

# Clinical and laboratory profile of urinary tract infection in diabetic patients

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## Abstract

**Background:** Diabetic patients have higher risk of urinary tract infection (UTI). The present study was undertaken to study clinical and laboratory profile of UTI in diabetics and also study yield of urine culture in UTI, common causative organisms and their antibiotic sensitivity pattern.

**Method:** Total 224 type 1 and type 2 diabetic patients, age > 18 years with or without symptoms of UTI with significant bacteriuria were enrolled in the study. Diagnosis of UTI was made on the basis of clinical history, symptoms and detailed clinical examination and confirmed by urine examination. Other investigations (CBC, serum creatinine, blood urea, HBA1C, fasting and post meal blood sugar and USG abdomen with pelvis) were also done. In addition, the organisms in urine cultures and antibiotic sensitivity patterns were investigated for bacteriuric patients.

**Results:** The highest numbers of patients were of fever 105 (46.67%) followed by asymptomatic UTI [98; 43.56%]. The presence of anemia and leucocytosis had statistically no significant association with UTI while poor glycaemic control has statistically significant association with UTI in diabetic patients. *E. coli* (32.14%) was commonest microorganism isolated in urine culture. Gram negative organisms were mostly sensitive to Imipenem, Piperacillin-tazobactam and Nitrofurantoin while gram positive bacteria were mostly sensitive to Linezolid, Nitrofurantoin, Vancomycin, Tetracyclin, Clindamycin and Azithromycin and showed increased resistance to Fluroquinolones and Cotrimoxazole. *Candida* sp. was sensitive to Fluconazole, Itraconazole.

**Conclusion:** UTI was more commonly associated in elderly diabetics with female predominance. The observed trends in clinical and laboratory profile, causative organism patterns, and antimicrobial susceptibilities will help to reduce morbidity and mortality.

**Keywords:** Diabetic, Urinary tract infection, Microorganisms, Antibiotic, Bacteriuria, Anemia, Leucocytosis, *E. coli*.

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## 1. Introduction

Diabetes mellitus (DM) has become a serious public health threat in both developed and developing countries, affecting more than 366 million people, and the number is expected to rise to 552 million by 2030 [1]. However the changing lifestyle and urbanization has caused an increase in the incidence in developing countries, including India [2]. It has been estimated that India has the largest number of diabetics in the world, with a prevalence

of about 40.9 million individuals [3]. Infections are frequent causes of morbidity and mortality in diabetic patients, evidence suggesting that UTI is the most common bacterial infections among diabetic patients because of sugar in urine, which serves as media for growth of bacteria [4].

An association between UTI and DM was first noted in an autopsy series in 1940's. Many autopsy studies

have shown an increased prevalence of UTI in diabetics [5]. Women with diabetes are about two to three times more likely to have bacteria in their bladders than women without diabetes. Interestingly, the same does not appear to be true for men. There also seems to be an increased risk of the infection spreading upwards into the kidneys in diabetic patients and diabetic women with UTI are also more likely to require hospitalization than non-diabetic women [6]. Diabetes affects many systems that protect against infection in general and against urinary tract infections specifically. Poor circulation in diabetics, reduced ability of white blood cells to fight infection, dysfunctional bladders that contract poorly, all contribute to the increased prevalence of UTI in diabetics. Asymptomatic bladder infections detected by a positive urine culture are also common among diabetics without any clinical evidence of UTI. Recurrent UTI are common in diabetics [7].

Hence a study was planned with the rationale to know the clinical and laboratory profile of UTI as well as clinical and microbial spectrum, and antimicrobial sensitivity of these organisms that cause UTI in diabetics in our locality of study.

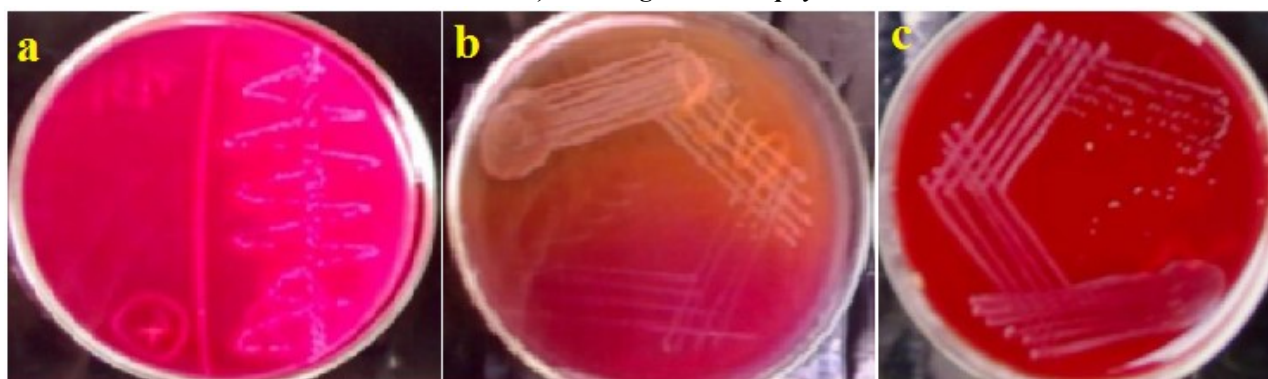
## 2. Materials and Methods

After obtaining Institutional Ethics Committee approval and written informed consent from all the patients, this descriptive observational study was carried out at in the Department of Medicine, at Tertiary Care Hospital in central India, during the period from November 2016 to November 2018. Study consisted of total 224 type1 and type 2 diabetic patients, age > 18 years with or without symptoms of UTI with significant bacteriuria. Patient with gestational diabetes, immune-compromised states-HIV, patients on steroids, malignancy, transplant recipients were excluded from the study.

A detailed history, physical examination and relevant clinical investigations were recorded as per case proforma. Diagnosis of UTI was made on the basis of clinical history, symptoms and detailed clinical examination and confirmed by urine examination. Other investigations include CBC, serum creatinine, blood urea, HBA1C, fasting and post meal blood sugar and USG abdomen with pelvis. CT scan KUB was done wherever necessary. Midstream urine sample of about 20ml was collected under sterile conditions and immediately transported to the microbiology laboratory of the hospital. After ensuring that the urine sample was uncontaminated by normal vaginal /urethral flora, it was centrifused at 3,000 R.P.M. for 5 minutes, after which the supernatant fluid was drained off, the deposit re-suspended and the last drop or two under a cover slip examined under a microscope (\*400 magnification). Presence of pyuria (>\_10 leukocytes/hpf) with a positive leukocyte esterase and /or nitrate test was considered as a positive urine analysis. Only those patients fulfilling these screening criteria for significant bacteria were included in the study.

For culture analysis, the urine samples were inoculated on Urechrom II media with calibrated loop (0.001 ml of sample), incubated aerobically at 37°C for 24 to 48 hours, and examined. The isolated microorganism was identified to the species level as per standard protocols. The plate was incubated, the number of colonies counted or estimated, and this number used to calculate the number of viable bacteria/ml of urine. Significant bacteriuria (SB) was defined as presence of >10<sup>5</sup> colony forming units (CFU) of isolated organisms per milliliter of urine sample in urine culture. Cultural media plates were examined under magnifying lens and identified using the standard microbiological procedures like colony morphology.

**Image 1: a) Mackonkeys agar with lactose fermenting of *E. Coli*, b) Mackonkeys agar with non-lactose fermenting colonies of *Pseudomonas* and c) Blood agar with *Staphylococcus aureus* colonies**



Antimicrobial susceptibility testing was performed using Kirby-Bauer disc diffusion method employing Mueller-Hinton Agar plate. The antibiotic discs representative of Penicillin group, Cephalosporins, Aminoglycosides, Quinolones and Nitrofurantoin were obtained in the following concentrations: Ampicillin (10µg), Amikacin (30µg), Gentamycin (10µg), Cefotaxime (30µg), Ceftriaxone (30µg), Nalidixic acid (30µg), Ciprofloxacin (5µg), Ofloxacin (5µg), Norfloxacin (10µg) and Nitrofurantoin (300µg). The inoculated plates were incubated at 37°C for 18-24 hours. Diameter of the zone of inhibition around the disc was measured to the nearest millimeter using a vernier caliper. The zone size around each antimicrobial disc was interpreted as susceptible or resistant based on the criteria indicated in tables provided by the manufacturer and CLSI (Clinical And Laboratory Standards Institute) guidelines, e.g. For *E. coli*.

### 2.1 Statistical analysis

Categorical variables were expressed in frequency and percentages (proportion). Continuous variables were presented as mean ± SD. Pearson chi square test was used to compare categorical variables while Student t- test was used to compare continuous variables. Statistical software STATA version 13 was used for data analysis.

## 3. Observations and Results

The present study consisted of total 224 cases of diabetes with symptomatic or asymptomatic UTI, among them 88 (39.28%) were males and 136 (60.71%) were

females, ( $p < 0.001$ , HS). Age of the patients ranged from 19 to 90 years with mean age was  $62.65 \pm 14.27$  years. The maximum number of cases [60 (26.78 %)] were in the age group of 61-70 year as shown in Table 1. There were 8 (3.57%) patients of type 1 diabetes and 216 (96.42%) patients of type-2 diabetes with UTI. Highest number of patient 135(60.27%) having diabetes duration > 10 year while 89(39.73%) patients having diabetes duration < 10 years. Thus, the duration of diabetes >10 years had statistically significant association with UTI in DM patients ( $p$  value <0.001).

**Table 1: Age distribution of patients**

Age in Years	No. of patients	Percentage
11-20	1	0.44
21-30	4	1.78
31-40	6	2.67
41-50	29	12.94
51-60	55	24.55
61-70	60	26.78
71-80	47	20.98
81-90	22	9.82
Total	224	100

Among the patients, highest number of patients were of fever 105 (46.67%) followed by asymptomatic UTI [98; 43.56%]. Some patients presented with more than one symptom. Hematuria was present only in two (0.89%) patients, (Figure 1).

**Figure 1: Clinical profile of the patients**

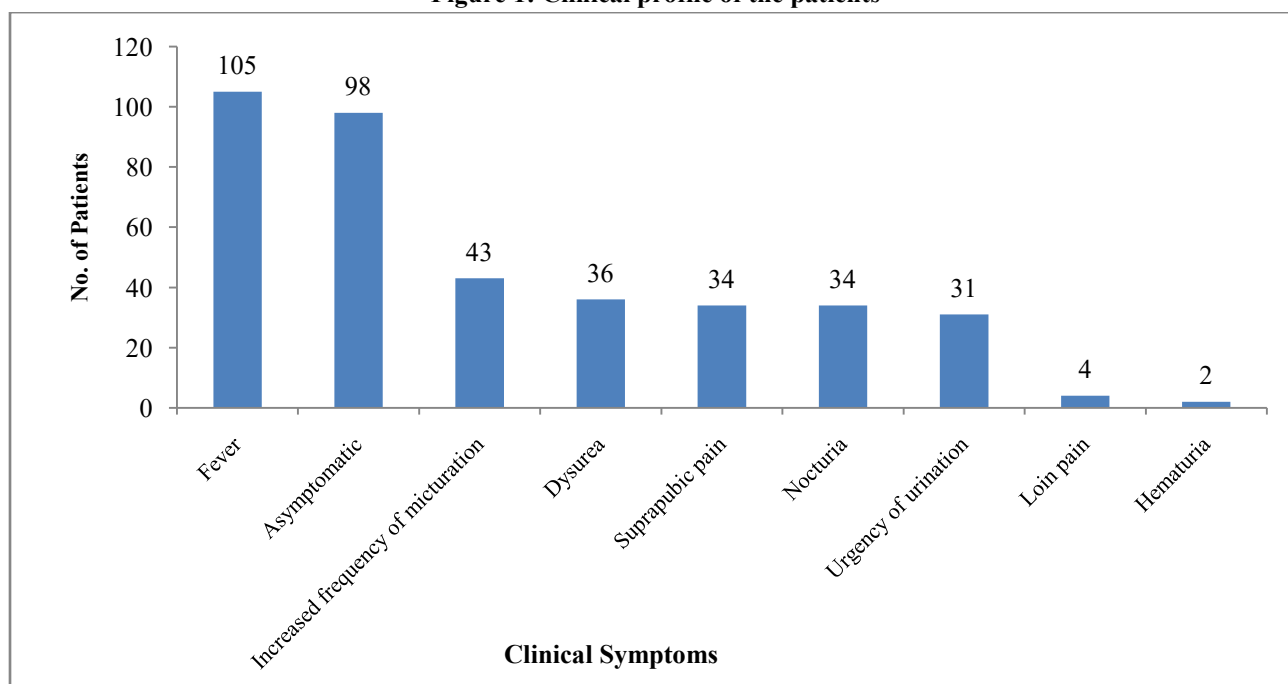


Table 2 showed laboratory profile of the diabetics' patients. A total of 211 patients had anaemia and presence of anemia was found to have statistically no significant association with UTI in DM patients, (p value 0.950, NS). There were 126 patients with symptomatic UTI out of which 90 patients had leukocytosis and there were 98 asymptomatic UTI out of which 60 patients had

leukocytosis. Presence of leukocytosis had statistically no significant association with UTI in DM patients, (p value 0.107). 202 patients had HbA1C more than 7% and 22 patients had HbA1C less than 7%. Poor glycaemic control had statistically significant association with UTI in DM patients, (p value < 0.001).

**Table 2: Laboratory profile of the patients**

Investigation	Mean $\pm$ SD	Range
Haemoglobin(gm)	9.14 $\pm$ 1.67	5-13
WBC( $\times 10^3$ cmm)	13.10 $\pm$ 2.91	3-24
Serum Creatinine(mg/dl)	1.54 $\pm$ 0.75	1-6
Blood Urea(mg/dl)	45.38 $\pm$ 6.79	4-60
HbA1C (%)	9.07 $\pm$ 1.59	0.9-13.2

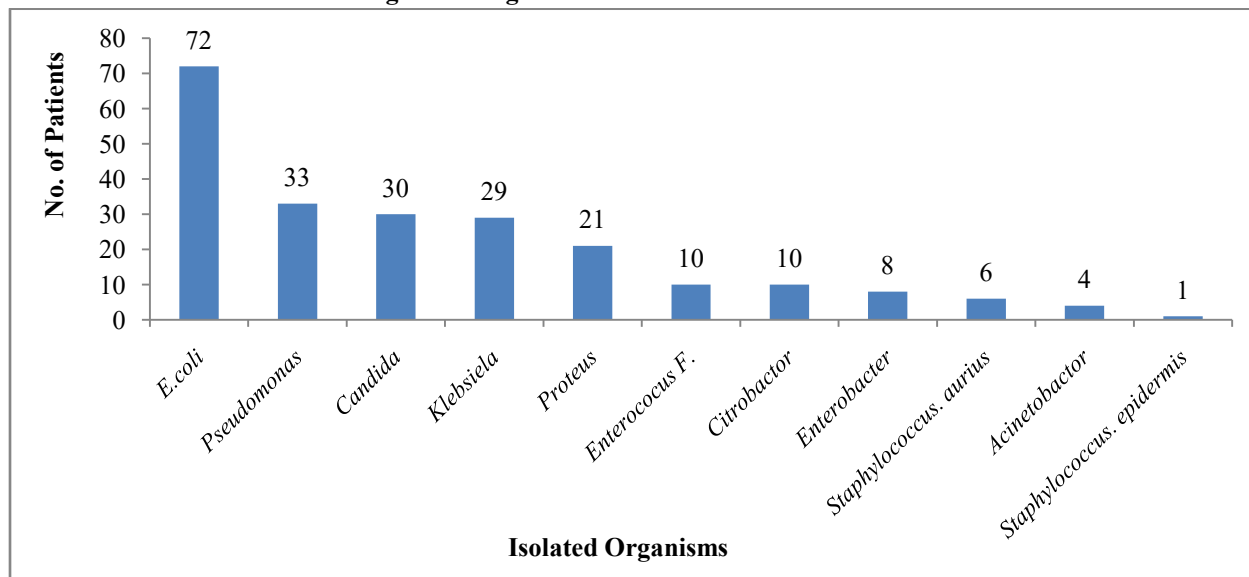
The maximum number of patients (90; 40.2%) had specific gravity > 1.028 and majority of patients (126; 56.25%) had urine pH between 6 – 6.99 as shown in table 3.

**Table 3: Distribution of patients according to Urine Examination**

Urine examination		No. of Patients	Percentage
Urine gravity	<1.02	75	33.5
	1.02-1.028	59	26.3
	>1.028	90	40.2
Urine PH	5-5.99	91	40.63
	6-6.99	126	56.25
	$\geq 7$	7	3.13

*E. coli* was commonest microorganism isolated in urine culture, followed by *pseudomonas* as shown in figure 2.

**Figure 2: Organisms isolated from urine culture**



Gram negative organisms like *E. coli*, *Pseudomonas*, *Klebsiella*, *Proteus*, *Citrobacter* spe and *Acinetobacter* were mostly sensitive to Imipenem, Piperacillin-tazobactam and Nitrofurantoin. Gram positive bacteria like *Enterococcus F.*, *Staphylococcus* were mostly

sensitive to Linezolid, Nitrofurantoin, Vancomycin, Tetracyclin, Clindamycin, Azithromycin and showed increased resistance to Fluroquinolones and Cotrimoxazole, (Table 4). *Candida* sp. was sensitive to Fluconazole, Itraconazole.

**Table 4: Drug sensitivity pattern of organisms**

Organisms	Maximum Sensitivity		Minimum Sensitivity	
	Drug	No. (%)	Drug	No. (%)
<i>E. Coli</i>	Imipenem	68 (94.4)	Ceftriaxone	2 (2.7)
<i>Pseudomonas</i>	Imipenem	31 (93.9)	Cotrimoxazole	7 (21.2)
<i>Klebsiella</i>	Imipenem	24 (82.7)	Ampicillin	2 (6.8)
<i>Proteus</i>	Nitrofurantoin	18 (85.7)	Ceftriaxone	5 (23.8)
<i>Enterococcus F.</i>	Linezolid	8 (80)	Erythromycin	2 (20)
<i>Citrobactor</i>	Imipenem	10 (100)	Levofloxacin	5 (50)
<i>Enterobacter</i>	Imipenem	6 (75)	Levofloxacin	2 (25)
<i>Staphylococcus. Aurius</i>	Vancomycin	5 (50)	Gentamycin	1(16.6)
<i>Acinetobactor</i>	Polymyxin B	3 (75)	Ampicillin	0 (0)
<i>Staphylococcus epidermis</i>	Vancomycin	1 (100)	Ampicillin	0 (0)

There was no significant correlation between urine culture isolates and age, gender and duration of diabetes of study population, (Table 5).

**Table 5: Correlation of urine culture isolates with age, gender and duration of diabetes**

Urine culture	Age of the patients								Gender		Duration of diabetes	
	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	Males	Females	<10	≥10
<i>E. Coli</i>	1	2	1	0	23	23	0	22	33	39	35	37
<i>Pseudomonas</i>	0	1	3	13	1	10	5	0	12	21	16	17
<i>Klebsiella</i>	0	0	1	2	14	8	4	0	9	20	8	21
<i>Proteus</i>	0	0	0	7	2	4	8	0	6	15	9	12
<i>Enterococcus F.</i>	0	0	0	1	1	2	6	0	3	7	5	5
<i>Citrobactor</i>	0	1	0	1	0	3	5	0	5	5	5	5
<i>Acinetobactor</i>	0	0	0	0	2	1	1	0	2	2	2	2
<i>Enterobacter</i>	0	0	1	3	0	0	4	0	2	6	5	3
<i>Staphylococcus. Aurius</i>	0	0	0	2	0	0	4	0	2	4	4	2
<i>Staphylococcus epidermis</i>	0	0	0	1	0	0	0	0	0	1	0	1

#### 4. Discussion

In the present study, the mean age of patients was  $62.65 \pm 14.27$  years and maximum numbers of cases (26.78 %) were in the age group of 61-70 years. This may be because of greater duration of diabetes in older patient. Similar findings were also seen in Vaishnav *et al* study [8]. The female to male ratio was 1.54:1. Thus, the female preponderance was noted which is comparable with the previous studies [9, 10]. Also, female gender was found to have significant relationship with UTI in diabetic patients (p value <0.001, HS). In general population also female genders have more prevalence of UTI compared to males. Risk factors for female gender being more prone for UTI are, ascent of bacteria from urethra to bladder is easier in females because of short urethra; the absence of bactericidal prostatic secretions and sexual intercourse may help transfer of bacteria from perineum to bladder. Highest numbers of patients were from group duration of diabetes > 10 year (60.27%). Longer duration of diabetes had significant relationship with occurrence of UTI. Similar findings were also seen in earlier studies [8, 11, and 12].

The prevalence of asymptomatic bacteriuria was found to be 43.56%. These patients included those enrolled from diabetic OPD and those enrolled who were admitted for other than UTI. Fever was the most common clinical presentation and was seen in patients of pyelonephritis, prostatitis, complicated UTI, CAUTI (catheter associated UTI). However admitted patient had other comorbidities and presence of other infections also, because of this fever is seen in majority of patients. These findings are correlated well with the study done by Jaipuria *et al* [9] and Srinivas *et al* [10].

According to American diabetic association poor glycemic control is defined as HbA1C >7% and good control as HbA1C <7%. In present study, poor glycaemic control was found to have statistically significant association with occurrence of UTI in diabetics. Borj *et al* [13] found that out of 100 diabetics with (59 males and 41 females) twenty- nine of diabetics had HbA1c levels >8.0%. Urine specific gravity normal range is 1.003 to 1.030. Urinary specific gravity correlates with urine osmolality and gives important insight into the patients' hydration status. It

is increased in glucosurea, which may be present in poor glycemic controlled DM patients [14].

In present study, maximum cases [90(40.2%)] had specific gravity more than 1.028. Specific gravity less than 1.02 was present in 75(33.5%) patients. Normal urine pH is slightly acidic, with usual values of 6.0 to 7.5, but the normal range is 4.5 to 8.0. A urine pH of 8.5 or 9 is indicative of a urea splitting organism, such as *Proteus*, *Klebsiella*, or *Ureaplasma Urealyticum*; therefore an asymptomatic patient with high urine pH means UTI. Alkaline pH also can signify struvite kidney stones, which are also known as infection stones [15]. In current study, urine pH 6 – 6.99 had seen in maximum number of patients [126 (56.25%)], Only 7(3.13%) patients had pH between 5 - 5.99.

Most common isolate was *E. coli*, found in 72 patients and second most common was *Pseudomonas*, grown in 33 patients. *Candida* was isolated in significantly greater number as compared to non-diabetics UTI in reference studies, in 13.3%. This may be because of immunological dysfunction which occurs in diabetic population. Similar findings reported in other studies [8,10,16]. Gram negative organisms *E. coli*, *Pseudomonas*, *Klebsiella*, *Proteus*, *Citrobacter spe* and *Acenetobacter* were mostly sensitive to Imipenem, Piperacillin-tazobactam and Nitrofurantoin. Gram positive bacteria *Enterococcus F*, *Staphylococcus* were mostly sensitive to Linezolid, Nitrofurantoin, Vancomycin, Tetracyclin, Clindamycin, Azithromycin and showed increased resistance to Fluroquinolones and Cotrimoxazole. *Candida* was sensitive to Fluconazole, Itraconazole. Thus imipenem was found to be useful in most UTI (94.40%), hence Imipenem can be useful for empirical treatment of UTI pending the culture reports.

Piperacillin-tazobactam was found to be of useful in 50% of patients of UTI. Ceftriaxone was not found to be useful and similarly ampicillin also showed wide resistance. Antibiogram and sensitivity patterns change from centre to centre and also time to time. These findings of our study are comparable with the previous studies [10, 17 and 18].

*E. coli* n=23(31.9%) was isolated from urine in patients of 51-60 years age group. *Pseudomonas* n=13(39.3%) was isolated from urine in 41-50 years age group, *Klebsiella* 14(48.27%) was commonly isolated from urine in patients of 51-60 years age group. In gender wise distribution, *E. coli* was found in n=39(54.16%) in females and in males n=33(45.83%). *E. coli*, *Klebsiella* and *Pseudomonas* were common in patients of >10year duration group of diabetes patients. But there was no significant correlation between urine culture isolates and age, gender and duration of diabetes. Similar findings were also noted in other studies [8-10].

## 5. Limitations of the Study

- Sample size may not be appropriate representative of the population.
- Patients are enrolled from tertiary care hospital where most of the patients are referred patients and thus true prevalence may differ from seen in general population.
- Present study was carried out in Government tertiary care hospital, where investigation and treatment resources are limited.
- Follow up of patient and recurrent UTI was not done as the study was descriptive observational.

## 6. Conclusion

UTI is more commonly associated in elderly diabetic patients with more risk in female gender. Asymptomatic bacteriuria was prevalent in 43.56% diabetic patient. Fever is most common symptom seen for UTI in diabetics, so any patient of fever, presenting with or without urinary symptom should be evaluated for presence of UTI. Poor diabetic control (HbA1c>7%) and longer duration of diabetes (>10 yrs) are associated with more risk of UTI in diabetics. *E. coli* was the most common causative organism and majority of isolated organisms were sensitive to antimicrobial agents like imipenem. Thus Imipenem can be used for empirical treatment for UTI in diabetics pending culture report. Piperacillin-tazobactam is second drug which can be used for empirical treatment of UTI in diabetics, however ceftriaxone and ampicillin showed wide resistance and thus should not be used for empirical treatment of UTI in diabetics. Good control of diabetes must be achieved to reduce the risk of UTI in diabetic.

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