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Utilization Of Antibiotics In Patients With Urinary Tract Infections

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Abstract

Objectives: This study aims to investigate the utilization of antibiotics among the patients attending in Silverline Hospital, Lekhnath Marg, Balaju, Kathmandu-44600, Nepal.
Methods: A hospital based cross sectional study was conducted in between June to September, 2022. A standard questionnaire was prepared, to conduct the survey based on patient's demographic data such as which utilization of drug, age, gender, therapy and medication.
Results: Out of 111 patients, antibiotics Levofloxacin is highly prescribed to the patients. It is prescribed to 92 (82.90%) people. Cefixime is prescribed for 37 (41.07%) people, Ciprofloxacin is prescribed for 29 (26.12%) patients, Ofloxacin is prescribed for 5 (4.5%) and Nitrofurantoin is prescribed for least for number of people and it is prescribed for 4 (3.6%) patients.
Conclusion: Fluroquinolones and Cephalosporins were the most commonly prescribed antibiotics in this study. Culture sensitivity test was carried out only in a limited number of cases, and present findings together with previous ones are suggestive of the need for periodic monitoring of antibiotic sensitivity pattern of the bacterial isolates to provide effective treatment and thereby to make it more cost effective particularly in the developing countries like Nepal. The continuous monitoring and reporting of prescribing pattern of antibiotics will surely help the physicians for effective treatment.

Key words: Utilization, Antibiotic, Drug, Infections, Female

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INTRODUCTION

A urinary tract infection (UTI) is a condition in which one or more parts of the urinary system become infected (Puca, 2014). Each type of UTI may result in more specific signs and symptoms, depending on which part of the urinary tract is infected (Wyndaele et al., 2012). UTIs are the most common of all bacterial infections and can occur at any time in the life of an individual (Akram et al., 2007; Azzarone et al., 2007). The most common UTIs occur mainly in women and affect the bladder and urethra. The cystitis is the infection of the bladder and urethritis is the infection of the urethra (Parsons, 2011). Furthermore, because the female urethra is close to the vagina, sexually transmitted infections, such as herpes, gonorrhea, chlamydia, and mycoplasma, can cause urethritis (Jepson et al., 2018). UTI is the second most common infectious disease in the community medical practice. Worldwide, about 150 million people are diagnosed with UTI each year, costing an excess of 6 billion dollars. The resistance pattern of community acquired uropathogens has not been extensively studied in Indian subcontinent (Kothari and Sagar, 2015). UTIs account for more than 100,000 hospital admissions annually, most often for pyelonephritis. They also account for at least 40% of all hospital acquired infections; the majority of these cases are catheter associated (Car, 2006). UTI may lead to life threatening complications like sepsis and renal scaring. Renal scaring is the most common cause of hypertension in later childhood and renal failure in adults. Recognition of UTI in children should be made as early as possible to prevent these complications. Therefore, investigations for early diagnosis of UTI are of most importance (Jones, 2010). Two clinical entities are recognized in patients with symptomatic UTI: lower UTI (cystitis) and upper UTI (pyelonephritis) (Rai et al., 2015).

In Nepal and other developing countries, UTI is the most common bacterial infection causing illness mostly in females due to illiteracy, unhygienic conditions and lack of proper toilet facilities. They are always vulnerable to infections by various organisms. Microbial resistance to nearly all classes of antimicrobials continues to rise despite increasing awareness and concern worldwide. In Nepal, Isolated pathogen frequency and antimicrobial resistant rates can vary dramatically even within the same nation. Therefore, to ensure the appropriate therapy current knowledge of organism that cause UTI and their susceptibility pattern is mandatory (Joshi, 2014). Up to 60% of women have at least one symptomatic UTI during their lifetime. Around 10% of women in the United States have one or more episodes of symptomatic UTIs each year. Young, sexually active women 18–24 years of age have the highest incidence of UTIs. About 25% of these women have spontaneous resolution of symptoms, and an equal number become infected (Sobel, 2014). The prevalence of UTIs in men is significantly lower than in women, occurring primarily in men with urologic structural abnormalities and in older adult men. Lower UTIs, also known as cystitis, are significantly more prevalent in women than in men. This is primarily because of anatomic differences, including shorter urethral length and moist periurethral environment in women. Urinary tract infections typically start with periurethral contamination by a uropathogen residing in the gut, followed by colonization of the urethra and, finally, migration by the flagella and pili of the pathogen to the bladder or kidney. Bacterial adherence to the uroepithelium is key in the pathogenesis of UTI. Infections occur when bacterial virulence mechanisms overcome efficient host defense mechanisms. Upper UTIs, also known as pyelonephritis, develop when uropathogens ascend to the kidneys by the ureters. Infections can occur when bacteria bind to a urinary catheter, a kidney, or a

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bladder stone or when they are retained in the urinary tract by a physical obstruction. In severe cases of pyelonephritis, the affected kidney may be enlarged, with raised abscesses on the surface (as revealed in imaging studies). Staphylococcus aureus bacteremia or endocarditis can lead to hematogenous seeding of the bacteria to the kidneys, causing suppurative necrosis or abscess formation within the renal parenchyma (Sobel, 2014). In contrast, gram-negative bacilli rarely cause kidney infection by the hematogenous route. According to an experimental model of pyelonephritis, the main renal abnormality reported is the inability to maximally concentrate the urine (Sobel, 2014). This concentration defect occurs early in the infection and is rapidly reversible with antibiotic therapy. An obstruction can led to progressive destruction of the affected kidney and subsequent renal insufficiency.

Initial diagnosis of acute uncomplicated cystitis is typically based on patient medical history, taking into account past individual and family health issues, sexual activity, and current symptoms. Common indicators of acute cystitis include urinary urgency and frequency, pain when voiding (dysuria), lower abdominal discomfort, and cloudy or dark urine. The diagnosis of patients presenting with these classic symptoms may be confirmed by urinalysis showing the presence of red blood cells, high nitrite levels, and leukocyte esterase in the urine. Although medical history and urinalysis are sufficient for the diagnosis of most uncomplicated UTIs, the gold standard for diagnosis of acute cystitis includes a bacteriological urine culture with identification of the causative agent and antimicrobial susceptibility testing. Using fresh, midstream urine, clinical confirmation of an uncomplicated UTI is classically defined as ≥105 colony-forming units (CFU)/mL of urine. However, this definition has recently been modified based on observations that many uropathogens are capable of eliciting clinical pathology in the urinary tract even with low levels of bacteriuria. Consequently, as little as 103 CFU/mL urine, in the presence of over UTI symptoms, is now considered sufficient for diagnosis of acute cystitis (Gupta, 2014). In the non-pregnant adult woman with a normal urinary tract, bacteriuria infrequently progresses to symptomatic cystitis or pyelonephritis. Common predisposing factors for UTIs are listed table below. The urethra is usually colonized with bacteria, and sexual intercourse can force bacteria into the female bladder. Furthermore, spermicides increase colonization of the vagina with uropathogens and adherence of Escherichia coli to vaginal epithelial cells. Patients with structural abnormalities develop UTIs largely from obstruction of the urine flow. Urinary stasis increases susceptibility to infection. Men of any age and pregnant women are susceptible to lesions that result in obstruction. (Sobel, 2014).

Drug utilization studies with the main focus on prescribing, and administering of drugs to facilitate the rational use of drugs in a population and promote appropriate use of monitored drugs and reduction of abuse or misuse of monitored drugs. Availability of antibiotics and its utilization in case of UTI is very essential for the effective management of it. Moreover, UTI management procedure or treatment guidelines is quite different from other diseases. It deals with prevention, Counselling, Lab testing and therapy. Utilization of antibiotics in UTI case and overcoming the resistance to drug is increased. The purpose of drug utilization review is to ensure drugs are used appropriately, safely, and effectively to improve patient health status. The use of drugs in appropriate, safe, and effective manner would decrease the treatment cost for the patients. Drug utilization review is an authorized and structured ongoing review of practitioner prescribing, pharmacist dispensing, and patient use of medications

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(Hoffmann, 1984). Drug utilization program always plays an important role in helping the health-care team to improve the prescribing, administration, and use of medications. Pharmacists can then, in collaboration with prescribers and other members of the health-care team, initiate action to improve drug therapy for patients (Fallik, 2015).

The present study might be beneficial to know about the most frequently prescribed UTI drugs, complications, most common age groups along with the rational use. The study might be beneficial to know about most frequently prescribed UTI drugs. This study helps in finding the appropriate drugs for UTI and further assist the patient who need more information and support. Also, this study will be helpful as a baseline study for further research. The main objective of this study was to understand the rationality of antibiotics used for treatment of UTI by conducting a drug utilization study. Antibiotic resistance is becoming a threat for the public health, lives of hospitalized individual and patients with chronic conditions therefore there is a need for antibiotic guidelines to prevent such resistance also to improve the patient's therapeutic outcome.

METHOD

The present study is important to identify the utilization of antibiotics in UTI. This research was also providing the reference for the early done research in UTI and its pharmacological management of it in Nepal as for stander treatment guideline. Research methodology provides the information about research design, sampling procedure, data analysis tool, instruments and data collection procedure in detail.

Study area

This study was carried out in Silverline Hospital of Kathmandu, Nepal. Silverline hospital formerly known as Janamaitri Hospital is a first non-profit private national charitable hospital of Nepal, located at Balaju, Ring Road in Kathmandu. Janamaitri Hospital has obtained approval from Government of Nepal for the operation and management of 24-hours emergency, ICU/CCU, OPD/IPD, and advanced diagnostic facilities, rehabilitation and research. The samples for this study was collected during the month of June to September, 2022.

Sampling design

It is cross sectional quantitative study. Data was collected from OPD patients whose was diagnosed as UTI in Urology department and internal medicine department. The total number of observed samples was 111. The inclusion criteria adopted for this study were: all in-patients who were diagnosed with urinary tract infections; all in-patients over 5 years of age, the male and female patients who have pus cell count 4 to 10 (pyuria) and RBC count 4 to 10 in urine regular examination and patients with urinary tract obstruction and infection occurred in Urinary tract. Similarly, the exclusion criteria adopted for this study were the in-patients with urinary tract infection who are unwilling to participate in the study and those patients who are unable to provide the informed consent.

Data Collection

The information such as socio-demographic information, clinical presentation, drugs prescribed, duration of drug therapy etc., were collected from patient or to any other person related to patient provided knowledge about the disease condition and filled up in data collection sheet. The validity of the research method was maintained by consulting with the experts, doctors and hospital staffs. The reliability of tool was maintained by taking permission from hospital with the help of experts and doctors. In this way, this study

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was carried out and necessary changes were made.

Data analysis

The collected data was entered, checked and edited manually and data analysis was done as per the objectives of the study. Data analysis was done with the help of SPSS version 25 and MS-excel. Approval letter was acquired from hospital for the purpose of data collection. The participants were informed about the purpose of object and purpose of study. There was no discrimination on the basis of cast, religion, socio-economic status. Participants were ensured that the collection of data will be used only for research purpose.

RESULTS

During the study period, a total of 111 patients diagnosed with Urinary tract infection and the results and analysis of 111 patients are presented here. In demographic studies, the patients were analyzed on the basis of age, sex and number of drugs prescribed.

Gender of the patients

Male patients showed highest number of occurrences of urinary tract infection 57 (51.4%) than female patients 54 (48.6%).

Age distribution of the patients

Out of 111 patients there are 9.9 percent patients are of age group 0 to 20, while 51.4 percent people are of age group 21 to 40, 24.3 patient age group are of age group 41 to 60, 10.8 percent of people are of age group 61 to 80, and 3.6 percent age of patients are of age group 80 above.

Material status of the patients

From the total 111 sample collected, we got the frequency of married people 95, and frequency of unmarried people is 16.

Therapy used for the patients

From the Table 4, we got the result that 47.7 patients used Empirical and 52.3 percent people are Definite therapy.

Antibiotics used in the patients

From the Table 5, we found the percentage of people to whom antibiotics are used. Among them 49.5% people were found to be using with single antibiotics whereas 50.5% people were found to be using with multiple antibiotics.

Sign and symptoms while attending hospital

While attending hospital, maximum number of patients have the sign and symptoms i.e., burning micturition (83), which holds 79.0% followed by the lower abdominal pain to 32 patients (30.5%) and blood in urine to 28 (26.7%) similarly fever 23 (21.9%) and so on.

Commonly prescribed drugs for UTI

The various antibiotics used in UTI patients. From the various antibiotics Levofloxacin is highly prescribed to the patients. It is prescribed to 92 (82.90 %) people. Cefixime is prescribed for 37 (41.07 %) people, Ciprofloxacin is prescribed for 29 (26.12%) patients, Ofloxacin is prescribed for 5 (4.5%) and Nitrofurantoin is prescribed for least for number of people and it is prescribed for 4 (3.6%) patients.

Commonly prescribed drug groups for UTI

The various antibiotics group used in UTI patients. From the various antibiotics group Fluoroquinolones was highly prescribed to the patients. It is prescribed to 126 (75.44%) people followed by the Cephalosporin which was prescribed for 37 (22.15%) people.

Duration of therapy per once visit in OPD

Out of 111 patients, majority of patients were given 7 days (80%) therapy while visiting the hospital and minority of

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the patients were given 10 days therapy (5%).

Comparison with National antibiotic treatment guideline.

According to National Antibiotics Treatment Guidelines (NATG) formulated by Government of Nepal, Ministry of Health and Population (2014) for urinary tract infection are as follows.

Symptoms and signs

- Acute agonizing pain over the loin often radiating to the groin and suprapubic region.
- Frequent passage of small amount of scalding usually cloudy urine sometime associated with stranger.
- Pain suprapubic or urethral region while passing urine.
- Usually high-grade fever with chills and rigor.
- Anorexia and vomiting.

Treatment procedure

According to prescription medicine prescribed for UTI in Helping Hands Community Hospital

a. Single antibiotic

- Levofloxacin 750 mg OD for 7 days OR
- Cefixime 200 mg BD for 7 days OR
- Ofloxacin 500 mg BD for 7 days .

b. Multiple antibiotics prescribed for UTI

- Levofloxacin 750 mg OD for 7 days and
- Cefixime 200 mg BD for 7 days.

OR

- Cefixime 200mg BD for 7 days and
- Levofloxacin 500mg BD for 7 days.

According to above comparison of prescribed drugs with national antibiotic treatment guideline slightly different in regimen of treatment were observed.

3.13. Price Variation of different antibiotics treated for UTI available at Silverline hospital

Among the different antibiotics available in Silverline hospital, the percentage price variation ranges from 25.0% to 50.94%. Cefixime 200 mg has the high percentage price variation with 50.94% with minimum price NRs. 13.25, maximum price NRs. 20 and mean price of NRs. 16.63. Levofloxacin has the lowest price variation 25.0% with minimum price NRs. 12 and maximum price NRs. 20. There is no price variation in ciprofloxacin 500 mg and Ofloxacin 400 mg.

Table 1: Microorganisms isolated from urine

S. N.	Microorganism isolated	Frequency	Percentage
1	No growth	16	27.58
2	*E. coli*	30	51.72
3	*Acinobactor baumanni*	5	8.6 %
4	*Klebsiella Pneumoniae*	4	6.89 %
4	Others	3	5.17 %

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Table 2: Sensitivity and resistance pattern of microorganisms

S. N	Microorganism	Sensitive drug	Resistance drug	Prescribed drug
1	*E. coli*	Ciprofloxacin, Levofloxacin, Nitrofurantoin, Cetriaxone	Amoxicillin, Ampicillin	Levofloxacin
2	*Acinobactor baumanni*	Ofloxacin, Cefixime, Levofloxacin, Nitrofurantoin	Amoxicillin, Ampicillin	Ofloxacin
3	*Klebsiella Pneumoniae*	Levofloxacin, Nitrofurantoin Ofloxacin, Cefixime, Ciprofloxacin,	Amoxicillin, Ampicillin	Ofloxacin, Levofloxacin
4	Others	Ciprofloxacin, Levofloxacin, Nitrofurantoin, Cetriaxone		Ofloxacin, Levofloxacin, Cefixime

Table 3: Treatment guidelines for UTI according to NATG (2014)

HP/SHP	PHC/District Hospital	Zonal & above or referral centre
• Amoxicillin 500 mg q8h for 14 days OR Cotrimoxazole 800+160 mg q12h for 7 days (for non-pregnant) In severe infection (for non-pregnant) • Ciprofloxacin 500 mg q12h for 7 days. Refer to hospital if fever does not subside within 7 days of treatment OR if infection reoccurs.	• As per SHP/HP OR • Nitrofurantoin 100 mg q8h for 14 days Parenteral therapy if patient is very sick • Inj Ampicillin 2 g IV q6h 2-3 days OR • Inj Gentamicin 5 mg/Kg IV q24h for 3 days (if sensitive to ampicillin) Then switch over to oral medicine as: • Amoxicillin 500 mg q8h for 12 days	• Amoxicillin 500 mg q8h for 14 days OR • Nitrofurantoin 100 mg q8h for 14 days Parenteral therapy if patient is very sick • Inj Ampicillin 2 g IV q6h 2-3 days OR • Inj Cefotaxime 1 g IV q6h 2-3 days OR • Gentamicin 5 mg/Kg IV q24h for 3 days Then switch over to oral medicine as: • Amoxicillin 500 mg q8h for 12 days OR • Cefixime 400 mg q6h for 12 days OR • Nitrofurantoin 100 mg q8h for 12 days

Table 4: Price Variation of different antibiotics treated for UTI available at Silverline hospital

Drug Name	Min. Price	Max. Price	Mean Price	% Price Variation
Cefixime 200 mg	13.25	20	16.63	50.94%
Cefixime 400mg	40	55	47.5	37.5%
Levofloxacin 500mg	12	15	13.5	25.0%
Levofloxacin 750mg	15	20	17.5	33.3%
Ciprofloxacin 500mg	8	8	8	0
Ofloxacin 400mg	8	8	8	0

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DISCUSSION

In the present study, out of 111 patients, male patients showed highest number of occurrences of urinary tract infection i.e., 57 (51.4%) than female patients 54 (48.6%). A Study conducted by Panayappan et al. (2017) in India, on prescribing pattern and rational use of antibiotics in UTI patients in a tertiary care hospital was conducted. The study indicates the female patients (54%) were more prone to UTI when compared to male patients (46%). In our study, data collected from Urology department and medicine department of the hospital not from the gynecology may affect the data. So male patients were more in this study than female patients. Out of 111 patients there are 9.9 percent patients are of age group 0 to 20, while 51.4 percent people are of age group 21 to 40, 24.3 patient age group are of age group 41 to 60, 10.8 percent of people are of age group 61 to 80, and 3.6 percent age of patients are of age group 80 above. From the total 111 sample collected, we got the frequency of married people 95, and frequency of unmarried people is 16. In a study by Huang and Stafford (2002), about National Patterns in the Treatment of UTI in women by ambulatory care physicians concludes that there are increasing in the use of fluoroquinolones and nitrofurantoin even though they are not highly recommended and not the most cost effective. One more study by Jancel and Dudas (2002), about the management of uncomplicated UTI has concluded that trimethoprim-sulfamethoxazole and trimethoprim are still considered first-line therapy for uncomplicated UTI in areas where resistance in the community is <10-20%. In this study, antibiotics Levofloxacin is highly prescribed to the patients. It is prescribed to 92 (82.90%) people. Cefixime is prescribed for 37 (41.07%) people, Ciprofloxacin is prescribed for 29 (26.12%) patients, Ofloxacin is prescribed for 5 (4.5%) and Nitrofurantoin and others is prescribed for least for number of people and it is prescribed for 4 (3.6%) patients.

In another study, it reveals that symptoms alone have low accuracy when assessed against the reference standard for diagnosing UTI. Empiric treatment of UTI based on symptoms may expose large number of patients to unnecessary antibiotics.

A study concluded by Gopal et al about antibiotic resistance patterns of outpatient pediatric UTI and has concluded that E. coli remains the most common pediatric uropathogen. Prospective observational study on prescribing pattern of antimicrobial agents in a tertiary care teaching hospital was conducted, and this study indicated that there is a need for motivating the physicians to prescribe antimicrobial agents by generic names with supportive bacteriological evidence. A prospective observational study was carried out on the excessive and inappropriate use of antibiotics in a Tertiary Care Teaching Hospital for 6 months in General Medicine and Pediatrics Department. This study results indicated that cephalosporin (72.72%) was mostly prescribed to inpatients, and penicillin's (57.29%) usage was found to be more in out patients. In our study, out of 100 patients, urine culture was done only for 30 patients. In that, 18 of them (60%) showed the isolation of E. coli followed by isolation of Proteus in 6 cases (20%) than Klebsiella in 4 cases (13.33%), and last is Pseudomonas in 2 cases (6.66%). A study conducted by Mahadevamma et al. (2012) in Banglore, India the prescribing pattern of antibiotics was studied in in-patients and out-patients. Among the 10 types of drugs prescribed, Ciprofloxacin was prescribed to only 13 (22.8%) in-patients whereas it is prescribed for 25 (23.8%) out-patients. Ceftriaxone was prescribed to 19 (33.3%) in-patients and 14(13.3%) of out-patients. Norfloxacin was prescribed to 4 (7.0%) in-patients and 15(14.0%) out-patients. Nitrofurantoin was

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not at all prescribed in in patients whereas in out-patients it was prescribed for 12(11.4%). Cefotaxim was prescribed to 4 (7.0%) of in patients and 07 (6.7%) of out-patients. Among the total of 07 Amoxicillin prescriptions, 03 (5.3%) were prescribed to in-patients and the rest 04(3.8%) were given to out-patients.

Among the different antibiotics available in Silverline hospital, the percentage price variation ranges from 25.0% to 50.94%. Cefixime 200mg has the high percentage price variation with 50.94% with minimum price NRs.13.25, maximum price NRs. 20 and mean price of NRs.16.63. Levofloxacin has the lowest price variation 25.0% with minimum price NRs.12 and maximum price NRs. 20. There is no price variation in ciprofloxacin 500 mg and Ofloxacin 400 mg. Prescribing by generic name can reduce the cost incurred on drugs and the risk of medication errors. Excess of prescribing by brand names may be considered as evidence of vigorous promotional activities by pharmaceutical companies. The number of drugs prescribed by generic name was 5.40 % in our study which is less compared to a similar study conducted by Mandavi et al in Punjab, India where 18% of the drugs were prescribed by generic name. Hence, more emphasis needs to be given to improve prescribing by generic names in developing countries like Nepal to make the treatment cost-effective. The number of antibiotics prescribed should be as low as possible and should be prescribed for appropriate medical indication.

CONCLUSION

Prescribing pattern of antibacterial and rationality of the medications used for treating patients with UTIs was appropriate but using brand names for prescribing drugs can increase the chance of medication related problems. Higher number of comorbidities was leading to polypharmacy which is a precursor for increasing possibility of drug-drug interactions, in return there is an increased requirement for close monitoring and management of possible interactions such as antibiotic resistance is becoming a threat for the public health, lives of hospitalized individual and patients with chronic conditions therefore there is a need for antibiotic guidelines to prevent such resistance. Fluroquinolones and Cephalosporins were the most commonly prescribed antibiotics in this study. Culture sensitivity test was carried out only in a limited number of cases, and present findings are suggestive of the need for periodic monitoring of antibiotic sensitivity pattern of the bacterial isolates to provide effective treatment. The continuous monitoring and reporting of prescribing pattern of antibiotics will surely help the physicians for effective treatment. The empirical therapy was found in around half of the population, so definite therapy was suggested for all of the patients as empirical therapy leads to the irrational use of the antibiotics drug. As the most common bacterial infection that requires medical care, UTIs vary greatly by clinical presentation and therapeutic management. Urinary tract infections affect a variety of patients with different biological and procedural risk factors (e.g., age, sex, pregnancy, catheters and urologic interventions). However, not all bacteriuria's require antibiotic therapy, particularly in the presence of ASB. Antibiotic stewardship practices are essential to promote judicious antibiotic use for UTIs. This can significantly reduce antibiotic resistance because UTIs are the most common infections leading to an antibiotic prescription.

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