Antimicrobial Sensitivity pattern of Bacteria Causing Urinary Tract Infection among Diabetic Patients

Pratima Thapa  
Pokhara University

Anita Sunar  
Pokhara University

Dipendra Lamichanne  
Pokhara University

Apeksha K.C  
Pokhara University

Arjan Dhungana  
Pokhara University

Rajan Paudel  
Pokhara University

Suresh Jaiswal  
Pokhara University

Bishnu Raj Tiwari (✉️ bishnurajtiwari@gmail.com)  
Pokhara University

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Abstract

Urinary tract infection is the presence and active multiplication of microorganism within the urinary tract. UTIs are group of infections that affects any part of urinary tract. The cross sectional descriptive study was conducted to determine the antibiotic susceptibility pattern of bacteria causing urinary tract infection in diabetic and non-diabetic patient from February 2016 to March 2016. Among the total 601 urine sample, 250 were diabetics and 351 were non diabetics. All samples were investigated by standard laboratory procedures. Out of diabetic patient 111(44.4%) were female and 139(55.6%) were male and among non-diabetic, 234(66.7%) were female and 117(33.3%) were male. The UTI prevalence rate was found to be 78 (13%) was statistically significant (p = 0.02), among the significant growth 6.8% diabetic and 6.2% non-diabetic. Escherichia coli (54) was the most predominant organism (42.5% in diabetic and 57.5% non-diabetic) followed by Staphylococcus aureus (8). Amikacin, Cotrimoxazole and Nitrofurantoin were most sensitive to E. coli isolated in diabetic and non-diabetic patients among the tested antimicrobials. High rate of resistance was observed with Norfloxacin and Nalidixic acid. Gentamicin, Cefotaxime, Cotrimoxazole and Ciprofloxacin were highly sensitive to S. aureus in diabetic patients while Oxacillin and Azithromycin were resistance and in non-diabetic patient highly sensitive antimicrobials were Azithromycin, Gentamicin, Cefotaxime, Cotrimoxazole, Vancomycin and Ofloxacin while Oxacillin was resistance. The antimicrobial susceptibility testing of bacterial isolates should be performed before the treatment of UTI.

Key words : Diabetic, Urinary tract infection, Antimicrobial sensitivity.

Background

The urinary tract infection (UTI) is one of the most common microbial disease encountered in medical practice affecting people of all age [1]. UTI has been classified by site of infection as upper urinary tract infection and lower urinary tract infection and by severity as complicated and uncomplicated UTIs. Worldwide prevalence of UTI was estimated to be around 150 million persons per year [2]. In Nepal about 20% female experience a single episode of UTI during their lifetime and 3% women have more than one episode of UTI per year [3]. Diabetic patients have a higher incidence of UTI than their non-diabetic counterparts [4, 5]. With higher severity UTI, which can be a cause of complications, ranging from dysuria (pain or burning sensation during urination) to organ damage and sometimes even death due to complicated UTI (pyelonephritis) [6]. Potential explanation of the increased UTI in diabetic patients might be the nerve damage caused by high blood glucose levels, affecting the ability of the bladder to sense the presence of urine and thus allowing urine to stay for a long time in the bladder and increasing infection probability [7, 8]. The major causative organisms are bacteria which are responsible for more than 95% of UTI cases [9]. The most prevalent causative organism of UTI is Escherichia coli and is solely responsible for more than 80% of these infections [10]. Klebsiella, Staphylococci, Enterobacter, Proteus, Pseudomonas, and Enterococci spp. are more often isolated from urine culture. Anaerobic organisms are rarely pathogens in the urinary tract [11]. Coagulase Negative Staphylococci are a common cause of urinary tract infection in some reports [12]. Staphylococcus saprophyticus tends to cause infection in
young women [13]. Treatment of UTI is often started empirically and therapy is based on information determined from the antimicrobial resistance pattern of the urinary pathogens [14]. The prevalence of antimicrobial resistance among urinary pathogens has been increasing worldwide due to aberrant use of antibiotics in practice [9]. Distribution of urinary pathogens and their susceptibility to antibiotics varies regionally so it becomes necessary to have knowledge of distribution of these pathogens and their susceptibility to antibiotics in a particular setting [15, 16]. Incorrect diagnosis, improper use of antibiotics by patients, unnecessary prescriptions, and the use of antibiotics as livestock food additives for growth promotion are the factors contributing towards resistance [17]. Successful antimicrobial therapy of an infection depends on concentration of antibiotic at the site of infection that is high enough to kill or inhibit the growth of microorganism. The choice of drug depends solely on the identification of the spp. by determination of the sensitivity characteristics of the microorganism. Hence, this study was undertaken to understand the incidence of spectrum of uropathogens and antimicrobial sensitivity pattern in both diabetic and non-diabetic patients with clinically suspected UTI.

**Materials And Methods**

A total of 601 Clean Catch Mid-Stream Urine (MSU) sample was collected in a sterile urine culture container from diabetic patients (250) & non diabetic persons (351) from Western Regional Hospital, Diabetic, Thyroid and Endocrinology Care Centre and Fishtail hospital, Pokhara, Nepal.

The cross sectional descriptive study was carried out at Microbiology Laboratory of School of Health and Allied Sciences, Pokhara University and Western Regional Hospital, Kaski from February 2016 to March 2016. Samples were excluded for study those who were under antimicrobials medication and consent cannot be obtained voluntarily were also excluded from the study. Urine samples were aseptically inoculated onto Blood Aagr and Macconky Aagr plate and incubated for 24 hours at 37 ± 1°C. Colony count of more than 10⁵ CFU/ml were considered significant and further processed for identification. Gram negative bacteria isolated from urine in this study were identified using conventional biochemical tests and antimicrobial susceptibility testing of significant isolates was done by Kirby Bauer disk diffusion method [3]. Carpet culture was performed in Muller Hinton Agar on UTI isolates for Antibiotic Sensitivity test by Kirby Bauer disk diffusion method. Antibiotics used for antibiotic sensitivity pattern were Amikacin (30mcg), Cefotaxime (30mcg), Ciprofloxacin (5mcg), Co-trimoxazole (25mcg), Azithromycin (15mcg), Nitrofurantoin (300mcg), Nalidixicacid (30mcg), Norfloxacin (10mcg), Gentamicin (30mcg), Oxacilin (1mcg), Ofloxacilin (5mcg), Novobiocin (30mcg) and Vancomycin (30mcg). After 24 hours incubation at 37 ± 1°C the antibiotics of the disk diffuses on the agar plate. Each plate was read for zone of inhibition and results were interpreted by following Clinical & Laboratory Standards Institute (CLSI) guidelines [18].

**Results**

Out of 601 patients, the total numbers of female were 345 and male were 256. The total number of diabetic were 250 (41.6%) and 351 (58.4%) were non diabetic. Out of 250 diabetic, 111 were female
(44.4%) and 139 were male (55.6%). Likewise from 351 non diabetic patient, 234 (66.7%) were female and 117 (33.3%) were male.

Among the total number of significant growth 78 (13%), 41 (6.8%) shows significant growth in diabetic was found higher than that of non-diabetic 37 (6.2%).

Table 1
Significant bacterial growth in comparison with diabetic and non-diabetic patients

|                  | Insignificant Growth | Significant Growth | Total |
|------------------|----------------------|--------------------|-------|
| Diabetic         | 209                  | 41                 | 250   |
| Non Diabetic     | 314                  | 37                 | 351   |
| Total            | 523                  | 78                 | 601   |

Significant growth was found higher above 45 years of age in case of diabetic and 25 to 45 years of age in case of non-diabetic. There is lesser significant growth in diabetic among category of less than 25 years than that of non-diabetic.

Table 2
Age wise distribution of significant growth.

| Age Group (years) | Diabetic | Non Diabetic |
|-------------------|----------|--------------|
| < 25              | 3        | 8            |
| 25–45             | 11       | 18           |
| > 45              | 27       | 11           |
| Total             | 41       | 37           |
Table 3
Significant Uropathogens

| Bacteria          | Diabetic          | Non diabetic     |
|-------------------|-------------------|------------------|
| E. coli           | 23 (56.09%)       | 31 (83.78%)      |
| S. aureus         | 7 (17.70%)        | 1 (2.70%)        |
| S. saprophyticus  | 6 (14.63%)        | 1 (2.70%)        |
| Proteus spp.      | 4 (9.75%)         | 1 (2.70%)        |
| Klebsiella spp.   | 1 (2.43%)         | 2 (5.43%)        |
| Enterobacter spp. | 0.00%             | 1 (2.70%)        |
| Total             | 100%              | 100%             |

From the significant growth, the prevalence of E. coli was higher in both diabetic (56.09%) and non-diabetic (83.78%) patients. Overall prevalence of E. coli, S. aureus, S. saprophyticus, Proteus spp. were found higher in diabetic than non-diabetic. But the prevalence of Klebsiella spp. Enterobacter spp. were higher in non-diabetic than diabetic patients.
Table 4
Isolated gram negative uropathogens with different antibiotics

| Organisms N = 63 | Patient type | E. coli | Proteus spp. | Klebsiella spp. | Enterobacter spp. |
|------------------|--------------|---------|--------------|-----------------|------------------|
| Antibiotics      |              |         |              |                 |                  |
| Amikacin (30 mcg)| Diabetic     | 14      | 5            | 4               | 2                |
|                  |              | 2       | 2            |                 | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  |              | 0       | 0            |                 | 0                |
|                  | Non-diabetic | 21      | 1            | 9               | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  |              | 1       | 0            |                 | 1                |
|                  |              | 0       | 0            |                 | 0                |
| Ciprofloxacin (5 mcg) | Diabetic | 7       | 0            | 16              | 3                |
|                  |              | 0       | 0            |                 | 1                |
|                  |              | 1       | 0            |                 | 0                |
|                  |              | 0       | 0            |                 | 0                |
|                  | Non-diabetic | 8       | 5            | 18              | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  |              | 0       | 0            |                 | 2                |
|                  |              | 1       | 0            |                 | 0                |
| Gentamicin (30 mcg) | Diabetic | 11      | 3            | 9               | 3                |
|                  |              | 0       | 0            |                 | 1                |
|                  |              | 1       | 0            |                 | 0                |
|                  |              | 0       | 0            |                 | 0                |
|                  | Non-diabetic | 16      | 9            | 12              | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  |              | 1       | 1            |                 | 1                |
|                  |              | 0       | 0            |                 | 1                |
| Norfloxacin (10 mcg) | Diabetic | 5       | 2            | 16              | 2                |
|                  |              | 0       | 0            |                 | 2                |
|                  |              | 1       | 0            |                 | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  | Non-diabetic | 11      | 2            | 18              | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  |              | 0       | 0            |                 | 1                |
|                  |              | 1       | 1            |                 | 1                |
| Nitrofurantoin (300 mcg) | Diabetic | 13      | 7            | 3               | 2                |
|                  |              | 1       | 1            |                 | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  |              | 0       | 0            |                 | 0                |
|                  | Non-diabetic | 17      | 6            | 8               | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  |              | 1       | 0            |                 | 1                |
|                  |              | 0       | 1            |                 | 0                |
| Nalidixic acid (30 mcg) | Diabetic | 3       | 0            | 20              | 2                |
|                  |              | 0       | 0            |                 | 2                |
|                  |              | 1       | 0            |                 | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  | Non-diabetic | 7       | 2            | 22              | 1                |
|                  |              | 0       | 0            |                 | 0                |
|                  |              | 0       | 0            |                 | 2                |
|                  |              | 1       | 0            |                 | 0                |
| Cotrimoxazole (25 mcg) | Diabetic | 12      | 1            | 10              | 2                |
|                  |              | 0       | 0            |                 | 2                |
|                  |              | 1       | 0            |                 | 0                |
|                  |              | 0       | 0            |                 | 0                |
|                  | Non-diabetic | 19      | 0            | 12              | 1                |
|                  |              | 0       | 0            |                 | 1                |
|                  |              | 1       | 0            |                 | 1                |
|                  |              | 0       | 0            |                 | 0                |

Note: S-Sensitive, I-Intermediate, R-Resistant, DM = Diabetic Mellitus, NDM = Non-Diabetic Mellitus

The total number of gram negative isolates in diabetics were 28 and non-diabetics were 35. Most sensitive drugs in diabetics were Amikacin (60.7%), Nitrofurantoin (53.5%), Cotrimoxazole (53.5%) and Gentamicin (50%). Likewise in non-diabetics most sensitive were Amikacin (68.5%), Cotrimoxazole (62.8%), Nitrofurantoin (54.2%) and Gentamicin (48.37%). Similarly most resistant drugs in diabetics were Nalidixic acid (78.57%), Norfloxacin (64.28%), Ciprofloxacin (60.7%) and Cotrimoxazole (42.85%). In the
same way in non-diabetics, resistant drugs were Nalidixic acid (68.57%), Ciprofloxacin (57.1%), Norfloxacin (54.28%) and Cotrimoxazole (37.14%).

In diabetics E.coli isolates were most sensitive to Amikacin (60.9%), Nitrofurantoin (56.5%), Cotrimoxazole (52.2%) and resistant to Nalidixic acid (87%), Norfloxacin (69.6%), Ciprofloxacin (69.6%). In non-diabetics all E.coli isolates were most sensitive to Cotrimoxazole (61.3%), Amikacin (60.9%), Nitrofurantoin (54.8%) and resistant to Nalidixic acid (71%), Norfloxacin (58.1%), and Cotrimoxazole (38%).

In diabetics Proteus spp. isolates were most sensitive to Gentamicin (75%), Ciprofloxacin (75%) and resistant to Norfloxacin (50%), Nalidixic acid (50%). In non-diabetics all Proteus isolates were 100% sensitive to all antibiotics.

In diabetic individuals, all Klebsiella isolates were sensitive to almost all antibiotics and did not show any resistant pattern. In non-diabetic all isolates were most sensitive to Cotrimoxazole (50%), Amikacin (50%), Nitrofurantoin (50%) and resistant to Nalidixic acid (100%).
Table 5
Isolated gram positive uropathogens with different antibiotics

| Organisms N = 15 | Patient type | S. aureus N = 8, Diabetic = 7, Non-Diabetic = 1 | S. saprophyticus N = 7, Diabetic = 6, Non-Diabetic = 1 |
|------------------|--------------|-------------------------------------------------|---------------------------------------------------|
| Antibiotics      | S | I | R | S | I | R |
| Gentamicin (30mcg) | Diabetic | 6 | 1 | 0 | 4 | 1 | 1 |
|                  | Non-diabetic | 1 | 0 | 0 | 0 | 1 | 0 |
| Amikacin (30mcg) | Diabetic | 3 | 0 | 4 | 6 | 0 | 0 |
|                  | Non-diabetic | 1 | 0 | 0 | 0 | 1 | 0 |
| Azithromycin (15mcg) | Diabetic | 2 | 1 | 4 | 1 | 0 | 5 |
|                  | Non-diabetic | 1 | 0 | 0 | 1 | 0 | 0 |
| Cefotaxime (30mcg) | Diabetic | 5 | 0 | 2 | 4 | 0 | 2 |
|                  | Non-diabetic | 1 | 0 | 0 | 0 | 0 | 1 |
| Cotrimoxazole (25mcg) | Diabetic | 5 | 1 | 1 | 2 | 1 | 3 |
|                  | Non-diabetic | 1 | 0 | 0 | 0 | 0 | 1 |
| Vancomycin (30mcg) | Diabetic | 4 | 0 | 3 | 6 | 0 | 0 |
|                  | Non-diabetic | 1 | 0 | 0 | 0 | 0 | 1 |
| Ofloxacin (5mcg) | Diabetic | 4 | 1 | 2 | 5 | 1 | 0 |
|                  | Non-diabetic | 1 | 0 | 0 | 0 | 0 | 1 |
| Oxicillin (1mcg) | Diabetic | 3 | 0 | 4 | 1 | 0 | 5 |
|                  | Non-diabetic | 0 | 0 | 1 | 1 | 0 | 0 |
| Ciprofloxacin (5mcg) | Diabetic | 5 | 0 | 2 | 5 | 1 | 0 |
|                  | Non-diabetic | 1 | 0 | 0 | 1 | 0 | 0 |

Note: S-Sensitive, I- Intermediate, R-Resistant

The total number of gram positive isolates in diabetic were 13 and non-diabetic were 2. Most sensitive drugs in diabetics were Gentamicin (76.92%), Vancomycin (76.92%), Amikacin (69.23%) and Cotrimoxazole (53.82%). Likewise in non-diabetics most sensitive drug were Azithromycin (100%) and Ciprofloxacin (100%). Similarly most resistant drugs in diabetic were Amikacin (69.23%), Oxicillin (69.23%) and Azithromycin (69.23%). In the same way in non-diabetics resistant drugs were Cotrimoxazole (7.69%), and Oxicillin (7.69%).
In diabetic, Staphylococcus aureus isolates were most sensitive to Gentamicin (85.7%), Cefotaxime (71.4%), Cotrimoxazole (71.4%) and Ciprofloxacin (71.4%) and resistant to Amikacin (57.1%), Oxacilin (57.1%), and Azithromycin (57.1%). Likewise in non-diabetic all isolates were 100% sensitive to Azithromycin, Gentamicin, Cefotaxime, Cotrimoxazole, Vancomycin and Ofloxacin and 100% resistant to Oxacilin.

In diabetics Staphylococcus saprophyticus isolates were most sensitive to Vancomycin (100%), Amikacin (100%), Ofloxacin (83.3%), Ciprofloxacin (83.3%) and resistant to Oxacilin (83.5%), Azithromycin (83.5%). Likewise in non-diabetics all isolates were most sensitive to Ciprofloxacin (100%), Azithromycin (100%) and 100% resistant to Cotrimoxazole, Oxacilin, Vancomycin, Cefotaxime, Amikacin and Ofloxacin.

**Discussion**

In this study, overall prevalence rate was found 78(13%) out of total cases and was statistically significant ($p = 0.02$), among them 6.8% diabetic and 6.2% non-diabetic. In this study significant growth in diabetic cases were higher as compared to non-diabetic cases. This is in accordance with the study done in the Dhulikhel hospital Kathmandu Nepal [19]. Similar type of study was also done in hospital of Bangladesh [20] where sample population was slightly lower than our study. Diabetic patients are more prone to urinary tract infection due to immune compromise, hyper glycosuria and neutrophil dysfunction. However, a study on a large series of diabetic and non-diabetic patients from a hospital in Italy, the culture positivity rate was 15% and 14% in diabetic and non-diabetic population respectively [21], which is almost similar with our finding (16.4% diabetic and 10.5% non-diabetics). A similar study [7] reported 20% UTI in diabetic patients in their study which is slightly higher than our finding (16.4%). This might be due to the differences in the sample size in these different studies.

It has shown in several studies that women are at increased risk to develop UTI then men [22]. In total sample, majority of the culture positive patients in our study were also female (57.4%) but in case of diabetic patient majority of culture positive patient were male (55.6%) it might be due to the high number male patient and female might be in antibiotic therapy.

The predominant numbers of pathogens isolated in our study were gram negative bacilli rather than gram positive pathogens. The rate of E. coli isolation we found in both diabetic and non-diabetic patients are almost similar in which predominant organism constituted 56% and 83% among diabetic and non-diabetic patients respectively. This is similar with the data obtained by various studies indicated that gram negative bacteria mostly E. coli and Klebsiella spp. are the predominant pathogens isolated in patients with UTI irrespective of risk factors associated with it [23–26]. This was followed by Klebsiella spp. (Diabetic 2.43%; Non diabetic 5.43%) and Enterococcus spp. (Diabetic 0%; Non diabetic 2.70%). In another study from Nepal, it was found that E. coli was most commonly grown organism (68.7%) followed by Enterococcus spp. (13.92%) [27].
The study from India has revealed Staphylococcus spp. as the second predominant isolates which is in accordance to our study [28]. There was no difference between the rate of isolation of organisms in diabetic and non-diabetic patients in our study which is in accordance with the study done in Bangladesh [20]. Pseudomonas spp. is another gram negative bacterium that is associated with UTI [21]. Irrespective of the status of diabetes and non-diabetic Pseudomonas spp. were not isolated from UTI patients in our study.

Regarding the antimicrobial sensitivity profile of the uropathogens, in our study 69% of the isolated E. coli strains were sensitive at similar rate to Amikacin, Gentamicin, Nitrofluratoin, Cotrimoxazole in both diabetic and non-diabetic patient. The significant differences between diabetic and non-diabetic patients to the sensitivity to Gentamycin, Ciprofloxacin and Nitrofurantoin was noted in a study from Bangladesh [20]. But sensitivity to Norfloxacin and Nalidixic acid were slightly different from diabetic and non-diabetic patients. One study was done in Iraq [19] by Abdul Sahib and found Ciprofloxacin resistant E. coli significantly higher in diabetic patient but in our study ciprofloxacin resistant E. coli significantly higher in non-diabetic patient than diabetic patient. Resistant pattern of E. coli in Nalidixic acid was almost similar in both diabetic and non-diabetic patient. This drug is more resistant in most of culture growth. Moreover this difference in sensitivity pattern of isolates could be attributed to time difference between the two studies or environment factors such as practices of self-medications, the drug abuse and indiscriminate misuse of antibiotics among the general population which has favored the emergence of resistance strains.

The limitations of our study were, first information regarding type and duration of diabetes was lacking and second was we could not elaborate the correlation of all the uropathogens among various regions, socioeconomic status, other health status due to the resource management and time factor during the research.

**Conclusion**

From the total isolates in this study, the highest prevalence, 54 (69.23%) was E. coli and lowest prevalence 1 (1.28%) was Enterobacter spp. Amikacin, Cotrimoxazole and Nitrofurantoin were highly sensitive to Gram Negative bacteria and resistant to Nalidixic acid and Norfloxacin in both diabetics and non-diabetics. Whereas Gentamicin, Cefotaxime, Cotrimoxazole were most sensitive and Oxacillin, Azithromycin were resistant to Gram positive isolates. E. coli is the predominant cause of UTI in both diabetic and non-diabetic patients. Antibiotics that are commonly used for the management of UTI cases are being less effective, so antibiotics should be prescribed only after performing the antimicrobial susceptibility testing.

**Abbreviations**

UTI
Urinary tract infections
MSU
Mid-Stream Urine
DM
Diabetes Mellitus
NDM
Non-Diabetic Mellitus
CLSI
Clinical & Laboratory Standards Institute
S
Sensitive
I
Intermediate
R
Resistant

**Declarations**

**Ethics approval and consent to participate**

Approval for the research was obtained from the School of Health and Allied Sciences, Pokhara University, Research Management Committee.

Informed consent was obtained from the participants.

**Consent for publication**

Consent for publication was obtained from the School of Health and Allied Sciences, Pokhara University.

**Availability of data and material**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

**Competing interests**

The authors declare that they have no competing interests.

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**Authors Contributions**
PT, AS, and DL collected isolates and performed the antimicrobial sensitivity testing. All authors contributed in designing the study, analysis of data, interpretation of the results, making the discussion and writing the manuscript. All authors read and approved the final manuscript.

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