

Urinary tract infection and antibiotic sensitivity pattern among diabetics

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ABSTRACT

Diabetes Mellitus is a major health problem of today's world. Urinary tract infection is its common complication. A descriptive, cross sectional study was designed to know the prevalence of culture positive Urinary Tract Infection in diabetic patients, to know their common clinical features and to find out the proportion of asymptomatic bacteriuria, to know the causative organisms and pattern of antibiotic sensitivity. Mid stream urine sample was collected using full aseptic precaution. Among 100 patients included, 53 were female and 47 were male. In total, 21% of them had culture positive Urinary Tract Infection. Urinary Tract Infection was more in female ($P=0.047$). Asymptomatic bacteriuria was found more common in female as compared to male. Common clinical features in symptomatic were burning micturation (90%), frequency of micturation (80%), suprapubic pain (60%), urgency (70%), loin pain (30%), and fever and vomiting (20%). Urinary Tract Infection was common among those who had prolong duration of diabetes ($P=0.039$) and among those receiving insulin as compared to those under oral medications ($P=0.08$). *Escherichia-coli* was most common organism followed by *klebsiella*, *proteus* and *pseudomonas*. Most of the urinary isolates were sensitive to ciprofloxacin, cotrimoxazole and ceftriaxone, where as resistance was high for ampicillin.

Keywords: Urinary tract infection, diabetes, antibiotic sensitivity.

INTRODUCTION

The worldwide prevalence of Diabetes Mellitus (DM) has raised dramatically over the past two decades.¹ It affects more than 120 million people world-wide and it is estimated that it will affect 220 million by the year 2020.² Patients with DM have a higher prevalence of Urinary Tract Infection (UTI) compared to non-diabetics. Symptomatic bacteriuria in patients with DM is serious and warrants proper clinical attention for diagnosis and treatment. UTI in diabetic patients are mostly considered as complicated.³ Most UTI in diabetic patients are relatively asymptomatic.⁴ This asymptomatic infection can lead to severe kidney damage and renal failure.⁵

The increased prevalence of asymptomatic bacteriuria (ASB) and symptomatic UTI in diabetic patient may be the result of difference in host responses between diabetic and non diabetic patients or to a difference in infecting bacterium itself.³

The clinical features of UTI in patients with diabetes are variable. Occasionally Fever may be less apparent. Hematuria or flank pain secondary to sloughing papillae may be noted in patients with papillary necrosis. Diabetic patients with urinary tract infection may be the source of metastatic infection. On the other hand any infection can cause poor diabetes control.⁶

Most of the studies have shown the presence of colony count of $>10^5$ organism per milliliter from properly collected midstream clean-catch sample to be significant.

In diabetic patient screening for UTI is very important to enable it to be properly treated and to prevent the development of

possible complications. This study aimed to find the prevalence culture positive UTI, their clinical presentation and pattern of antibiotic sensitivity in our setting. This will guide for further management of our patients in future.

MATERIALS AND METHODS

This was a descriptive cross-sectional study conducted in the department of medicine in Tribhuvan University Teaching Hospital. It included diabetic patient presented in medical OPD and admitted in various wards of medicine department over duration of one year, between March 2007 to February 2008. A total of 100 patients of DM were randomly enrolled in the study.

A known diabetic or newly diagnosed diabetic with or without medication were included. Both having controlled and uncontrolled blood sugar were included.

Diagnosed diabetics who were already started on antibiotics and who took antibiotic within last 2 weeks were excluded.

DM was diagnosed according to World Health Organization (WHO) criteria with symptoms of diabetes plus random blood glucose concentration equal or more than 11.1 mmol/l (200 mg%) or fasting plasma glucose equal or more than 7.0 mmol/l (126 mg%).

Mid stream urine was collected from a patient with full aseptic precautions. It was collected in a sterile container and closing the lid as soon as urine was collected. The

method for collection, isolation and identification of urine sample was followed as described by American Society of Microbiology. Culture of each uncentrifuged urine sample was done by semi quantitative method on 5% Blood agar (BA) and Mac Conkey agar (MA) plates. An inoculating loop of standard dimension was used to take up approximately fixed and a known volume (0.001 ml) of urine for inoculation. After incubating the plates aerobically at 37°C for 24 hours colonies were counted. The antibiotic sensitivity test of the pathogens was determined by Kirby-Bauer method of disk diffusion techniques as recommended by Clinical Laboratory standard Institute (CLSI). Sample showing $>10^5$ colony forming unit (CFU) per milliliter (ml) was taken significant.

SPSS version 14.0 for windows was utilized to analyze the data. P-value was calculated and value <0.05 was considered significant.

Fasting Blood Sugar (FBS) ranged between 2.70 mmol/l (49 mg%) to 27 mmol/l (486 mg%) while 2hr Postprandial Blood Sugar (PPBS) ranged between 4.90 (88 mg%) to 21 mmol/l (378 mg%)

Among the enrolled 100 patients, FBS and PPBS were above the upper limit of normal range in 66% (>7.2 mmol/l; 130 mg%) and in 75% (10mmol/l; 180mg% and above) respectively.

RESULTS

Among the 100 included patients, 53% were female and 47% were male. Among 53 female 41 were post menopausal. The age ranged from 21-98 years with a mean age of 59.32 ± 12.91 years. Height and weight ranged between 1.29 m - 1.80 m and 46 kg - 86 kg, the mean being 1.57 ± 0.13 m and 62.87 ± 9.25 kg respectively. The body mass index ranged between 15.78 kg/m^2 to 42.88 kg/m^2 with mean of $25.80 \pm 4.75 \text{ kg/m}^2$.

The Systolic Blood pressure (SBP) ranged between 90 to 180 mm of Hg and Diastolic Blood pressure (DBP) ranged between 48 and 110 mm of Hg. The mean were 127.88 ± 19.15 and 79.80 ± 11.55 mm of Hg.

The average duration of diabetes mellitus was 10.49 ± 7.49 years. A total of 10 patients were newly diagnosed diabetic. Twenty four were diagnosed DM for less than 5 years, 29 were between 5 years and 10 years duration and 37 were having diabetes for more than 10 years duration.

Twenty five patients were not under any medication during study enrollment, 47 were taking oral hypoglycemic agents (OHA), 22 were under insulin and 6 were taking both insulin and OHA. The baseline characteristics of enrolled patients are shown in Table-1.

Table-1: Baseline characteristics of enrolled subjects.

Particulars	Values
Age (Mean \pm SD)	59.32 \pm 12.91 years
Sex (Male/Female)	47/53 No and %
Height (Mean \pm SD)	1.57 \pm 0.13 m
Weight (Mean \pm SD)	62.87 \pm 9.25 kg
BMI (Mean \pm SD)	25.80 \pm 4.75 kg/m ²
Duration of DM (Mean \pm SD)	10.49 \pm 7.49 years
Systolic BP (Mean \pm SD)	127.88 \pm 19.15 mm of Hg
Diastolic BP (Mean \pm SD)	79.80 \pm 11.55 mm of Hg
Medication for DM	
No. and %	
No Medication	25
OHA	47
Insulin	22
Insulin + OHA	6

A total of 21 urine C/S sample showed growth of organisms more than 10^5 CFU which is shown in Table-2.

Table-2: Profile of Urinary C/S report

	Frequency	Percent
No growth	79	79.0
Growth	21	21.0
Total	100	100.0

Among 53 females 15 (28.3%) had growth and among 47 male 6 (12.76%) had growth. Escherichia-Coli (E-Coli) was the most common organism in 11 (52.38%) cases. The other organisms isolated were klebsiella in 3 (14.28%) cases, pseudomonas, proteus, enterococcus in 2 (8.52%) cases and acinetobacter in 1 (4.76%) case. The organism isolated are shown in Table-3.

Table-3: Isolated organisms in culture positive cases

Organism isolated	Frequency	Percent
E-coli	11	52.38
Klebsiella	3	14.29
Pseudomonas	2	9.52
Proteus	2	9.52
Acinetobacter	1	4.76
Enterococcus Fecalis	2	9.52
Total	21	100

Pattern of antibiotic sensitivity and resistance of the organisms were variable. E-coli- was sensitive to ciprofloxacin in 81.8%, ceftriaxone in 90.9% and imipenem in 100%. It was sensitive in 70% cases to cotrimoxazole. Klebsiella was 100% sensitive to ciprofloxacin and 66% to ceftriaxone. It was also 100% sensitive to imipenem. Pseudomonas was 100% sensitive to imipenem and ceftriaxone, while 50% sensitive to ciprofloxacin. The antibiotic sensitivity pattern of urinary isolates are shown in Table-4.

Table-4: Pattern of antibiotic sensitivity with percentage

Antibiotics	E-Coli	Klebsiella	Pseudo-monas	Proteus	Entero-coccus	Acineto-bacter
Ciprofloxacin	s-9 %-81.8	s-3 %-100	s-1 %-50	s-1 %-50	s-2 %-100	s-1 %-100
Cotrimoxazole	s-7 %-70	s-2 %-66.6	s-1 %-50	s-1 %-50	s-1 %-50	s-0 %-0
Amikacin	s-5 %-71.4	s-1 %-33.3	s-1 %-50	s-0 %-0	s-1 %-50	s-1 %-100
Gentamycin	s-5 %-62.5	s-2 %-66.6	s-0 %-0	s-1 %-1	s-1 %-50	s-0 %-0
Ceftriaxone	s-10 %- 90.9	s-2 %66.6	s-1 %-50	s-2 %-100	s-2 %-100	s-1 %-100
Ampicillin	s-5 %-50	s-0 %-0	s-0 %-0	s-1 %-50	s-1 %-50	s-0 %-0
Imipenum	s-6 %-100	s-2 %-100	s-2 %-100	s-1 %-50	s-1 %-100	s-1 %-100
Nitrofurantoin	s-6 %-54.5	s-2 %-66.6	s-1 %-50	s-1 %-50	s-1 %-50	s-0 %-0

s – sensitive no., % - percentage

Organisms were found resistant to ampicillin to great extent. Only in 50% cases, E-coli was sensitive to it. All the isolated klebsiella and pseudomonas was resistant to ampicillin. Resistance was 50% for proteus and enterococcus.

Among 21 culture positive cases, 10 had urinary symptoms, present in 5 male and 5 female. Burning micturition was the common symptom present in 9 (90%), followed by frequency of micturition in 8 (80%), urgency in 7 (70%) cases. Suprapubic and loin pain were present in 6 (60%) and 3 (30%) cases respectively. Fever and vomiting was present in only 2 (20%) cases. Total of 11 patients (52.23%) having C/S positive UTI were asymptomatic. Of them 10 were female and 1 was a male. Thus 66.6% female and 16.66% male were having asymptomatic bacteriuria.

Statistical analysis showed sex had positive correlation with UTI. Among 53 female 15 had growth and among 47 male 6 had growth with $P=0.047$.

UTI was found more common in post menopausal female, according to number, but correlation was only marginal ($P=0.05$).

UTI was found more common in those patients who were under insulin as compared to those who were taking OHA. Among 25 patients not under any medication 3 had growth. Among 47 patient under OHA 5 had growth and among 22 patients under insulin 10 had growth. Among 6 patients taking both (insulin+OHA) 1 had growth. The growth was high for insulin group with significant correlation ($P=0.08$).

UTI was more common among the cases having prolonged duration of DM. Only 2 of newly detected had UTI. For those who had DM for more than 10 years, 14 had UTI. Prolong the duration of Diabetes; UTI was more prevalent, with significant correlation ($P= 0.039$).

No statistically significant correlation was obtained between the degree of sugar control and growth of organism with $P=0.055$ and 0.16 respectively for fasting and PP.

P values of different variables in relation to UTI among diabetics are shown in Table-5.

Table-5: P values of variables for UTI in Diabetics

Variables	P values
Sex	$P=0.047$
Menopausal Status	$P=0.05$
Duration of DM	$P=0.039$
Medication of DM	$P=0.08$
Fasting Control Status	$P=0.055$
PP control Status	$P=0.16$

DISCUSSION

The observed prevalence of UTI among diabetic patients in this study (21%) was almost similar to defined in the literatures. This study found UTI in female more common as compared to male ($P=0.047$) and major percent of female with UTI were asymptomatic. UTI was found more common among post menopausal. There was organism isolation in 12 specimens obtained from 41 post menopausal females ($P=0.05$). Huvo and Rocha had shown the prevalence of UTI up to 41% in female with DM.⁷ Geerlings and colleagues had shown the same in up to 26% of female.⁸ Sotiriopoulos and colleagues found 9.6% of bacteriuria in diabetics.⁹ This study showed culture positive UTI among 28.3% of diabetic female; 66.6% of them were asymptomatic. In male also, the result observed was similar to what had been described in the past. This study found 12.76% UTI in male. They were almost symptomatic (83.33%) except 1 (16.66%).

Several factors might have contributed to the variability of UTI in diabetics. Majority of the studies have taken organism isolation of $>10^5$ significant. However some authors advocates less than this can even be significant. The race, ethnicity and geographical variation might have contributed well. The difference in results of community based and hospital based studies is expected. Besides, healthy lifestyle, prompt diagnosis and treatment of other comorbid condition and significant awareness of disease gravity may contribute for differences in results.

There was high prevalence of UTI among those patients having diabetes for more than 10 years duration as compared to those with less than 10 years with significant correlation ($P=0.039$). Schmitt and colleagues too have shown a statistically significant longer diabetic duration in bacteriuric subjects than in those without bacteriuria.¹⁰

This study found greater proportion of patients under insulin therapy was having UTI ($P=0.008$). Women taking insulin are mainly at higher risk, possibly because of more severe diabetes, since the use of insulin may be a marker for disease severity.¹¹

Studies have shown no correlation between the degree of glycemic control and prevalence of UTI.¹² This study also did not find any statistically significant correlation between diabetic control and UTI ($P=0.055$ for fasting and $P=0.16$ for PP).

Regarding urinary isolates E-coli was the most common organism found in 11 (52.38%) cases followed by klebsiella in 3 (14.28%) cases. Literatures show up to 90% of UTI caused by E-coli in diabetic patients. Bonadio and colleagues had shown E-Coli was

responsible for 56.1% of UTI in DM, which almost coincides with this result.¹³ Previously articles described that there exist no major difference among the organism causing UTI in diabetic as compared to non diabetic.¹⁴ This study also found the common organism causing UTI in ordinary subjects were the major cause of UTI in diabetics.

The sensitivity pattern of majority of urinary isolates in our study was similar to what has been reported previously. E-coli was found sensitive to ciprofloxacin in 81.8% and to ceftriaxone in 90.9% cases. It was 100% sensitive to Imipenem. Sensitivity to cotrimoxazole was in 70% cases. In addition this agent can lead to hypoglycemia and is not a recommended first choice of drug in DM.¹⁵ This pattern was almost similar as shown by Mario and colleagues except for imipenem.¹⁶

The resistance of ampicillin was high for almost all organism isolated. It was sensitive to E-Coli only in 50% cases. Similar results were found for proteus and enterococcus.

The clinical features of UTI in patients with diabetes are essentially the same as in people without diabetes.

Among the culture positive UTI, result showed 11 out of 21 (52.23%) were asymptomatic. The result was more for female, 10 out of 15 (66.66%) being without

symptoms. Controversy exist whether to treat them or not. Geerlings in his publication mentioned that ASB doesn't lead to complication and screening and treatment is not warranted.³ However Mahadeva, Pajica and Zeljko in their study mentioned that all UTI should be treated regardless of symptoms. Untreated infection can lead to renal parenchymal infection which may impair renal function in long term.⁴ Larger population based study is further awaited to address this dispute.

In conclusion, prevalence of UTI among diabetics in this study was comparable to published literature. The commonly used antibiotics were fairly sensitive to the urinary isolates. Female sex, particularly post menopausal, insulin users and prolong disease duration were at risk. Prevalence of ASB was common.

REFERENCES

- Alvin CP, Diabetes Mellitus. In Fauci SA, Braunwald E, Kasper LD *et al.*, editors. Harrison's Principles of Internal Medicine (17th ed.). Vol II. New York: McGraw-Hill 2008; 2275-04.
- Kumar P, Clark M, editors. Kumar and Clark Clinical Medicine (6th ed.). Philadelphia: Elsevier Saunders 2005; 1101-51.
- Geerlings SE. Urinary tract infections in patients with diabetes mellitus: epidemiology, pathogenesis and treatment. *Int J Antimicrobial Agents* 2008; 31: 54-7.
- MahadevaSB, Pajica P, Zeljko M. Kidney infection in Diabetes Mellitus. *Diabetologica Croatica* 2002; 31: 85-03.
- Keane EH, Boyko EJ, Reller LB, Hamman RF. Prevalence of asymptomatic bacteriuria in subjects with NIDDM in Sant Luis valley of Colorado. *Diabetic Care* 1988; 11: 708-12.
- Leibovici L, Yeheehzkelli Y, Portter A, Regev A, Krauze I, Harel D. Influence of diabetes mellitus and glycemic control on the characteristics and outcome of common infections. *Diabet Med* 1996; 13: 457-63.
- Huvos A, Rocha J. Frequency of bacteriuria in patients with diabetes mellitus. *New Engl J Med* 1959; 261: 1213-6.
- Geerlings SE, Stolk RP, Camps MJL *et al.* Asymptomatic bacteriuria may be considered a complication in women with diabetes. *Diabetes Care* 2000; 23: 744-49.
- Sotiropoulos A, Skourtis S, Merkouris P *et al.* Incidence and outcome of asymptomatic bacteriuria in female with Type 2 diabetes mellitus over a 1-year follow-up period and association with risk factors. *Diabet Med* 2005; 22: 1625-6.
- Schmitt JK, Fawcett CJ, Gullickson G. Asymptomatic bacteriuria and hemoglobin A1. *Diabetes Care* 1986; 9: 518-20.
- Turner CR, Cull CA, Frighi V, Holman RR. Glycemic control with diet, sulfonylurea, metformin, or insulin in patients with type 2 diabetes mellitus: progressive requirement for multiple therapies (UKPDS 49). UK Prospective Diabetes Study (UKPDS) Group. *J Amer Med Assoc* 1999; 281: 2005-12.
- Bokyo EJ, Fihn SD, Scholes D, Chen CL, Normand EH, Yarbro P. Diabetes and risk of acute urinary tract infection among post menopausal women. *Diabetic Care* 2002; 25: 1778-83.
- Bonadio M, Meini M, Gigli C, Longo B, Vigna A. Urinary tract infection in diabetic patients. *Urol Int* 1999; 63: 215-19.
- Nicolle LE. A practical guide to antimicrobial management of complicated urinary tract infection. *Drugs Aging* 2001; 24: 54-54.
- Poretzky L, Moses AC. Hypoglycemia associated with trimethoprim/sulfamethoxazole therapy. *Diabetes Care* 1984; 508-9.
- Mario B, Silvia C, Giovanna M, Tiziana T. The influence of Diabetes mellitus on the spectrum of uropathogens and antimicrobial resistance in elderly patients urinary tract infection. *BMC Infectious Disease* 2006; 6: 54.