

Original Research Article

## “A STUDY ON CLINICAL PROFILE OF URINARY TRACT INFECTION IN DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL”

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### ABSTRACT:

**Background:** Diabetic Patients are at high risk of developing various infections especially if the diabetes is uncontrolled. Urinary tract infections (UTI) are one of the common infections in diabetics. Knowledge about the clinical and microbiological profile of UTI in diabetic patients will not only aid in early diagnosis but also helps in early initiation of appropriate empirical antibiotic therapy ensuring early recovery.

### OBJECTIVES:

1. To study the clinical pattern of urinary tract infections in diabetics.
2. To study the common causative organisms and their antibiotic sensitivity pattern in diabetics.
3. To study the common causative organisms in different level of glycaemic control (defined by HbA1c) in diabetic patients.
4. To study the relationship of duration & poor control of diabetes mellitus (defined by HbA1c>8%) to the incidence of UTI.

**MATERIAL & METHODS: Study Design:** Prospective hospital based observational study. **Study area:** The study was conducted in the In-patient department, Department of General medicine at KMCT Medical college, Manassery, Kozhikode, Kerala, India. **Study Period:** June 2019 – May 2020. **Study population:** This study was conducted in 170 Diabetic patients above 18 years of age with symptoms of UTI with significant pyuria who were admitted under department of General Medicine, KMCT medical college, Kerala, who satisfied the inclusion criteria and gave consent for study. **Sample size:** study consisted a total of 170 subjects. **Sampling method:** Simple Random sampling method.

**Results:** Fever was the most common clinical presentation followed by dysuria. E. coli was the most commonly isolated organism followed by Klebsiella. Most of the organisms were sensitive to Amikacin. Antibiotic resistance and Pyelonephritis were higher in patients with

poor glycaemic control. The most common ultrasonographic abnormality was prostatomegaly.

### **CONCLUSION:**

Patients with poor glycaemic control are at high risk of resistant UTI and Pyelonephritis. Good glycaemic control with routine monitoring of HbA1C is mandatory in diabetic patients to prevent UTI and to avoid its complications. E. coli was the most common organism isolated followed by Klebsiella. Most of the organisms were sensitive to Amikacin. Hence, Amikacin can be recommended as empirical antibiotic for Diabetic patients who are admitted with UTI.

**Key words:** Urinary tract infections, antibiotic sensitivity, diabetic patients

### **INTRODUCTION:**

Description of Diabetes has been mentioned historically with the symptom of polyuria at 1500 BC in the Egyptian Papyrus Ebers descripts. Knowledge about diabetes has evolved progressively since then from the era of tasting urine to measure blood glucose levels, to measurement of HbA1c levels.<sup>1</sup> With the advancement of screening and diagnostic tools and invention of insulin and newer OADs (oral ant diabetic agents), the mortality and morbidity due to poor diabetic control are significantly reduced.

Diabetic Patients are at high risk of developing various infections especially if the diabetes is poorly controlled. Urinary tract infections (UTI) are one of the common infections in diabetics. Diabetes affects the cell mediated innate immunity, decreases the function of polymorphonuclear cells and monocytes/macrophages and decreases their ability to secrete IL-1 and IL-6. Their function improves once the hyperglycemia is adequately controlled.<sup>2</sup> Some microorganisms become more virulent in a high glucose environment. Alteration in humoral innate immunity and decrease in C4 complement activity have also been described in diabetic patients. Autonomic neuropathy and cystopathy secondary to diabetes causes bladder dysfunction and stasis of urine, which further increase the risk UTI in diabetics and increase the overall prevalence of UTI in diabetics.<sup>3</sup>

An observational study conducted in UK general practice research noticed that the incidence rate of UTI was 46.9 per 1,000 persons among diabetics and 29.9 for non-diabetics.<sup>4</sup>

An American database study conducted in 2014 found that UTIs were more common in patients with diabetes compared to those without diabetes (9.4% vs. 5.7%, respectively).<sup>5</sup>

The causative organisms and their sensitivity patterns due to the emergence of antibiotic resistance are changing over the last few decades. Knowledge about the disease, the spectrum of bacteria and their sensitivity pattern to antibiotics and the common complications of UTI will help to reduce morbidity and mortality. The significance of this study lies in the fact that determination of common pathogens of UTI in diabetic patients in different level of glycaemic control (defined by HbA1c) and the resistance pattern of antibiotics help the clinicians to get useful information regarding the choice of antibiotics in diabetic population.

In recent years, there have been numerous researches to identify the clinical profile of urinary tract infections in diabetic patients. However, such studies on diabetic patients in South India are limited. With this background we intend to look at the clinical & laboratory profile of UTI in diabetic patients admitted at a tertiary care center.

**OBJECTIVES:**

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**Study Design:** Prospective hospital based observational study.

**Study area:** The study was conducted in the In-patient department, Department of General medicine at KMCT medical college, Manassery, Kozhikode, Kerala, India.

**Study Period:** June 2019 – May 2020.

**Study population:** This study was conducted in 170 Diabetic patients above 18 year of age with symptoms of UTI with significant pyuria who were admitted under department of general medicine, KMCT medical college, Kerala, who satisfied the inclusion criteria and gave consent for study.

**Sample size:** study consisted a total of 170subjects.

**Sampling method:** Simple Random sampling method.

**Inclusion criteria:** Diabetic patients >18 year of age with symptoms of UTI with significant pyuria and positive urine culture.

**Exclusion criteria:**

1. Gestational diabetes
2. Patients on urinary catheter
3. Patients with Anaemia (defined by Haemoglobin in males<13 & in females <12) to avoid false HbA1c levels.
4. Immunocompromised states like- HIVAIDS, Patients on steroids, Patients with Malignancy, Transplant recipients

**Ethical consideration:** Institutional Ethical committee permission was taken prior to the commencement of the study.

**Study tools and Data collection procedure:**

This Descriptive Cross-sectional study was conducted after obtaining approval from hospital ethics committee & scientific committee. 170 patients who were admitted in General medicine department, KMCT Medical College were chosen for this study, over a period of one year. Patients having a history of diabetes or with fasting venous blood glucose value>126mg/dl or post prandial blood sugar >200mg/dl and HbA1c level >6.5% with clinical and microbiological features of urinary tract infections, were included in this study.

A detailed history was taken after taking consent from the patients, including duration of diabetes and type of medications for diabetes, history in relation to urinary tract infection like burning micturition, frequency, urgency, dysuria, suprapubic pain and hematuria. Any symptoms suggestive of acute Pyelonephritis like fever, chills, nausea, vomiting and flank pain were noted. Previous histories of urinary tract instrumentation or catheterization were also duly noted.

A detailed examination of all systems with special emphasis on temperature, pulse rate, blood pressure, suprapubic tenderness, renal angle tenderness, tenderness/ mass on deep abdominal palpation was carried out.

Midstream, clean catch urine samples were collected and sent to laboratory for routine urine evaluation and for culture and sensitivity.

HbA1c estimation was done, and patients were divided into good (<7%), moderate (7-8%), poor (>8%), very poor (>10%) according to the glycaemic control based on HbA1c values.

Other investigations including Complete blood count, FBS, PPBS and USG abdomen were done in all patients.

#### Statistical analysis:

Data entry was done in Microsoft Excel software. Data analysis was done in Statistical Product and Service Solutions (SPSS). Continuous variables were analysed by mean, standard deviation, median, mode, minimum and maximum. Qualitative variables were described by percentage distribution among groups. Comparison of quantitative variables was done by t-test and qualitative variables were compared by Chi square test. P value of less than 0.05 was taken as level of significance.

#### OBSERVATIONS & RESULTS:

**Table 1: Age wise distribution**

Gender	N (%)	MeanAge	SD
Male	88(51.8)	72.29	10.68
Female	82(48.2)	63.84	15.17
Total	170(100)	68.21	13.64

Among the 170 patients, 88 were males which constitutes for 51.8% and the mean age of male population was 72.29. 82 subjects were females which constitutes for 48.2% and the mean age of female subjects was 63.84.

Mean duration of diabetes in this study is  $12.11 \pm 6.72$ . Among these 170 patients, 60.6% were taking OHA, 8.2% were taking insulin, 24.1% were taking both and 1.8% was not on treatment.

**Table 2: Clinical presentation**

Clinical presentation	n (%)
Fever	145(85.3)
Dysuria	59(34.7)
Frequency	33(19.4)
Vomiting	40(23.5)
Pyuria	4(2.4)

<b>Haematuria</b>	3(1.8)
<b>Suprapubic Pain</b>	34(20)
<b>Flank Pain</b>	10(5.9)
<b>Suprapubic Tenderness</b>	24(14.1)
<b>Renal Angle Tenderness</b>	9(5.3)

Majority of the patients presented with fever (85.3%), followed by dysuria (34.7%). 23.5% of the patients had vomiting, 20% had suprapubic pain and 19.4% had increased frequency. Flank pain was present in 5.9% of the subjects while 2.4% had pyuria and 1.8% had haematuria. On examination 14.1 % of the subjects had suprapubic tenderness and 5.3 % had renal angle tenderness. Fever was the most common presentation and haematuria was the least common presentation in this study.

Leukocytosis was seen in majority of diabetics with UTI, mean average was 14716.66 cells per cubic millimetre and mean Hb was 12.84g/dl. Mean values of FBS and PPBS were 165.76 and 258.58 mg/dL respectively.

On evaluation of diabetic control by measuring HbA1c, Mean HbA1c was 7.94±2.70%. Among these 170 patients, 51.8% had good control, 17.1% had moderate control, 12.9% had poor control and 18.2% had very poor control of diabetes.

Majority of the patient had acidic urine (97.1%), only 2.9% had alkaline urine. Haematuria was seen in 4.7% of the patients.

**Table 3: Organisms isolated from urine culture**

<b>Organisms Isolated &gt;10*5CFU</b>	<b>N</b>	<b>%</b>
<b>E.coli</b>	102	60
<b>Klebsiella</b>	31	18.2
<b>Pseudomonas</b>	13	7.6
<b>Candida spp</b>	8	4.7
<b>Proteus</b>	6	3.6
<b>Enterococcus</b>	5	2.9
<b>Acinetobacter</b>	3	1.8
<b>MRSA</b>	1	0.6
<b>Mixed</b>	1	0.6
<b>Total</b>	170	100

E.coli was the predominant organism isolated (60%), followed by Klebsiella (18.2%), pseudomonas (7.6%), Candida spp (4.7%), Proteus (3.6%) and Enterococcus (2.9%). Acinetobacter (1.8%) and MRSA (0.6%) were the least common organisms. Mixed growth (0.6%) is probably due to urine sample contamination.

**Table 4: Antibiotic Sensitivity Pattern**

	S	R
<b>Ampicillin</b>	20(12.3)	142(87.7)
<b>Meropenem</b>	150(92.6)	12(7.4)
<b>Cefazolin</b>	45(27.8)	117(72.2)
<b>Cefuroxime</b>	51(31.5)	111(68.5)
<b>Ceftriaxone</b>	73(45.1)	89(54.9)
<b>Cefipime</b>	100(61.7)	62(38.3)
<b>Cefoperazone-Sulbactam</b>	129(79.6)	33(20.4)
<b>Gentamycin</b>	106(65.4)	56(34.6)
<b>Amikacin</b>	160(98.8)	2(1.2)
<b>Norfloxacin</b>	78(48.1)	84(51.9)
<b>Ciprofloxacin</b>	78(48.1)	84(51.9)
<b>Nitrofurantoin</b>	125(77.2)	37(22.8)
<b>Cotrimoxazole</b>	96(59.3)	66(40.7)
<b>Fosfomycin</b>	135(83.3)	27(16.7)

Majority of the organisms were sensitive to Amikacin (98.8%), followed by Meropenem (92.6%), Fosfomycin (83.3%), Cefoperazone-Sulbactum (79.6%), Nitrofurantoin (77.2%) and Cotrimoxazole (59.3%). Most of the organisms were resistant to Ampicillin (87.7%), Cefazolin (72.2%) and Cefuroxime (68.5%), Norfloxacin (51.9%) and Ciprofloxacin (51.9%).

Among these antibiotics E.coli was mostly sensitive to Amikacin followed by Meropenem and Nitrofurantoin. Klebsiella was mostly sensitive to Amikacin followed by Meropenem, Fosfomycin and Cefoperazone -Sulbactum. Enterococcus was exclusively sensitive to Linezolid and Vancomycin.

Ultrasound abdomen results of 64.7% of the subjects were normal, 17.1% had cystitis, 8.2% had Pyelonephritis and 1.2% had emphysematous Pyelonephritis. Hydrouretronephrosis and renal abscess were detected in 0.6% each. Prostatomegaly was detected in 12 male patients (7.1% of total number of subjects).

**Table 5: Incidence of upper and lower UTI**

	N	%
<b>Lower UTI</b>	152	89.4
<b>Upper UTI</b>	18	10.6
<b>Total</b>	170	100

Of the 170 patients evaluated in this study, majority (89.4%) had lower UTI. 10.6 % of the patients had features consistent with upper UTI.

**Table 6: Association between diabetic control and organisms isolated**

	Acinetobacter	Candida spp	E.coli	Enterococcus	Klebsiella	mixed	MRSA	Proteus	Pseudomonas	Total	P value
<b>Good</b>	3	2	52	3	18	1	0	6	3	88	0.02*
	3.4%	2.3%	59.1%	3.4%	20.5%	1.1%	0.0%	6.8%	3.4%	100.0%	
<b>Moderate</b>	0	1	14	1	5	0	0	0	8	29	
	0.0%	3.4%	48.3%	3.4%	17.2%	0.0%	0.0%	0.0%	27.6%	100.0%	
<b>Poor</b>	0	1	15	0	3	0	1	0	2	22	
	0.0%	4.5%	68.2%	0.0%	13.6%	0.0%	4.5%	0.0%	9.1%	100.0%	
<b>Very Poor</b>	0	4	21	1	5	0	0	0	0	31	
	0.0%	12.9%	67.7%	3.2%	16.1%	0.0%	0.0%	0.0%	0.0%	100.0%	

**Chi square value: 43.81. P value of 0.02 is statistically significant**

Among different categories of glycaemic control, E.coli was the most common organism found in all categories. Klebsiella was the second most common organism in all categories except in group with moderate control, where Pseudomonas was the second most common organism isolated. Candida spp were isolated in patients with very poor control of diabetes.

**Table 7: Association between incidence of UTI and age**

	Mean age	SD	P value
<b>Lower UTI</b>	69.13	13.72	0.01*
<b>Upper UTI</b>	60.50	10.72	



P value <0.05 is statistically significant; \*\* <0.001 is statistically highly significant, Independent t test. Mean age of patients with UTI was above 60 in patients with either lower UTI or upper UTI.

**Table 8: Association between UTI and control of diabetes (defined by HbA1c)**

	Good	Moderate	Poor	Very Poor	P value
<b>Lower UTIn(%)</b>	85(55.9)	25(16.4)	20(13.2)	22(14.5)	0.001*
<b>Upper UTIn(%)</b>	3(16.7)	4(22.4)	2(11.1)	9(50)	

p value <0.05 is statistically significant; \*\* <0.001 is statistically highly significant, chi square test.

Incidence of upper UTI was common in very poorly controlled diabetes (50%) and lower UTI was common in good (55.9%) to moderate (16.4%) control of diabetes.

**Table 9: Association between symptoms and control of diabetes**

		Fever	Dysuria	Frequency	Vomiting	Pyuria	Haematuria	Suprabubic Pain	Flank Pain	P value
<b>Good</b>	n	74	34	24	18	1	2	16	2	0.03*
	%	43.3%	19.9%	14.0%	10.5%	0.6%	1.2%	9.4%	1.2%	
<b>Moderate</b>	n	25	9	4	11	1	1	9	2	
	%	40.3%	14.5%	6.5%	17.7%	1.6%	1.6%	14.5%	3.2%	
<b>Poor</b>	n	19	3	3	3	2	0	4	1	
	%	54.3%	8.6%	8.6%	8.6%	5.7%	0.0%	11.4%	2.9%	
<b>Very poor</b>	n	28	4	2	8	0	0	5	5	
	%	53.8%	7.7%	3.8%	15.4%	0.0%	0.0%	9.6%	9.6%	
<b>Total</b>	n	146	50	33	40	4	3	34	10	



	%	45.6%	15.6%	10.3%	12.5%	1.2 %	0.9%	10.6%	3.1%	
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**P value of 0.03 is statistically significant**

Fever was the most common clinical presentation in all categories of glycaemic control.

## DISCUSSION:

In this study 170 diabetic patients with signs and symptoms of UTI with urine culture positivity were included.

Among the 170 patients, 88 were males and 82 were females and the mean age of males and females were 72.29 and 63.84 respectively. There was significant (p-0.01) correlation between age and incidence of UTI in this study, higher incidence was seen in older age group. Similar finding was seen in a study conducted by Mustafa et al<sup>6</sup>, at Sabah General Hospital Malaysia, where it was found that the peak incidence of UTI occurred in diabetic patients aged 60 years and above. These findings were similar to the present study.

Among the 170 patients, 88 were males which constitutes for 51.8% and 82 were females which constitutes for 48.2%. In this study UTI was predominantly seen diabetic males. These findings were comparable to the study done by Jegadeeswaran et al<sup>7</sup>, where males (53.3%) dominated females (46.7%).

Analyzing the control of diabetes by HbA1c and its association with the incidence of UTI found that there is highly significant (p-0.001) correlation between increased incidences of upper UTI (50%) with poor control of diabetes defined by HbA1c.

Mean duration of diabetes in this study was 12.11 years  $\pm$ 6.72. In the present study the incidence of UTI was more common when the duration of diabetes is more than 12 years. It indicates that longer duration of diabetes increases the risk of developing UTI. Similar finding was seen in a study conducted by Swaine L Chen et al, where increased susceptibility of UTI in diabetics were associated with increased duration and severity of diabetes.<sup>8</sup>

In our study, patients who were taking OHA only for diabetes constituted 60.6%. 8.2% of the subjects were on insulin alone while 24.1% of them took both OHA and insulin. Among the 170 patients, (based on HbA1c) 51.8% had good control, 17.1% had moderate control, 12.9% had poor control and 18.2% had very poor control of diabetes. In a study conducted by Edward J et al<sup>9</sup>, it was found that incidence of UTI was higher in patients who used oral hypoglycemic agents and insulin compared to control group. However, in our study incidence of UTI was found to be more in diabetics who were taking OHA than insulin. In a prospective observational study conducted by Sylvester JS et al,<sup>10</sup> out of the 100 diabetics with UTI 43% had poor glycaemic control, patients on OHA had better glycaemic control than those on insulin and UTI was commonly seen with poor glycaemic control group. However, in our study incidence of UTI was found to be higher in diabetics who were taking OHA compared to patients on insulin.

Most common presenting complaint was fever (85.3%) followed by dysuria (34.7%) and vomiting (23.5%). On examination suprapubic tenderness (14.1%) was more common than renal angle tenderness (5.3%). Hematuria was the least common presentation in this study, and it was significantly associated with UTI caused by Enterococcus species than other

organisms. Similar presenting complaints were seen in a study done by Sivakumar et al<sup>11</sup>, where in diabetics with UTI, fever (60%) was the predominant presenting complaint followed by dysuria (48.5%).

In this study most of the patient who had bacteriuria also had pyuria. Similar observation was seen in a study conducted by Mohammed Ali et al<sup>12</sup>, found that that pyuria had a significant correlation with bacteriuria.

In ultrasonography of genitourinary tract features of prostatomegaly (7.1%) were the most common finding in diabetics with UTI in our study. This was not consistent with the study conducted by Signe et al<sup>13</sup> in patients with UTI, where hydronephrosis (17%) was the most common followed by urolithiasis.

In this study E.coli, Klebsiella, Pseudomonas, Proteus, Enterococci, Acinetobacter, MRSA and Candida species were isolated from urine culture. E.coli (60%) was the most common organism obtained from urine culture followed by Klebsiella (18.2%). This is similar to the results observed in a retrospective study done by Dash et al<sup>14</sup>, where it was found that Gram-negative aerobic rods are causative agent in 78.2% (E coli was most common i.e. 68.8%) cases while Gram-positive cocci and Candida species were responsible for 20.8% and 1% respectively. Multiple studies conducted in India from different locations by Jah BK et al<sup>15</sup>, Janifer J et al<sup>16</sup>, Goyal A et al<sup>17</sup>, Sing L et al<sup>18</sup>, also found that E.coli is the most common organism causing UTI in diabetics. Among the gram-positive cocci Enterococcus (2.9%) was the most common one followed by staphylococcus aureus. A study done by Jegadeeswaran et al<sup>19</sup>, also found that common Gram-positive bacteria in diabetics with UTI were Enterococcus faecalis (10.90%) and Staphylococcus aureus (2.91%).

Most of the organisms were susceptible to antibiotics like Amikacin, Meropenem, Cefoperazone-Sulbactam, Nitrofurantoin and Fosfomycin. E.coli was sensitive to above mentioned antibiotics most of the time. Among the antibiotics Amikacin was the most effective inject able antibiotic followed by Meropenem. Nitrofurantoin was the most effective oral antibiotic. Majority of the bacteria showed resistance to Ampicillin, Fluroquinolones, first and second generation Cephalosporins but third and fourth generation Cephalosporins were effective in most of the cases. Among them Cefixime, Ceftriaxone and Cefeperozone-Sulbactam were the most commonly prescribed first line agents in our study. Similar antibiotic sensitivity pattern was observed by Ramanath et al<sup>20</sup>, and in that study prescribing trends for in-patients was Ceftriaxone (68%) Cefotaxime (12.2%) and Ciprofloxacin (7.3%), and the prescribing trends for out-patients were Ciprofloxacin 28.4%, Norfloxacin 22.1% and Nitrofurantoin 18.9%. However in our study ciprofloxacin and Norfloxacin were not widely prescribed due to emerging resistance in our territory. Another retrospective study conducted by Shill et al<sup>21</sup>, in Bangladesh found that amoxicillin showed maximum resistance (78%) followed by ciprofloxacin (72.8%), Meropenem (9%) and Amikacin (23.6%).

Enterococcus species showed maximum sensitivity to Linezolid and Vancomycin our study. A prospective study conducted by Chaudhary et al over 6 months in 125 diabetics with UTI,<sup>22</sup> observed that, Imipenem was 95% effective for Gram-negative organism while Vancomycin was 100% effective for gram-positive cocci. We obtained similar results. Vancomycin and Linezolid showed 100% sensitivity to Enterococcus species. A retrospective study done by Jegadeeswaran et al<sup>23</sup>, also found that, Gram-positive bacteria were mostly sensitive to Nitrofurantoin, Linezolid and Vancomycin.

In our study patients with poor control of diabetes tend to have higher rates of resistance to antibiotic therapy and ESBL (Extended Spectrum Beta Lactamase) organisms were commonly seen in diabetics with poor control of blood sugar, and this is probably due to recurrent UTI and multiple antibiotic uses in the past. Due to the emerging resistance to antibiotics, diabetics with UTI with culture positivity for ESBL organisms should be managed appropriately with Carbapenems as a first line agent. Though Amikacin is more effective and less costly, its nephrotoxicity limits its wide use as a first line agent for ESBL. A study conducted by M.Srinivas et al<sup>24</sup> and a study conducted in Kerala by Prabhu et al<sup>25</sup>, showed higher prevalence of ESBL organisms in patients with poor diabetic control.

Among complications of UTI, increased incidence of Pyelonephritis was seen in patients with very poor control of diabetes (defined by HbA1c>10). Poor control of diabetes was associated with increased risk of developing Pyelonephritis, emphysematous Pyelonephritis, renal abscess and serious fungal UTI. In the present study Pyelonephritis was seen in 14 patients, emphysematous pyelonephritis was found in 2 patients and renal abscess was found in 1 patient.

The study of control of diabetes by HbA1c and its association with the incidence of organism proves that E.coli was the most common in all stages of diabetic control and there is no significant change in organisms with control of diabetes as defined by HbA1c levels. pH of urine was acidic in most of the patients with UTI (97.1%). Alkaline pH (2.9%) was significantly associated with Proteus species.

#### **CONCLUSION:**

The incidence of UTI increases as the age advances and the duration of diabetes increases. Antibiotic resistance and Pyelonephritis were found to be higher among patients with poor glycaemic control. Good glycaemic control with routine monitoring of HbA1C is mandatory in diabetic patients to prevent UTI and to avoid its complications. E. coli was the most common organism isolated followed by Klebsiella. Most of the organisms were sensitive to Amikacin. Hence, Amikacin can be recommended as empirical antibiotic for Diabetic patients who are admitted with UTI.

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