (15.32%) in empirical, 48 (35.03%) in definitive, while the least prescribed were azithromycin 500 mg, 5 (3.64%), amoxicillin-clavulanic acid 625 mg 1 (0.72%) and norfloxacin 400 mg, 1 (0.72%). A previous study shows that nitrofurantoin was the most prescribed antibiotics in

empirical and definitive therapy.[12] As the selection of antibiotics in treatment of UTI are guided by local microbial sensitivities this result can be due to different antibiotic susceptibility pattern in the two different regions. Also, the infection in a specific area can be caused by gram-positive organisms.[13]

In most of the cases, both empirical and definitive therapy were prescribed for 5-7 days 74 (61.15%) followed by five days 39 (32.23%) each. Sometimes the treatment is longer than one week. Mostly definitive cases took a long time. This finding is in agreement with the previous study conducted in Kerala of India where around 66% was treated with empirical therapy of seven days.[14] While looking at the symptoms of UTI, this study finds dysuria in 36.5%, fever in 21.9%, and lower abdominal pain in 16.1% as the chief complaints followed by burning micturition and flank pain. An earlier study in Nepal displayed that lower abdominal pain was the most experienced symptoms and frequency of micturition as the second most ordinary symptom.[15] The variation observed in the symptoms could be due to the environmental and the health conditions of the respondents.

Our study reports that the majority of patients received nonantibiotic supportive therapy such as pantoprazole 40 mg tablet 46.71%, disodium hydrogen citrate 35.03%, and paracetamol 500 mg tablet 30.65%. The study done by Prakasham et al demonstrated that paracetamol was found to be used in 80% of the patients.[14] The choice of supportive therapy is influenced by the symptoms and other associated factors of a patient. Most importantly, in this study, for some significant number of cases; 20 (14.59%) patients were prescribed with multivitamins which was a cost burden to patients even though multivitamins don't have any relation to the treatment of UTI. Such an economic burden for patients has to be avoided. While observing the inpatient cases the antibiotic prescribed for 16 complicated cases, amikacin 500 mg and ceftrazone 1 gm were highly used, while the least used were gentamycin 80 mg.This therapy pattern was slightly different from Gupta et al.[16]

The average cost for empirical therapy (NRs. 65.44) was higher than the definitive therapy cost (NRs. 255.54). The total direct cost of empirically prescribed cases was NRs. 125016, average NRs. 820.44 and definitive therapy cost was NRs. 45832, average NRs. 305.54 was calculated as per the cost rate of the study site at the study period. The total direct cost of medical management for 16 cUTI patients was NRs. 199765, average NRs. 2316.55 including registration, urine analysis, investigation bed charge, and other consumable charges as well as discharge medicine cost.

CONCLUSION

In the current research done in the tertiary care hospital of Western Nepal, gram-negative bacteria presented a higher occurrence. Commonly organisms were *E. coli* and *Staphylococcus*. Females were more prone to UTI infection and the age group 25-54 had a higher prevalence rate. Dysuria, fever, and pain were the most common symptoms associated with UTI. With lower cost, higher sensitivity, and high prescription, cefixime, and nitrofurantoin were better drugs for the management of UTI among OPD patients.

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