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COMPARISON OF ANTIMICROBIAL RESISTANCE PATTERN BETWEEN COMPLICATED AND UNCOMPLICATED URINARY TRACT INFECTIONS

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ABSTRACT

Objective: To determine the antibiotic resistance pattern of patients attending with UTI and to compare antimicrobial resistance pattern between complicated and uncomplicated UTI.

Background: Urinary Tract Infection (UTI) is one of the most common bacterial infections seen in clinical practice worldwide every year, with about 150 million people getting infected. Multidrug resistant uropathogens have considerably complicated empirical antibiotic therapy especially in lower middle-income countries like Pakistan where antibiotics are used in irrational manner. There is limited data available on the antimicrobial resistance pattern of complicated and uncomplicated UTIs in Balochistan which restricts the clinicians to work towards locally adapted empirical antibiogram.

Place and Duration of Study: Department of Medicine / Urology OPD, Sandeman Provincial Hospital and Bolan Medical College, Quetta from April 12, 2026 to July 13, 2026.

Methodology: The method used was a cross-sectional analytical study with non-probability consecutive sampling of 203 cases of patients who had UTI aged 18, with a urine culture of ≥50,000 CFU/mL and with clinical symptoms. There was an operational definition for complicated vs uncomplicated UTI. Urine culture was performed and antibiotic susceptibility testing using the disc diffusion method was carried out for 20 antibiotics. The chi-square / Fischer exact test was used for comparisons of the resistance frequencies among groups. The raw data were analysed by SPSS 24.0.

Results: The mean age was 38.2 ± 14.6 years with female predominance (68.5%). Complicated UTI was identified in 44.3% (90/203) and uncomplicated UTI in 55.7% (113/203) of patients. The most frequently reported pathogen was Escherichia coli (58.6%). Significant differences were found between complicated and uncomplicated UTI for ampicillin (82.2% vs 70.8%), ciprofloxacin (68.9% vs 54.0%), ceftriaxone (63.3% vs 48.7%), co-trimoxazole (74.4% vs 62.8%) and nitrofurantoin (32.2% vs 20.4%) (all $p<0.05$). Nitrofurantoin and amikacin had the lowest resistance rates for both groups.

Conclusion: More complicated UTIs actually show significantly higher antimicrobial resistance rates compared to all uncomplicated UTIs for multiple antibiotic classes. Ampicillin and co-trimoxazole are no longer useful as empirical agents in either group. Nitrofurantoin and amikacin are still relatively active and should still be considered as a priority in local guideline for empirical treatment. To guide rational antibiotic prescribing at the local level continuous antibiotic surveillance is necessary in Quetta.

KEYWORDS: Urinary tract infection, Antimicrobial resistance, Complicated UTI, Uncomplicated UTI, Uropathogens, Quetta

INTRODUCTION

UTI is among the most commonly seen bacterial urinary infections in community and hospital settings and it is estimated that 150 million people worldwide suffer from UTIs annually, with a significant cost of morbidity as well as health-care spending and antibiotic use [1,12]. UTI is defined by the presence of pathogenic microorganisms in the urinary tract (urethra, bladder, kidneys and prostate) and will be confirmed by positive urine culture showing a bacterial count ≥50,000 CFU/ml of urine with a recognised uropathogen [2]. It is the second most common bacterial infection worldwide and affects all age groups, being most common among ~16 to 64 years [11,12].

UTIs can be divided into two overall types: uncomplicated and complicated. Uncomplicated UTI is usually occurs in non-pregnant pre-menopausal women without urinary tract abnormality, and can usually be treated with a short course of empirical antibiotic treatment[13,14]. In contrast, complicated UTI refers to those infections that occur

in someone who has predisposing anatomic or functional abnormalities, substrate for urinary tract problems, immunocompromising illness, urinary obstruction, renal stones, urinary catheterisation or to systemic illness (e.g. sepsis or diabetes mellitus), and may require culture directed long-term therapy [11]. So accurate categorisation of UTI type is essential to selecting the right antibiotic and to manage clinical aspects[11].
As a result, the increase of antimicrobial resistance (AMR) in common uropathogens has posed a great clinical and public health problem in recent years, especially in the lower and middle - income countries, where abuse of antibiotics and self-medication is common, and also directly contribute to the development of AMR [6]. It is important to understand that the pattern of antimicrobial resistance in uropathogens, as well as what is occurring, depends on many complex factors including selection of the microbial population, the susceptibility of the host, the antibiotic resistance of the local and present population of microorganisms, the antibiotic policies of clinicians and the healthcare delivery system, and it is constantly changing [7]. It is therefore imperative to monitor locally the susceptibility patterns in order to develop rational empirical antibiograms. Very high levels of resistance to co-trimoxazole, ciprofloxacin, cefuroxime and amoxicillin have been reported among uropathogens in tertiary care hospitals in South Asia and nitrofurantoin, as a rule, had lower levels of resistance [2,8]. But, there are still few studies that specifically compare the antimicrobial resistance of complicated and uncomplicated UTIs from Balochistan to base localised tailored prescription decisions. To find out and compare the antimicrobial resistance pattern in complicated UTI and uncomplicated UTI hence this study was conducted at Sandeman Provincial Hospital, Quetta.

MATERIALS AND METHODS

Study Design and setting

This is a cross-sectional analytical study, conducted in the Department of Medicine and Urology OPD at Sandeman Provincial Hospital (SPH) / Bolan Medical College, Quetta from April 12, 2026 to July 13, 2026. After written informed consent was obtained, consecutive patients with symptomatic UTI and who met the inclusion criteria were enrolled.

ETHICAL APPROVAL

The study was conducted after obtaining approval from the Research Evaluation Unit (REU), CPSP (Ref: CPSP/REU/MED-2022-001-20314, dated April 11, 2026) and the Ethical Review Committee of the institute. Written informed consent was obtained from all study participants prior to enrolment.

Sampling Technique and Sample Size

Using the WHO sample size formula [15]: $n = (Z^2 \times p \times (1-p)) / e^2$, at 25.38% frequency of nitrofurantoin resistance in E. coli [2] in combination with a margin of error of ± 6%, confidence level of 95% (Z = 1.96), a sample size of 203 was obtained. Non probability consecutive sampling was used.

Inclusion Criteria

- Male and female subjects ≥ 18 years of age.
- Symptomatic and laboratory confirmed UTI: urine culture positive for bacterial growth ≥50,000 CFU/mL of a recognised uropathogen.
- Both Upper UTI (pyelonephritis) and Lower UTI (cystitis).

Exclusion Criteria

- Recurrent UTI (three or more in past 12 months).
- Known Renal failure or Chronic liver disease
- Women who are clinically and/or physically examined as having an active menstruation, tubo-ovarian disease, appendicitis, or colitis which may impair the interpretation of a urine culture; men with clinically and/or physically examined epididymitis or orchitis.

Operational Definitions

Uncomplicated UTI was defined as UTI in a non-pregnant, immunocompetent, adult female, aged 18-65 years, without any structural or functional urinary tract anomaly, diabetes, renal calculi, urinary obstruction or urinary catheter. Complicated UTI was defined as UTI in any of the following: pregnant patients, immunocompromised patients, diabetes mellitus, renal calculi, urinary obstruction, urinary catheter, sepsis, and upper urinary tract (pyelonephritis).

Antibiotic Resistance Interpretation: Antibiotic susceptibility testing was performed using the standard Kirby-Bauer disc diffusion method on Mueller-Hinton agar. Zones of inhibition were measured in millimeters and categorized as Susceptible, Intermediate, or Resistant according to the Clinical and Laboratory Standards Institute (CLSI M100) guidelines.

Data Collection Procedure

UTI patients coming to Medicine and urology OPD of SPH Quetta were screened. After obtaining appropriate written informed consent, all the baseline demographic and clinical data such as age, gender, place of residence, weight, height, BMI, duration of symptoms, smoking status, diabetes, hypertension, immunocompromised status, pregnancy, sepsis, renal stone, renal stone obstruction and renal catheterization were collected on a predesigned proforma. Midstream urine samples were taken in sterile containers and analyzed within 2 hours in the hospital microbiology laboratory. The causal organism was identified using Gram stain, blood agar and MacConkey agar cultivation and colony morphology. Disc diffusion susceptibility testing was carried out using 20 different antibiotics: Amoxicillin, Ampicillin, Ampicillin-Sulbactam, Piperacillin-Tazobactam, Cefuroxime, Cefixime, Ceftazidime, Ceftizoxime, Ceftriaxone, Cefepime, Nalidixic acid, Ciprofloxacin, Nitrofurantoin, Tetracycline, Co-trimoxazole, Clarithromycin, Erythromycin, Amikacin, and Gentamicin. Results were analysed according to the zone size criteria in the operational definition. The principal investigator categorised the UTI type (complicated or uncomplicated) and all findings were recorded on the proforma.

Statistical Analysis

SPSS 24.0 was used for data entry and analysis. Normality of quantitative variables (age, BMI and duration of symptoms) was measured using the Shapiro-Wilk test and the data was presented as mean ± SD or median (IQR) accordingly. Qualitative variables were expressed as frequencies and percentages such as gender, UTI type and causative organism, comorbidities and individual antibiotic resistance rate. The chi-square test or Fischer exact test was used to compare the frequencies of antibiotic resistance between complicated and uncomplicated UTI group. Stratified analysis was performed for effect modifiers such as age, sex, residence, BMI, diabetes, hypertension, smoking, and causative organism and post-stratification was used for the chi-square/Fisher exact tests. A p-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 203 Laboratory-confirmed UTI patients were enrolled in this study. The mean age was 38.2 ± 14.6 years with female predominance (68.5%, n=139). Complicated UTI was identified in 44.3% (90/203) of patients and uncomplicated UTI in 55.7% (113/203). Baseline demographic and clinical characteristics are given in table 1.

Table 1: Demographic and clinical characteristics of study population (n=203).

Variable	Complicated UTI (n=90)	Uncomplicated UTI (n=113)	p-value
Mean age (years)	41.6 ± 15.2	35.4 ± 13.6	0.002
Female gender	54 (60.0%)	85 (75.2%)	0.019
Urban residence	48 (53.3%)	62 (54.9%)	0.820
Diabetes mellitus	38 (42.2%)	26 (23.0%)	0.003
Hypertension	32 (35.6%)	17 (15.0%)	<0.001
Renal calculi	28 (31.1%)	0 (0%)	<0.001
Immunocompromised	18 (20.0%)	6 (5.3%)	0.001
Pregnancy-associated	12 (13.3%)	0 (0%)	<0.001
Urinary catheter in situ	16 (17.8%)	0 (0%)	<0.001
Mean duration of symptoms (days)	5.4 ± 3.8	3.1 ± 2.4	<0.001

Escherichia coli was the most prevalent overall (58.6%, n=119), followed by Klebsiella pneumoniae (18.7%, n=38), Staphylococcus aureus (11.3%, n=23), Enterococcus spp. (7.4%, n=15) and other organisms (4.0%, n=8), as illustrated in Figure 1.

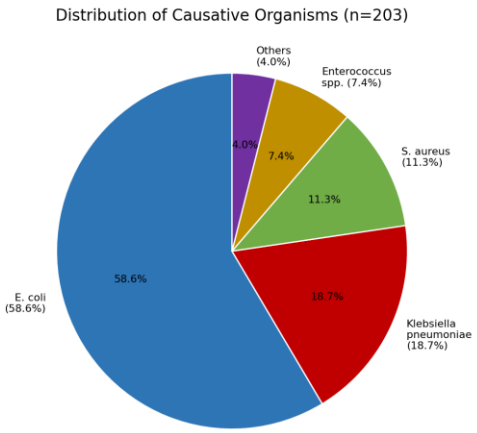

Figure 1. Proportion of Individuals in Study Population (n=203) with each of the Causative Organisms.

Table 2 shows the antibiotic resistance rates of the complicated UTI group compared to uncomplicated UTI group as important antibiotics tested. Significantly higher resistance was observed in the complicated UTI group for ampicillin (82.2% vs 70.8%; p=0.044), ciprofloxacin (68.9% vs 54.0%; p=0.022), ceftriaxone (63.3% vs 48.7%; p=0.033), co-trimoxazole (74.4% vs 62.8%; p=0.041), gentamicin (45.6% vs 31.9%; p=0.041) and nitrofurantoin (32.2% vs 20.4%; p=0.048). Amikacin had a trend for increased resistance in complicated UTI (22.2% vs 12.4%) but was not statistically significant (p=0.055). The results are further demonstrated with the following Figure 2.

Table 2: Comparison of the percentage of antibiotic resistance rate in complicated UTI and uncomplicated UTI.

Antibiotic	Complicated UTI (n=90)	Uncomplicated UTI (n=113)	p-value
Ampicillin	74 (82.2%)	80 (70.8%)	0.044
Co-trimoxazole	67 (74.4%)	71 (62.8%)	0.041
Ciprofloxacin	62 (68.9%)	61 (54.0%)	0.022
Ceftriaxone	57 (63.3%)	55 (48.7%)	0.033
Cefuroxime	54 (60.0%)	58 (51.3%)	0.218
Gentamicin	41 (45.6%)	36 (31.9%)	0.041
Tetracycline	38 (42.2%)	41 (36.3%)	0.383
Nitrofurantoin	29 (32.2%)	23 (20.4%)	0.048
Amikacin	20 (22.2%)	14 (12.4%)	0.055
Piperacillin-Tazobactam	15 (16.7%)	12 (10.6%)	0.201

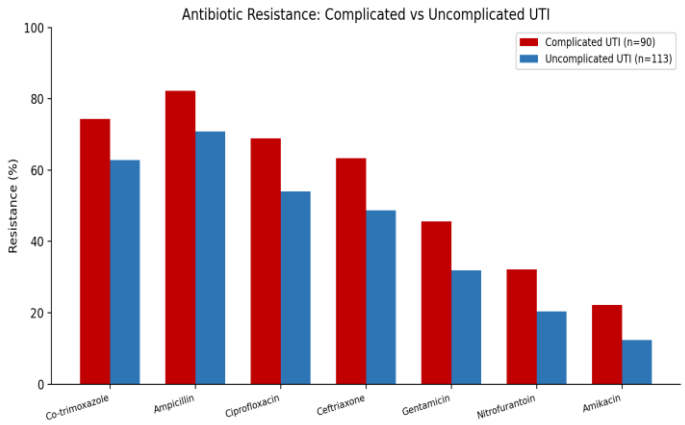

Figure 2. Antibiotic Resistance Rates: Complicated vs Uncomplicated UTI.

DISCUSSION

The present cross-sectional study conducted on 203 patients with confirmed UTI in SPH Quetta has revealed that antimicrobial resistance is significantly higher in complicated UTI than uncomplicated UTI in all antibiotic groups with p values as p = 0.044 for ampicillin (82.2% vs 70.8%), p = 0.022 for ciprofloxacin (68.9% vs 54.0%), p = 0.033 for ceftriaxone (63.3% vs 48.7%), p = 0.041 for co-trimoxazole (74.4% vs 62.8%) and p = 0.048 for nitrofurantoin (32.2% vs 20.4%). E. coli was the uropathogen most commonly found in the two groups (58.6% overall). These results are in line with previous literature and highlight the significance of this in clinical practice for the selection of empirical antibiotic therapy. Klein and Hultgren have shown that urinary tract anatomy, the virulence potential of the infecting organism and host immune characteristics all play an important role in the host-pathogen interaction in UTI and the susceptibility directly reflects these factors, and that complicated and uncomplicated UTI differs with respect to these clinical properties [1].

The high levels of ampicillin resistance for both groups (82.2% and 70.8%) were consistent with the worldwide trend of loss of ampicillin as an acceptable empirical antimicrobial agent for UTI, as a result of the widespread plasmid-mediated beta-lactamase activity of E coli and Klebsiella spp. Amoxicillin resistance has also been seen to be as high as 66% in urinary E. coli isolates from Bangladesh tertiary care hospital and the complicated UTI has been found to be consistent with higher resistance to all beta-lactams tested by Majumder et al. [2]. As mentioned earlier, significant differences between complicated UTI and uncomplicated UTI were observed regarding ciprofloxacin resistance in this study (68.9% vs 54.0%), possibly because the complicated UTI population was disproportionately affected by healthcare exposure, catheter use and prior antibiotic therapy all of which are associated with fluoroquinolone resistance [6].

A comprehensive review by Gharavi et al., on antimicrobial susceptibility trends of uropathogens isolated from urine samples of Iranian patients revealed that resistance to co-trimoxazole and ciprofloxacin in uropathogens was highly associated with ESBL producers, with the rate of resistance being significantly higher in patients with complicated UTI, in a manner similar to that noted in the present study [7]. In a similar study in a university teaching hospital, Ong et al. found more than 700,000 positive urinary cultures of E. coli over six years with a consistent increasing trend in resistance to ciprofloxacin and co-trimoxazole, which have the highest prevalence in CAUTIs and nosocomial UTI and form the majority of complicated UTIs [6].

The lowest overall resistance rate observed in both groups (complicated 32.2% versus uncomplicated 20.4%) was for nitrofurantoin, which is in line with the literature from both international and regional studies supporting the use of nitrofurantoin for uncomplicated lower UTI because the drug is both highly active in the urine and in the bladder wall [2,8]. Malik et al. also analyzed the microbial resistance in UTIs present in Pakistan and found that among others, nitrofurantoin remains the one with clinically relevant activities against uropathogens, suggesting its incorporation into first line empirical treatment of uncomplicated cystitis [9].

The higher nitrofurantoin resistance rate in the complicated group (32.2%) than in the uncomplicated group (20.4%; p=0.048), however, argues against using nitrofurantoin in complicated lower UTIs, especially in cases of upper urinary tract involvement and/or systemic spread. Amikacin demonstrated the lowest resistance rate for both the groups (22.2% and 12.4%), which is in line with the findings of Czajkowski et al. and Farias et al., where aminoglycosides continued to have the best activity against multidrug-resistant uropathogens, including ESBL producers, and therefore they remain as a valuable reserve for complicated UTI requiring parenteral therapy [4,5].

From a hospitalisation and intravenous drug therapy point of view, the 63.3% resistance to ceftriaxone use in the complicated group is of concern as it significantly reduces the empirical treatment options for attendance at an emergency department with pyelonephritis or urosepsis in this group. The diabetes mellitus (42.2%), hypertension (35.6%) and renal stone (31.1%) rates were high in this population of difficult UTIs as it is reported throughout Pakistan that diabetes mellitus, hypertension and renal stone are raised in Balochistan, hence contributing towards the vulnerability of urinary tract [10].

CONCLUSION

Antimicrobial resistance is significantly higher in complicated UTIs compared to uncomplicated UTIs and this resistance is seen in various types of antibiotics at Sandeman Provincial Hospital, Quetta. In both groups, ampicillin and co-trimoxazole are no longer effective empirical drugs. Nitrofurantoin and amikacin have a comparatively low level of resistance, and should be given first-line preference for empirical treatment in uncomplicated and complicated UTI, respectively[13]. To tackle the rising resistance and minimise morbidity due to undertreated or inappropriate UTI in this group, the surveillance of antimicrobial resistance and antibiotic prescribing based on antimicrobial susceptibility testing (AST) should continue at local level.

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