**Original article:**

# Prevalence of uropathogens in diabetic patients types 1 and 2, and their correspon -ding resistance pattern

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**Abstract**:

**Background**: The prevalence of urinary tract infection (UTI), both symptomatic and otherwise is high in patients with diabetes mellitus. Rampant non-evidence based overuse of antibiotics has led to emergence of new resistance patterns. People with diabetes are more prone for urinary tract infections. Incidence of infection increases with longer duration and uncontrolled glucose levels.

**Objectives**: To study the clinical patterns and causative organisms of Urinary tract infection in both Type I and II Diabetes Mellitus

**Key words**: Urinary tract infection, Klebsiella

## Introduction

Diabetes mellitus is one of the most common endocrine diseases in the world. Due to its micro and macro vascular complication it can affect multiple organs. Diabetes mellitus refers to a group of metabolic diseases of multiple aetiologies. It is characterised by chronic hyperglycaemia with disturbances of protein, carbohydrate and fat metabolism resulting from defects in insulin secretion, insulin action, or both. Due to the high content of glucose in the urine and defect in the host immune factors, people with diabetes are more prone for urinary tract infections. Hyperglycaemia causes neutrophil dysfunction by increasing intracellular calcium levels and interfering with actin, diapedesis and phagocytosis.

People with diabetes can develop acute and chronic complications of diabetes. Acute complications include diabetic ketoacidosis and non-ketotic hyper-osmolarstate. Serious long-term complications include diabetic retinopathy, cardiovascular disease, chronic renal failure,perirenal abscess, emphysematous cystitis, emphysematous pyelonephritis, fungal infections, xantho – granulomatous pyelonephritis, and papillary necrosis. (17)Urinary tract infections include a spectrum of clinical entities in which the presence of bacteriuria is the common denominator. Other types of microorganisms such as viruses and fungi may also infect the urinary tract but usually do so under special circumstances of systemic infection or decreased host resistance. Asymptomaticbacteriuria, acute pyelonephritis and complications of UTI are reported to be more common in patients with diabetes. (18)Incidence of UTI is more common among females. (13, 19)Women with diabetes mellitus (DM) have asymptomatic bacteriuria (ASB) more often than women without DM and they have an increased risk of developing a symptomatic UTI than those without ASB.(21)Bacteriological studies usually reveal the involvement of gram negative enteric organisms that commonly cause urinary tract infections, such as E. coli, Klebsiella species, and

the Proteus species.(22)In another study from India, it was found that E. coli was the most commonly grown organism (64.3%), followed by Staphylococcus aureus (21.4%), and Klebsiellapneumoniae (14.3%). (22, 23) Lloyds et al. have shown that Enterococci spp. accounted for 35% of urinary tract isolates. (24)

**Background & Objective**

There is an increased susceptibility to diabetes mellitus in Indian population. The recent studies on a South Indian population has showed that incidence of diabetes was 20.2 / 1000 person years. Patients with type 1 and type 2 diabetes mellitus are at increased risk of various infections. The prevalence of urinary tract infection (UTI) is high in patients with diabetes mellitus. The prevalence of urinary tract infection (UTI), both symptomatic and otherwise is high in patients with diabetes mellitus. Rampant non-evidence based overuse of antibiotics by enthusiastic healthcare workers and in some cases by self-medicating patients has led to emergence of new resistance patterns, creating a dilemma in the management of these patients. Not many studies have been done in Mangalore to assess the prevalence of UTI in the urine of diabetic subjects. This study attempts to address this gap.

**The objective of this study**

1. To study the clinical patterns of Urinary tract infection in both Type I and IIDiabetes Mellitus

2. To study causative microorganisms and their drug susceptibility in Urinary tract infections with both Type I and II Diabetes Mellitus.

**Materials & Methods**

This is a descriptive study of 100 diabetic patients with UTI admitted in Yenepoya Medical College Hospital. Clean voided midstream urine samples were collected in sterile containers after giving proper instructions and samples was processed in the laboratory within 2 hours of collection. The urine cultures were done by inoculating urine samples on blood agar and MacConkey agar plates using a calibrated loop (0.001ml) and incubated at $37^0$C for 24-48 hours. Antimicrobial sensitivity was done by Kirby-Bauer disc diffusion method.

Inclusion criteria

1. History of diabetes or with FBS =/>126mg/dl and PPBS=/>180.

2. Clinical and microbiological features of urinary tract infections

3. Both Type I and Type II diabetics

4. Irrespective of their sex, duration of diabetes, treatment taken, adherence and all patients above age of 18 years

Exclusion criteria

1. History of receiving antibiotics within two weeks prior to culture.

2. Patients on continuous indwelling catheter.

3. Menstruating women.

**Results**

In 100 diabetics with symptoms of UTI, 43 were found to be bacteriuria. The urinary tract infection did not show any correlation with the age of patients. The incidence of Urinary tract infection was higher among the female patients .A duration of diabetes more than 6 years increases chances for developing urinary tract infections. Bacteriuria were less in patients taking insulin and combined (insulin and oral hypoglycaemic) treatment for diabetes. The patients with neuropathy had higher chances for developing bacteriuria.Asymptomatic bacteriuria did not show an increased incidence in female population.Glycated haemoglobinA1C was found to be high in diabetic patients with urinary tract infections. E .coli was the commonest organism isolated from urine culture and Klebsiella was the second common organism isolated.

| Comparison on Type of Diabetes | | | PATIENT GROUP | | |
|---|---|---|---|---|---|
| | | | Without Bacteruria | With Bacteruria | |
| Diabetes Type | I | Count | 6 | 2 | 8 |
| | | % within patient group | 10.5% | 4.7% | 8.0% |
| | II | Count | 51 | 41 | 92 |
| | | % within patient group | 89.5% | 95.3% | 92.0 |
| **Total** | | Count | 57 | 43 | 100 |
| | | % within patient group | 100% | 100% | 100% |

Of the hundred patients evaluated in this study only eight (8%) patients had Type I diabetes and 92 (90%) patients were Type II diabetics.

| Duration of Diabetes | | | Patient Group | | Total |
|---|---|---|---|---|---|
| | | | Without Bacteruria | with Bacteriuria | |
| duration | <1yr | Count | 6 | 3 | 9 |
| | | % within patient group | 10.5% | 7.0% | 9.0% |
| | 1-5yrs | Count | 12 | 11 | 23 |
| | | % within patient group | 21.1% | 25.6% | 23.0% |
| | 6-10 | Count | 21 | 25 | 46 |
| | | % within patient group | 36.8% | 58.1% | 46.0% |
| | 11-15yrs | Count | 11 | 4 | 15 |
| | | % within patient group | 18.8% | 14.8% | 16.3% |
| | .>15yrs | Count | 7 | 0 | 7 |
| | | % within patient group | 12.3% | .0% | 7% |
| Total | | Count | 57 | 43 | 100 |
| | | % within group | 100.0% | 100.0% | 100.0% |

Chi-square=9.89 p= 0.042

Mean duration of Diabetes since diagnosis

| Patient group | N | Mean | STD deviation | T | P |
|---|---|---|---|---|---|
| Without bacteruria | 57 | 8.714 | 5.9452 | 2.599 | 0.011 |
| With bacteruria | 43 | 6.158 | 2.8605 | | |

Treatment taken for Diabetes

*Mean duration of diabetes was **6.158** years for bacteruric patients and **8.714** for non bacteruric patients with a p value of 0.011.*
*This difference statistically significant for urinary tract infection*

| Treatment | Without Bacteruria (n=57) | With Bacteruria (n=43) |
|---|---|---|
| Insulin | 17 | 11 |
| % | 29.8% | 25.6% |
| Oral | 28 | 22 |
| % | 49.1% | 51.2% |
| Both | 8 | 7 |
| % | 14.0% | 16.3% |
| No Treatment | 6 | 3 |
| % | 10.5% | 7.0% |

Evaluation of Complications of Diabetes

| Complications | Without Bacteruria (n=57) | With Bacteruria (n=43) |
|---|---|---|
| Retinopathy | 16 | 17 |
| % | 28.1% | 39.5% |
| Neuropathy | 20 | 25 |
| % | 35.1% | 58.1% |
| Nephropathy | 9 | 11 |
| % | 15.8% | 25.6% |
| Diabetic foot | 6 | 16 |
| % | 10.5% | 37.2% |
| Hypertension | 16 | 16 |
| % | 28.1% | 38.1% |
| IHD | 14 | 7 |
| % | 25.0% | 16.3% |
| Others | 4 | 0 |
| % | 7.0% | .0% |

Diabetic Foot

| | | | Group | | Total |
|---|---|---|---|---|---|
| | | | Males with Bacteriuria | Females with Bacteriuria | |
| Diabetic Foot | yes | Count | 10 | 6 | 16 |
| | | % within group | 62.% | 22.2% | 37.2% |
| | no | Count | 6 | 21 | 27 |
| | | % within group | 37.5% | 77.8% | 62.8% |
| Total | | Count | 16 | 27 | 43 |
| | | % within group | 100% | 100% | 100% |

Neuropathy

| | | | Patient Group | | Total |
|---|---|---|---|---|---|
| | | | Males with Bacteriuria | Females with Bacteriuria | |
| Neuropathy | yes | Count | 20 | 25 | 45 |
| | | % within patient group | 35.1% | 58.1% | 45.0% |
| | no | Count | 37 | 18 | 55 |
| | | % within patient group | 64.9% | 41.9% | 55.0% |
| Total | | Count | 57 | 43 | 100 |
| | | % within patient group | 100% | 100% | 100% |

Complications
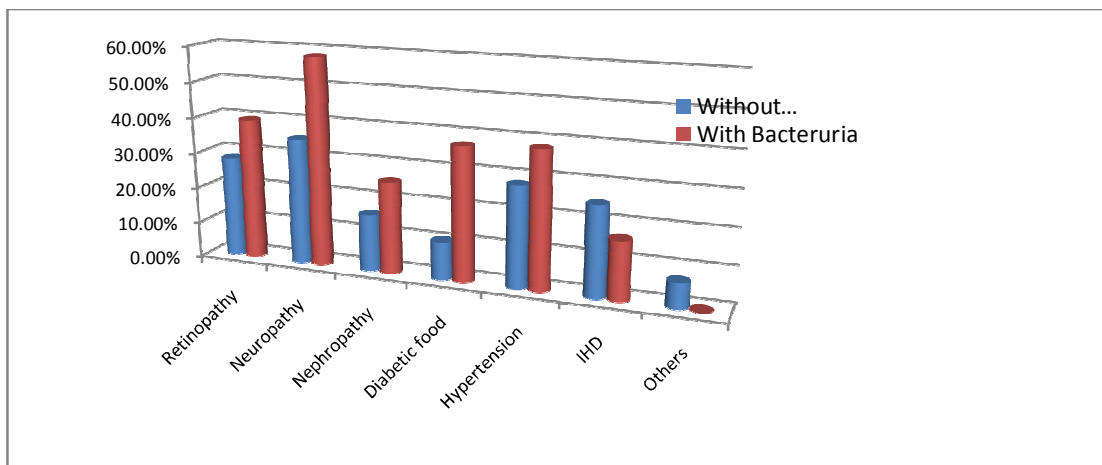
Symptoms of Urinary Tract Infections

| UTI Symptoms | Without Bacteriuria (n=57) | With Bacteriuria (n=43) |
|---|---|---|
| Asymptomatic % | 0 0% | 14 32.6% |
| Fever % | 14 24.6% | 12 27.9% |
| Dysuria % | 28 49.1% | 18 41.9% |
| Frequency % | 19 33.9% | 17 39.5% |
| Urgency % | 29 50.9% | 4 9.3% |
| hematuria % | 12 21.1% | 2 4.7% |
| pyuria % | 0 .0 % | 1 2.3% |
| Suprapubic pain | 12 21.1% | 16 37.2% |
| Flank pain | 11 19.3% | 6 14.0% |

Frequency Of Micturition

| | | | Group | | Total |
|---|---|---|---|---|---|
| | | | Males with Bacteriuria | Females with Bacteriuria | |
| Frequency | yes | Count | 10 | 7 | 17 |
| | | % within group | 62.5% | 25.9% | 39.5% |
| | no | Count | 6 | 20 | 26 |
| | | % within group | 37.5% | 74.1% | 60.5% |
| Total | | Count | 16 | 27 | 43 |
| | | % within group | 100% | 100% | 100% |

Table 15: Asymptomatic Bacteriuria

| | | | Group | | Total |
|---|---|---|---|---|---|
| | | | Males with Bacteriuria | Females with Bacteriuria | |
| Asymptomatic | yes | Count | 4 | 10 | 14 |
| | | % within group | 25.0% | 37.0% | 32.6% |
| | no | Count | 12 | 17 | 29 |
| | | % within group | 75.0% | 63.0% | 67.4% |
| Total | | Count | 16 | 27 | 43 |
| | | % within group | 100% | 100% | 100% |

Evaluation of Tenderness

| Examination | Without Bacteriuria (n=57) | With Bacteriuria (n=43) |
| --- | --- | --- |
| Suprapubic Tend: % | 11 19.3% | 14 32.6% |
| Rental Angle Tend: % | 8 14.0% | 1 23.3% |
| Deep Palpation % | 1 1.8% | 1 2.3% |
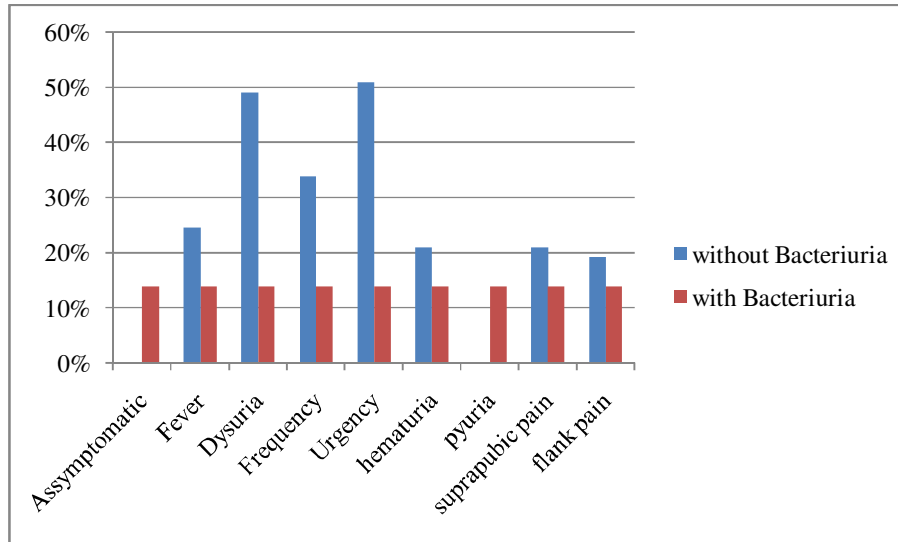


The symptoms urgency (p=0.042) frequency (p=.026) and hematuria (p=0.021),

were statistically significant in non – bacteruric patients when compared between bacteruric.
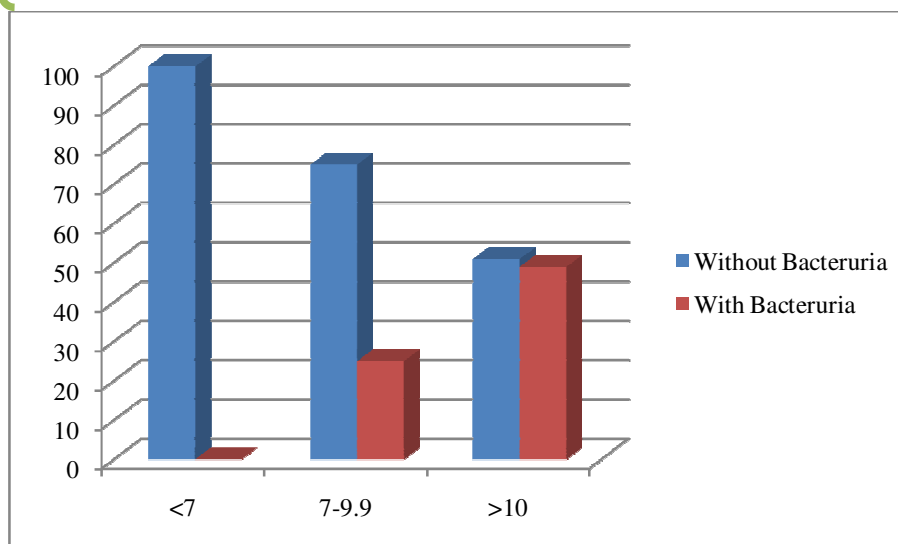
| | | | Patient group | | Total |
|---|---|---|---|---|---|
| | | | Without bacteruria | With bacteruria | |
| HbA1c new | <7 | Count | 3 | 0 | 3 |
| | | %within HbA1c | 100% | 0% | 100.0% |
| | 7-9.9 | Count | 15 | 6 | 21 |
| | | %within HbA1c | 75.0% | 25.0% | 100.0% |
| | >10 | Count | 39 | 37 | 76 |
| | | %within HbA1c | 51.0% | 49.0% | 100.0% |
| Total | | Count | 57 | 43 | 100 |
| | | %within HbA1c | 57.0% | 43.0% | 100.0% |

All patients (n = 43) in the bacteruric group had HbA1c above 7 37 patients in the bacteruric group above 10. This was statistically significant with a p value 0.0434 for urinary tract infections

Urine culture
Organism Isolated

| Organism | Number | Percentage |
|---|---|---|
| E-Coli | 30 | 69.8% |
| Klebsiella | 7 | 16.2 |
| Enterococci | 4 | 9% |
| Pseudomonas | 1 | 2% |
| Candida | 1 | 2% |

Gender based study on Organism

| | | | Group | | Total |
|---|---|---|---|---|---|
| | | | Males with Bacteriuria | Females with Bacteriuria | |
| $>10^5$ | candida | Count | 0 | 1 | 1 |
| | | % within group | 0% | 3.7% | 2.3% |
| | E-coli | Count | 10 | 20 | 30 |
| | | % within group | 62.5% | 74.1% | 69.8% |
| | Enterococci | Count | 2 | 2 | 4 |
| | | % within group | 12.5% | 7.4% | 9.3% |
| | Klebsiella | Count | 3 | 4 | 7 |
| | | % within group | 18.8% | 14.8% | 16.3% |
| | Pseudomonas | Count | 1 | 0 | 1 |
| | | % within group | 6.3% | .0% | 2.3% |
| Total | | Count | 16 | 27 | 43 |
| | | % within group | 100.0% | 100.0% | 100.0% |

Chi-square=2.89 p=0.583

Culture and sensitivity

| Organisms n= 43 | Ampicillin % | Cefuroxime % | Ceftriaxone % | Cotrimoxazole % | Gentamycin % | Piperacillin/ tazobactum % | Cefaperazone % | Ciprofloxacin % | Norfloxacin % |
|---|---|---|---|---|---|---|---|---|---|
| Ecoli (30, 69.7) | **52.4** | 20.7 | 12.7 | 20.55 | 6.1 | **90** | 84 | 26.66 | |
| Klebsiella (7, 16.3%) | **89.7** | | 12.5 | 16.7 | 17.8 | **88.4** | 82.4 | 22.1 | 14 |
| Enterococcus (4, 9.3%) | 23.7 | | 12.5 | 32.8 | **60.7** | **70.4** | 83.5 | 13.2 | 8.2 |

- Gram negative bacilli were found to be highly sensitive to sulbactum / cefoperazone (84%) and piperacillin / tazobactum (90%)

- Gram positive cocci were 70.4% sensitive to sulbactum / cefoperazone and 83.5 % sensitive to piperacillin / tazobactum respectively.

- Gram negative bacilli were more sensitive to ampicillin than gram positive bacilli ( 54.2, 89.7 vs 23.7)

- Gram positive bacilli were more sensitive to gentamycin than gram negative bacilli (6.1, 17.8 vs 60.7)

**Discussion**

Many studies have shown an increased prevalence of bacteriuria in diabetics whereas almost equal number of studies failed to show a significant association. O' Sullivanet al study showed that bacteriuria in 150 diabetics was13.3% and in 150 controls was 12% which failed to achieve statistical significance. (1)Vejlsgradet al found 9.3% incidence ofbacteriuria in diabetics. This was statistically significant. (2)The present study did not show an increased prevalence of bacteriuria in diabetics. There was no significant correlation between age and incidence of bacteriuria in the present study in diabetic patients. This was in contrast to other studies by Ooi BS et al, O'Sullivan DJ et al, Vejlsgaard et al who found significant incidence in older age group.(3,1,2)Jaspani et alfound no significant correlation with age.(4)In this study, incidence of urinary tract infection was found to be significantly high in females (p=.043 sig). This is probably due to anatomical reasons. This observation was same with almost all previous studies viz. Shah BV et al 5, Ooi BS et al, O'Sullivan DJ et al, Jaspani et al. (5, 3, 1, 4)The present study did not show any statistically significant incidence of bacteriuriabased on type of diabetes (I or II), this was in concordance with the study done by to studies by C. R. Cardwell et al and D M Fleming. (6, 7)Mean duration of diabetes in this study was 6 years for bacteriuria patients and 9 yearsin patients without bacteriuria. There were similar results in studies done by Ooi BS et al, Jaspani et al, but Shah BV et al, and Keane et al didn't find any correlation with duration of diabetes in their study. (3, 4, 5, 8)In the present study there was no significant correlation between with bacteriuriaand type of treatment taken for diabetes. Majority of the

patients with urinary tract infections were not willing for insulin regimen for control blood sugars, though it was advised. Shah BVet al, Jaspaniet al and Szucset al had similar observations. (5, 4, 9)Zhanel et al found bacteriuria was higher with patients on oral hypoglycaemics. (10) No significant difference in bacteriuriawas noted, between patients who were regular on treatment and follow up.

Among the complications of diabetes, neuropathy (p value =0.027) was found to have higher incidence for bacteriuria in the present study. Other complications like retinopathy, nephropathy, hypertension, IHD or others like (myopathy) did not show significant correlation for bacteriuria. The studies done by Suzzanne E Geerlingset al and Schmitt JKetal showed that presence of longstanding complications (peripheral neuropathy, peripheral vascular disease) increased the risk of developing asymptomatic bacteruria. (11, 12)Zhanelet al found significant association with heart disease. (10)

Comparison between bacteriuria and non bacteriuria group based on symptoms of urinary tract infections in diabetics did not show much significance in this study. Of the 43 patients evaluated with bacteriuria 14 patients (32.6%) had asymptomatic bacteriuria.The pH of urine was significantly higher in the bacteriuriagroup; specific gravity was not significantly different between the two groups. In this study the following organisms Escherichia Coli, Klebsiella, Enterococci, and Pseudomonas were isolated. Of which E. coli (69.8%), was found to be predominant, the next being Klebsiella (16.3%). One sample contained Candida along with E. coli. Studies done by Bonadio M et alhad found an increased incidence of E-coli 54.1% in diabetic patients with bacteriuria, the next prevalent

organism being Enterococcus spp: 8.3%.(13) Similar results were seen in studies done by Shah B. V et al, Zhanelet al, O'Sullivan et al, Szucs S et aland Bonadio et al.(5,10,1,9,13) Klebsiella was the second common organism isolated (35.71%), matches with observations by Shah B. V et aland Zhanelet al.(5,10) Proteus was the second common organism in some studies. Most of the organisms were susceptible to antimicrobials like piperacillinand tazobactum. E.coli isolates in majority of the patients were sensitive to both ampicillin and piperacillintazobactum.The studies done by BonadioMet al, Shah B. V et al, Zhanelet al did correlate with the present study.(13,5,10)In the present study evidence of pyelonephritis was found in 12 patients and 21 patients had a normal ultrasound evaluation in the bacteruric group. The post voiding l residual urine above 100ml had not shown statistical significance as a risk factor for urinary tract infections in diabetics.

The gram negative pathogens were highly resistant to cotrimoxazole, ciprofloxacin, cotrimoxazole and ceftazidime. Diabetic patients are at a high risk of development of UTIs, so it is recommended that continued surveillance of resistance rates among uropathogens is needed to ensure appropriate recommendations for the treatment of these infections. (14)Other studies also recommended that continued surveillance of resistance rates among uropathogens is needed to ensure appropriate recommendations for the treatment of these infections. (15, 16)Keeping the emergence of new resistance patterns in mind, it is suggested that the antibiotic therapy should be started only after obtaining the sensitivity report from the Microbiology laboratory. This would not only help in the careful use of antibiotics but also would curb the dissemination of antimicrobial resistant strains in the community as well as in the hospital.

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