# How to Reverse the Course of Resistance? A Study of our Local Antibiogram

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## ABSTRACT

**Background:** Urinary Tract Infection are classified as complicated and uncomplicated UTI. Uncomplicated UTIS include urinary tract infections without structural and neurological abnormalities. They are further classified as lower and upper UTIs (Cystitis and Pyelonephritis respectively)

**Objective:** To determine UTI causative organisms and antibiotic resistance with respect to commonly used antibiotics.

**Material & Methods:** A descriptive case study was conducted at the department of Urology, Nawaz Shareef Kidney Hospital Swat for duration of 6 months (March 2017-August 2017). Sample size of 172 patients was calculated with 95% confidence interval, 32.8% prevalence (E.coli) and 7% margin of error. Participants were selected with simple random sampling. Ethical approval and Consent forms were taken. Urine cultured samples were tested within an hour after sampling. Data was analyzed using SPSS version 22.0. Correlation and fisher's exact test was applied. P value =0.05 was considered significant.

**Results:** Total 172 patients were included in study. Mean age of patients was 41.6 years±11.6 SD. There were 56(32.6%) males and 116(67.4%) females. Causative agents were E.Coli in 132(76.7%), Klebsiella spp in 17(9.9%), Staphylococcus saprophyticys in 11(6.4%) and Pseudomonas aeruginosa in 12(7%) patients. Overall resistance patterns were, Ciprofloxacin, Levofloxacin, Nalidixic acid, ceftriaxone & Trimethoprim-sulfomethoxazole 47.7%, 16.3%, 11.6%, 16.9% and 7.6% respectively. Quinolones & Cephalosporins showed resistance in 68( 97.1%) in complicated UTIs.In more than 95%(67) of cases urine cultures showed sensitivities to Nitrofurantoin & Fosfomycin in oral antibiotics & Tazobactum ,Imipinem,cepoperazone/sulbactum, & Amikacin among parenteral antibiotics.30(42.8%) patients with UTI were diabetics,25(35.7%) having urolithiasis & 15(21.4%) cases had some urological intervention. 50(71.42%) cases had used empirical antibiotics prescribed by local physicians & quacks .

A negative correlation between diabetes mellitus & UTI was observed. Statistically significant association between antibiotics and antibiogram patterns is reported (p=0.000).

**Conclusion**: Escherichia coli and Klebsiella spp were predominant pathogens for UTI development.

However, variable antimicrobial resistance patterns were seen followed by high resistance of E.coli towards quinolones & ceftriaxone. Routine surveillance and monitoring are required for updating clinicians regarding most prevalent pathogens and empirical treatment of UTI.

***Key words:*** *Urinary tract infection (UTI), Antibiotics Resistance, Urine culture & sensitivity(C/S)*

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## INTRODUCTION

Urinary tract infections (UTI) are most common bacterial infections creating 6 billion US $ health care expenditure[1]. Globally, UTI's are responsible for affecting 150 million individual each year[2]. In United States, UTI is responsible for 10.5 million office visits including 0.9% ambulatory visits and 3 million emergency visits. UTIs are very common in older men, infant boys and females leading to a significant morbidity[3].

UTI's are classified as complicated and uncomplicated UTI. Uncomplicated UTIS include urinary tract infections without structural and neurological abnormalities. They are further classified as lower and upper UTIs (Cystitis and Pyelonephritis respectively)[4]. Complicated UTIs are associated with significant factors affecting urinary tract and host defense (renal failure, urinary obstruction, urinary retention, renal transplantation, presence of foreign bodies like calculi or drainage devices. UTI complications include pyelonephritis along with sepsis, Pre-term birth, renal damage and antibiotic resistance[5].

UTIS are usually caused by Gram positive, negative and certain fungi. Uropathogenic

Escherichia coli (UPEC) is most common pathogen for complicated and uncomplicated UTI. Klebsiella pneumonia, Proteus mirabilis, staphylococcus aureus, Enterococcus faecalis and Candida spp are also involved in uncomplicated UTI development[6].

One of greatest advances in modern medicines is discovery of antibiotics. However, increase used and excessive availability of antibiotic leads to microbial resistance. In developing world, antibiotic resistance is increasing day by day. In 2014, World Health Organization (WHO),

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reported that antibiotic resistance is a global threat to modern medicines[7]. Wariso et al. reported that most common cultured isolate was Escherichia Coli (32.8%).

Resistance of isolates was reported 76.6%, 31.2% and 22.7% with fluorinated quinolones, aminoglycosides and nitrofurantion[8]. Kumari et al. reported that most strains of E.Coli were resistant to ciprofloxacin and Ampicillin. Moreover, Ps. Aeuginosa showed high resistance to aminoglycosides and ceftazidime[9]. Antibiotic selection for UTI is critical to prevent potential complications of untreated disease.

A number of studies have been done internationally on this topic but these are not enough to reach any conclusion in settings of Pakistan. So present study aims to determine UTI causative organisms and antibiotic resistance with respect to commonly used antibiotics.

## MATERIAL & METHODS

A descriptive case study was conducted at department of Urology, Nawaz Sharif Kidney Hospital, Swat for duration of 6 months (March 2017-August 2017).

Sample size of 172 patients was calculated with 95% confidence interval, 32.8% prevalence (E.coli)[8] and 7% margin of error. Participants were selected with simple random sampling (Lottery method). Ethical approval was taken from ethical review board of Nawaz Shareef kidney Hospital, Swat. Consent forms were taken from all participants. All patients of age >18 years, both genders, patients suffering with [dysuria] [dysuria and fever], [fever& lower urinary tract symptoms, were included. Mentally retarded, patients with congenital anomalies, patients already using antibiotics or allergic to antibiotics were excluded from study. Urine cultured samples were tested within an hour after sampling.

A UTI positive sample is one that is cultured at concentration = 105 cfu/ml (or at 104 cfu/ml) and =5 leukocytes per high power were seen on microscope. Bacterial identification was based upon biochemical characteristics and standard culture of isolates. Standard single disc method was used for identification of antibiotic susceptibility and resistance through zone diameter as shown in Table 1.

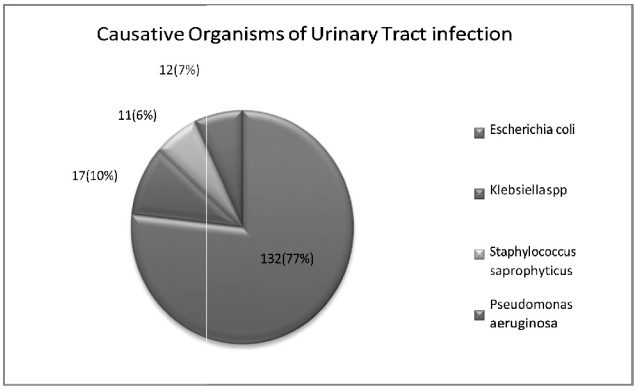
Data was analyzed using SPSS version 22.0. Mean and standard deviation was calculated for age. Frequency and percentages were calculated for qualitative variables P value =0.05 was considered significant.

## RESULTS

Total 172 patients were included in study. Mean age of patients was 41.6 years±11.6 SD. There were 56(32.6%) males and 116(67.4%) females. Total 78(45.3%) patients were in age group 18-35 years, while 94(54.7%) were in 36-70 years age group. Among all the patients 172(100%) , 77(44.8%) had diabetes mellitus while while 95(55.2%) did not had DM. Causative agents were E.coli in 132(76.7%), Klebsiella spp in 17(9.9%),Staphylococcus saprophytics in 11(6.4%) &Pseudomonas aeruginosa in 12(7%) patients as shown in figure 1.

Among all the males 56(32.6%), 53(30.8%) had UTI due to E.Coli and 3(1.7%) due to P. Aeruginosa.

**Figure 1: Causative Organisms of Urinary Tract Infection**




Among all females 116(67.4%), 79(45.9%) had UTI due to E.coli, 17(9.9%) K.spp, 11(6.4%) staphylococcus saprophyticus and 9(5.2%) P. Aeruginosa 12(7%). Among all those in age group 18-35 years 78(45.3%), 51(29.7%) had UTI due to E.coli, 15(8.7%) K.spp, 7(4.1%) staphylococcus saprophyticus and 5(2.9%) P. aeruginosa. Similarly among all those in age group 36-70 years 94(54.7%), 81(47.1%) had UTI due to E.coli, 2(1.2%)K.spp, 4(2.3%) staphylococcus saprophyticus and 7(4.1%) P.aeruginosa ($x^2$ =16.566, p=0.001, df =1). Negative correlation between diabetes mellitus(r = -0.06), and causative agents was found. Statistically significant association between antibiotics and antibiogram patterns is reported (p=0.000) as shown in Table 1

Among all the causative agents resistant to amikacin 82(47.7%), 53(30.8%) were resistant to E.Coli, 12(7%) K spp, 8(4.7%) staphylococcus saprophyticus and 9(5.2%) were resistant to P. aeruginosa. Among all those resistant to ciprofloxacin 28(16.3%), 28(16.3%) were resistant to E.coli.

Among all those resistant to Nitrofurantoin 20(11.6%), 17(9.9%) were resistant to E. coli and 3(1.7%) P.aeruginosa. Among all those resistant to gentamicin 29(16.9%), 27(15.7%) were resistant to E. coli and 2(1.2%) K.spp. Among all those resistant to nalidixic acid 13(7.6%), 7(4.1%) were resistant to E.coli, 3(1.7%) K.spp and3(1.7%) were resistant to Staphylococcus saprophyticus.

## DISCUSSION

Worldwide, UTIs are most common diseases with high prevalence among females. Management of UTI has been improved due to availability of new antibiotics. However, due to increase in antibiotic resistance, management of UTI became jeopardized[10].

In present study, total 172 patients were included. Mean age of patients was 41.6 years±11.6 SD. There were 56(32.6%) males and 116(67.4%) females. Causative agents were E.Coli in 132(76.7%), Klebsiella spp in 17(9.9%), Staphylococcus saprophyticys in 11(6.4%) and Pseudomonas aeruginosa in 12(7%) patients. Kibret & Abera reported that E.coli was dominant isolate 63.6%. However, other isolated were K.spp 8.5% and P.spp 8.2%. They reported resistance rates of erythromycin 85.6%, Amoxicillin 88.9% and tetracycline 76.7%[11]. oli et al. reported that most common pathogens for UTI were E.coli 28.5%, S.Aureus 28%, Salmonella spp 22.8% and P. aeruginosa 20.5%[12].

**Table 1: Association between antibiotic and antibiogram patterns**

| Antibiotics | Antibiogram | | | Total | P value |
|---|---|---|---|---|---|
| | Resistance | Intermediate | susceptibility | | |
| Amikacin | 40(23.3%) | 19(11%) | 23(13.4%) | 82(47.7%) | 0.000 |
| Ciprofloxacin | 7(4.1%) | 12(7%) | 9(5.2%) | 28(16.3%) | |
| Nitrofurantoin | 18(10.5%) | 0(0%) | 2(1.2%) | 20(11.6%) | |
| Gentamicin | 18(10.5%) | 3(1.7%) | 8(4.7%) | 29(16.9%) | |
| Nalidixic acid | 0(0%) | 12(7%) | 1(0.6%) | 13(7.6%) | |
| Total | 83(48.3%) | 46(26.7%) | 43(25%) | 172(100%) | |

**Table 2: Association between antibiotic resistance and causative agents**

| Antibiotics | Causative agents | | | | Total | P value |
|---|---|---|---|---|---|---|
| | E.Coli | Klebsiella spp | Staphylococcus saprophyticus | Pseudomonas aeruginosa | | |
| Amikacin | 53(30.8%) | 12(7%) | 8(4.7%) | 9(5.2%) | 82(47.7%) | 0.000 |
| Ciprofloxacin | 28(16.3%) | 0(0%) | 0(0%) | 0(0%) | 28(16.3%) | |
| Nitrofurantoin | 17(9.9%) | 0(0%) | 0(0%) | 3(1.7%) | 20(11.6%) | |
| Gentamicin | 27(15.7%) | 2(1.2%) | 0(0%) | 0(0%) | 29(16.9%) | |
| Nalidixic Acid | 7(4.1%) | 3(1.7%) | 3(1.7%) | 0(0%) | 13(7.6%) | |
| Total | 132(76.7%) | 17(9.9%) | 11(6.4%) | 12(7%) | 72(100%) | |

In present study, overall resistance patterns were amikacin, Ciprofloxacin, Nitrofurantoin, Gentamicin, Nalidixic acid 47.7%, 16.3%, 11.6%, 16.9% and 7.6% respectively. Kashef et al reported that susceptibility of E.coli was mostly seen with nitrofurantoin 71.3%, ciprofloxacin 68.1% and trimethoprim-sulfamethoxaxole 38.2%[13]. Beyene & Tsegaye reported that E.coli and K.pneumoniae were highly resistant to ampicillin and amoxicillin (100%)[14]. Demilie et al. reported that a resistant rate of 50-100% of gram positive isolates was seen against amoxicillin, penicillin G, tetracycline, amoxicillin and ampicillin[15].

In present study, among all the causative agents resistant to amikacin 82(47.7%), 53(30.8%) were resistant to E.Coli, 12(7%) K spp, 8(4.7%) staphylococcus saprophyticus and 9(5.2%) were resistant to P.Aeruginosa. Among all those resistant to ciprofloxacin 28(16.3%), 28(16.3%) were resistant to E.coli. sood & Gupta et al. most common community acquired pathogen was 61.84%[16]. Bahadin et al. reported that enterobacteriaaceae family is found commonly resistant to amoxicillin and clavulanate[17]. This study is implicated on Urologists, Nephrologists, General Medical & Surgical Practioners.

**Strength:**
Study provides first-hand information or documentation on microbial susceptibility (scientific Evidence).
**Limitation:**
Study did not provide molecular bases of antibiotic resistance patterns.

## CONCLUSION

Escherichia coli and Klebsiella spp were predominant pathogens for UTI development.
However, variable antimicrobial resistance patterns were seen followed by high resistance of E.coli towards amikacin. Routine surveillance and monitoring are required for updating clinicians regarding most prevalent pathogens and empirical treatment of UTI.

Patients with complicated UTI should not be prescribed empirical antibiotics until their C/S is available & educated about the rational use of medication. All patients with recurrent & complicated UTIs should be subjected to urine C/S & culture specific antibiotics should be prescribed in consultation with an infectious disease specialist.

## REFERENCES


1. Theodros G. Bacterial pathogens implicated in causing urinary tract infection (UTI) and their antimicrobial susceptibility pattern in Ethiopia. Revista CENIC. Ciencias Biológicas. 2016;41(1):16.
2. Nerurkar A, Solanky P, Naik SS. Bacterial pathogens in urinary tract infection and antibiotic susceptibility pattern. J Pharm Biomed Sci. 2015;21(2):13.
3. Tseng MH, Lo WT, Lin WJ, Teng CS, Chu ML, Wang CC. Changing trend in antimicrobial resistance of pediatric uropathogens in Taiwa. Pediatr Int. 2014;50(3):797-800.
4. Haider H, Zehia N, Munir AA, Haider A. Risk factors of urinary tract infection in pregnancy. J Pak Med Assoc. 2014;60(5):213-216.
5. de Francesco MA, Giuseppe R, Laura P, Riccardo N, Nino M. Urinary tract infections in Brescia, Italy: Etiology of uropathogens and antimicrobial resistance of common uropathogens. Med Sci Monit. 2013;13(3):136-144.
6. Leegaard TM, Caugant DA, Froholm LO, Hoiby EA. Apparent difference in antimiovrobial susceptibility as a consequence of national guidelines. Clin Microbiol Infect. 2014;6(2):290-91.
7. Biadglegne F, Abera B. Antimicrobial resistance patterns of bacterial isolates from urinary tract infections at Felege Hiwot Hospital, Ethiopia. Ethiop J Health Dev. 2009;23(2):236-238.
8. Wariso K, Siminialayi I, Odigie J. Pattern and antibiogram of urinary tract infection at the University of Port Harcourt Teaching Hospital. Asian Pacific Journal of Tropical Medicine. 2010;3(1):66-9.
9. Kumari N, Ghimire G, Magar JKG, Mohapatra TM, Rai A. Antibiogram pattern of isolates from UTI cases in Eastern part of Nepal. Nepal Med Coll J. 2005;7(2):11-68.
10. El-Mahmood AM, Atimi AT, Tirmidhi B, Mohammed A. Antimicrobial susceptibility of some quinolone antibiotics against some urinary tract pathogens in a tertiary hospital, Yola, Adamawa State, Nigeria. J Clin Med Res. 2009;1(2):2634.
11. Kibret M, Abera B. Prevalence and antibiogram of bacterial isolates from urinary tract infections at Dessie Health Research Laboratory, Ethiopia. Asian Pac J Trop Biomed. 2014 ;4(2):1648.
12. Oli AN, Akabueze VB, Ezeudu CE, Eleje GU, Ejiofor OS, Ezebialu IU, et al. Bacteriology and Antibiogram of Urinary Tract Infection Among Female Patients in a tertiary Health Facility in South Eastern Nigeria. Open Microbiol J. 2017;11:292300.
13. Kashef N, Djavid GE, Shahbazi S. Antimicrobial susceptibility patterns of communityacquired uropathogens in Tehran, Iran. J Infect Dev Ctries. 2010;4(4):2026.
14. Beyene G, Tsegaye W. Bacterial uropathogens in urinary tract infection and antibiotic susceptibility pattern in jimma university specialized hospital, southwest ethiopia. Ethiop J Health Sci. 2011;21(2):1416.
15. Demilie T, Beyene G, Melaku S, Tsegaye W. Urinary bacterial profile and antibiotic susceptibility pattern among pregnant women in north west ethiopia. Ethiop J Health Sci. 2012;22(2):1218.
16. Sood S, Gupta R. Antibiotic Resistance Pattern of Community Acquired Uropathogens at a Tertiary Care Hospital in Jaipur, Rajasthan. Indian J Community Med. 2012;37(1):3944.
17. Bahadin J, Teo SSH, Mathew S. Aetiology of community-acquired urinary tract infection & antimicrobial susceptibility patterns of uropathogens isolated. Singapore Med J. 2011 Jun;52(6):415 20.