



**ORIGINAL RESEARCH PAPER**

**General Medicine**

**A COMPARATIVE CROSS-SECTIONAL STUDY OF THE CLINICAL AND MICROBIOLOGICAL PROFILE OF URINARY TRACT INFECTIONS IN DIABETICS AND NONDIABETICS- A HOSPITAL BASED STUDY.**

**KEY WORDS:** urinary tract infection; diabetes mellitus; microbiological profile UTI; clinical profile UTI; comparative study diabetic and non-diabetic

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**ABSTRACT**

**INTRODUCTION:** In developing countries like India, infections are common presenting manifestations of Diabetes and urinary tract infection being the commonest. Impaired immunity, poor metabolic control, incomplete bladder emptying (autonomic neuropathy) and emergence of infections by resistant pathogens may all contribute. The objective of the study is to compare the clinical and microbiological profile of urinary tract infections among the diabetic and the non-diabetic group.

**METHODOLOGY:** All the patients above the age of 18 years visiting our hospital with symptoms of urinary tract infection, satisfying the inclusion criteria, after an informed consent were studied with regards to their symptoms and the diagnostic workup for urinary tract infection. A sample size of 150 with 75 patients each of Diabetic and Non-diabetic were compared and analysis done using appropriate statistics.

**RESULTS:** Diabetics showed a higher incidence of lower urinary tract infection symptoms with higher level of blood leucocytosis (p= 0.026) and urinary abnormalities ( urine leucocytes p=0.007 , ketonuria p = 0.023, proteinuria p= 0.004) compared to non-diabetics. Incidence of complicated UTI was also more among the Diabetics as compared to Non-diabetics (cystitis 28% vs 8% p < 0.001, pyelonephritis 10.66% vs 5.35%, renal abscess 5.3% in diabetics). The most common cause of UTI was E.coli followed by Klebsiella, Proteus, Staph aureus, Pseudomonas, Enterococci and Coagulase negative staphylococcus in descending order but there wasn't significant difference in the spectrum of organisms among the two groups. The uropathogens showed higher levels of resistance against the commonly used antibiotics in Diabetics.

**CONCLUSIONS:** Although the microorganisms causing UTI in Diabetics are similar to the ones causing infection in the Non-diabetic population, yet they exhibit a surprisingly different antibiotic sensitivity pattern. Hence it is imperative to cautiously evaluate any episode of urinary tract infection in the diabetic population and have a complete microscopic and culture profile of urine done so as to provide the antibiotic with maximum efficacy.

**INTRODUCTION:**

- India is considered to be the Diabetic capital of the world with as many as 50million people suffering from diabetes. According to a World Health Organization fact sheet <sup>1</sup> on diabetes, an estimated 3.4 million deaths are caused due to diabetes. The WHO also estimates that around 80 percent of diabetes deaths occur in low and middle income countries and projects that such deaths will double between 2018 and 2030.
- Patients with diabetes mellitus are at increased risk of infections , with the urinary tract being the most frequent site. Factors like impaired cellular & humoral immunity, poor metabolic control, incomplete bladder emptying due to autonomic neuropathy and emergence of infections by resistant pathogens may all contribute to urinary tract infections in diabetes <sup>2</sup>.
- Urinary tract infections range from a spectrum consisting of insignificant pyuria, asymptomatic bacteriuria, cystitis, prostatitis, acute & chronic pyelonephritis and urinary catheter related infections.
- The same spectrum of UTI exists in diabetes although complicated by conditions like bacteraemia, acute papillary necrosis, renal abscess, emphysematous pyelonephritis, xanthogranulomatous pyelonephritis, acute kidney injury due to recurrent UTI <sup>3</sup>.
- Diabetics are also specifically more prone to upper UTI's than non-diabetics. The cause for this is not fully understood but assumed to be due to bladder dysfunction due to autonomic neuropathy.
- Studies done suggest that in diabetes **age, duration of diabetes and poor glycemic control are three important independent risk factors** causing UTI in diabetes patients.

**AIMS AND OBJECTIVES OF THE STUDY**

1. To study the clinical profile of urinary tract infections in diabetics and nondiabetics.
2. To find the spectrum of different microorganisms responsible for causing UTI and their comparison within the diabetics and nondiabetics.
3. To find the antibiotic susceptibility patterns of the uropathogens in the diabetic and nondiabetic population.
4. To obtain an antibiotic pattern of the microorganisms causing the most common infections reported at our hospital.
5. To find the incidence of complicated urinary tract infections among the Diabetic population under study.

**MATERIALS AND METHODS**

**Inclusion Criteria:** All the patients above the age of 18 presenting with the symptoms suggestive of urinary tract infection and satisfying the following inclusion criteria:-**The**

**diabetic group** of cases will be selected based on the definition for diabetes (includes all diagnosed type 1 and type 2 diabetes cases who are on oral medications and / or insulin therapy. Fasting plasma glucose  $\geq$  126mg/dl and / or 2 hr plasma glucose  $\geq$  200mg/dl, HbA1c  $\geq$  6.5% Or Random plasma glucose  $>$  200mg/dl along with symptoms of diabetes.

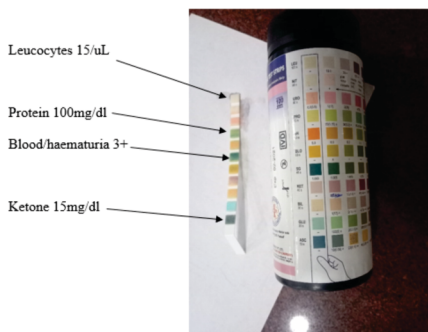
The other group consists of **non-diabetics** (fasting blood sugar  $<$  126mg/dl) with comparable age group with no past history of taking any antidiabetic medications.

**a. Exclusion Criteria**

- Subjects with age  $<$  18 years.

- Pregnancy, Gestational Diabetes mellitus & Diabetes insipidus.
- Immunocompromised patients ( HIV, Malignancy, Patient on steroids, Transplant recipients )
- History of receiving antibiotics within 14 days prior to urine culture.
- Patients on continuous indwelling catheter.
- Patients who are moribund or bedridden for prolonged periods & cases of stroke.
- Known case of renal & urologic diseases.
- Known autoimmune diseases or existing Cardiovascular diseases taking treatment.
- Severe Psychiatric illness or addiction.
- Patients diagnosed of sexually transmitted diseases
- Patients unwilling to participate in the study or those who did not approve of the informed consent.

Over a duration of 6 months the number of cases diagnosed of having urinary tract infections were included under the study after satisfying the inclusion and exclusion criteria. A prospective observational cross sectional study was done after choosing subjects by universal sampling technique and appropriate statistics applied. Subjects were given sterile wide mouthed universal containers into which a clean catch midstream urine sample of about 10 – 20 ml was collected on the morning of the test. In patients who are already catheterized (within past 3 days), urine sample was collected from a fresh urinary catheterization under all aseptic precautions. Analysis of urine sample was done based on its physical, biochemical characteristics, and microscopically analysed and the sample sent for culture and antibiotic sensitivity testing. Routine blood tests were also conducted.



**Figure 1: Dipstick Urine analysis showing pyuria, proteinuria, hematuria and ketonuria**



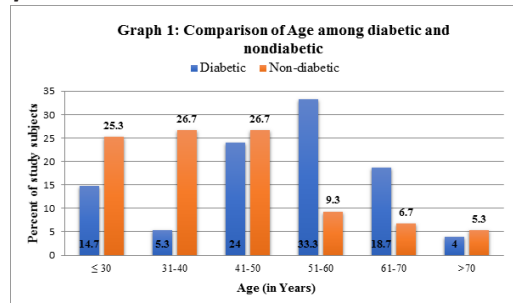
**Figure 2: MacConkey agar showing Lactose fermenting colonies of E.coli**



**Figure no.3: Muller Hinton Agar Showing Antibiotic Sensitivity Testing**

**OBSERVATIONS & RESULTS:**

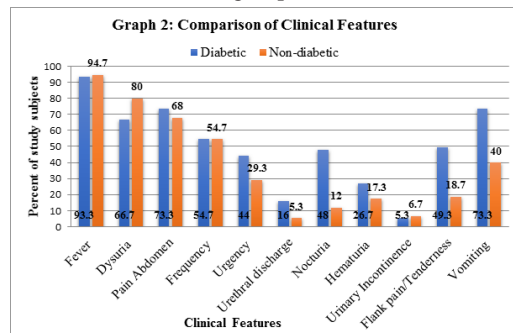
The study included in total of 150 subjects with both the Diabetic and the Non-diabetic group containing 75 each. Both these groups had cases which were age and gender matched and then analysis was done to evaluate the difference in clinical and microbiological profile obtained in urine analysis.



The age distribution reveals the maximum diabetic population to be in the age group of 51-60years, whereas most of the nondiabetic subjects presenting with UTI fell in the age group of 31-50years. This difference could well be explained based on the most common age at which diabetes is first diagnosed which falls in the age group of 45-64years as per the data published by the CDC ( centre for disease control).

The two groups showed no difference in the age and gender matching and hence these two groups could be compared with respect to their diabetic status without having a confounding bias.

As per the gender wise distribution , females formed 57.3% of the cases among the nondiabetic whereas males predominated the diabetic group.



Amongst the clinical symptoms suggesting of UTI , fever was the most common symptom followed by dysuria ( burning sensation while micturition).

Although not many studies done previously found a clinically significant difference between the symptomatology of UTI between the diabetic and non-diabetic. But owing to the more number of cases of cystitis, pyelonephritis & urosepsis among the diabetics its not uncommon to find symptoms of pus per urethra, flank pain, pain abdomen and abdominal tenderness to be present among the diabetics in a significantly higher percentage when compared to the non-diabetics.

Considering diabetes mellitus itself being an important risk factor for the occurrence of recurrent urinary tract infections , around 28 % of the diabetic group had experienced a past history of UTI whereas this number was significantly lower among the nondiabetic ( 10.7%).

Comparing the clinical profile of these two groups, the only statistically significant difference was observed for the presence of lower abdominal tenderness more so in diabetics than non-diabetics again indicating the diagnosis of Cystitis being more common in the Diabetes group.

((Chi-Square Test, P Value \*Significant < 0.001\* for “ Lower abdominal tenderness”))

**Table 1: Comparison of renal function tests**

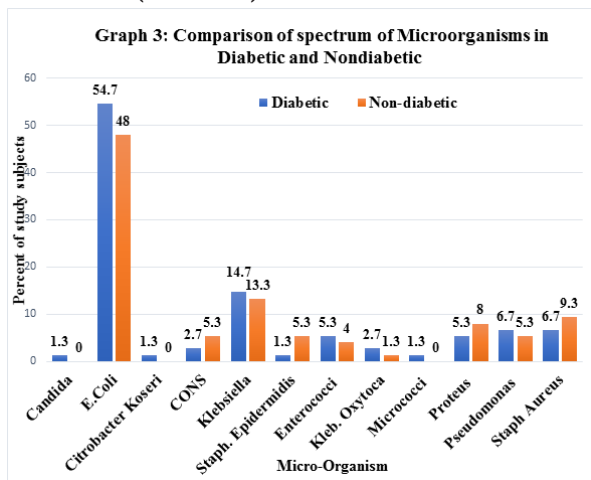
RFT	Diabetic (n=75) Mean (SD)	Non-Diabetic (n=75) Mean (SD)	P Value
Blood Urea	70.61 (63.51)	43.61 (41.30)	0.002*
Serum Creatinine	2.85 (10.67)	1.73 (2.80)	0.381

Mann Whitney Test, P Value \*Significant

Acute kidney injury is a common complication of urinary tract infection in diabetics. Several studies indicate the presence of hypovolemia, hypotension, urosepsis, use of nephrotoxic drugs and associated comorbidities playing a role of causing AKI in diabetic UTI. As observed in the figure the mean values of blood urea were significantly higher in the diabetic cases as compared to the non-diabetics indicating associated prerenal failure or already pre-existing early stage diabetic nephropathy as one of the many possibilities of AKI

Considering the incidence of complicated infections in diabetes mellitus, complicated UTI in the form of pyelonephritis, renal abscesses and urosepsis was observed in our study. But the number of cases of cystitis were significantly higher in the diabetic than nondiabetic group (28% vs 8%). And all 5 cases of urinary tract infection getting complicated into Renal abscesses were amongst the diabetic group. And although the occurrence of pyelonephritis and urosepsis was higher in diabetic population as compared to nondiabetic but it was not statistically significantly.

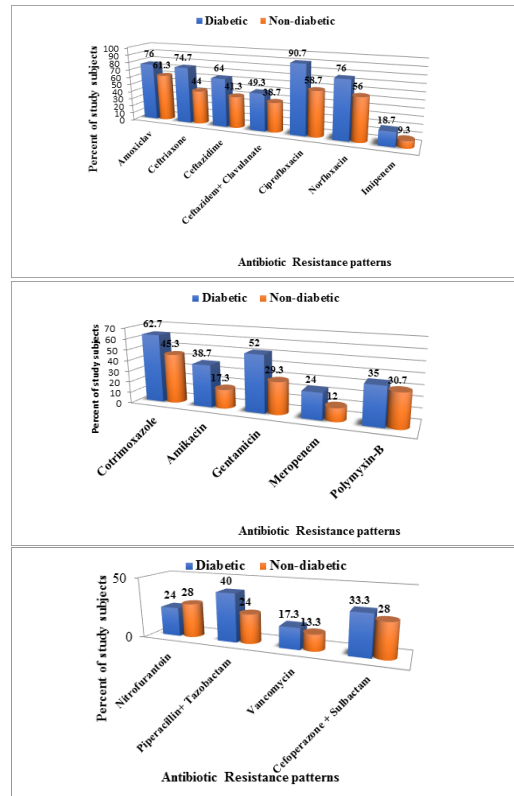
Microalbuminuria is an important assessment in the evaluation of cardiovascular mortality in diabetic population. In our study microalbuminuria was observed in comparable percentage of subjects of both diabetic and non-diabetic groups. But moderate to heavy proteinuria i.e macroalbuminuria (> 300mg/dl) was noticed in significantly higher percentage of diabetic group when compared to the non-diabetic (20% vs 4%).



Among the diabetic subjects, E.coli was the commonest organism causing UTI in both males and females (23% in males vs 18 % in females). The second most common pathogen was the Klebsiella spp in both the groups. Atypical organisms causing UTI were found more in female subgroup when compared to males.

Among the non-diabetic group under study, E coli was the commonest organism among male and female subgroups ( 14 % in male vs 22% in female). And the occurrence of Staph aureus, Proteus and Pseudomonas infection was more common among the male subgroup than females.

**Graph 4: Showing The Percentage Of Subjects With Resistant Against The Antibiotics Tested Amongst The Diabetic And Non-diabetic**



The antibiotics pattern exhibited present an astonishing pattern amongst both the groups. The isolates of microorganisms found among the diabetics show at least more than 50 percent subjects having resistance to amoxiclavulanate, ceftriaxone, ciprofloxacin, norfloxacin, cotrimoxazole and gentamicin.

And the organisms causing UTI amongst the nondiabetic population have more than 50 % subjects showing resistance against amoxiclav, ceftriaxone, ceftazidime, ciprofloxacin and norfloxacin.

Although the microbiological profile of UTI appears to be similar with only a few insignificant differences among the diabetics and non-diabetics E. coli, being the most common cause amongst both the groups alike, exhibits high resistance to ciprofloxacin, norfloxacin, cotrimoxazole, ceftriaxone, amikacin, piperacillin tazobactam (in the descending order of percentages) when the isolates are from diabetics.

Whereas E. coli isolated from the non-diabetics exhibit high resistance to norfloxacin, ciprofloxacin, cotrimoxazole, ceftriaxone, amikacin and piperacillin tazobactam (in the decreasing order of percentages).

**DISCUSSION**

As incidence of UTI is more common in females as compared to males, similar distribution was seen as in total cases under study female population was slightly higher than males. And this difference was more significant in the nondiabetic population. This is probably due to anatomical reasons. This observation was same with almost all previous studies viz. Shah BV et al<sup>4</sup>, Ooi BS et al<sup>5</sup>, O’Sullivan DJ et al<sup>6</sup>, Viggs et al<sup>7</sup>, Jaspani et al<sup>8</sup>.

One such study was done by Aswani Srinivas M, Chandrashekar UK which compared the clinical profile of urinary tract infections in diabetics and non-diabetics done in 2014<sup>9</sup>. A total of 181 diabetics (83 males and 98 females) and

124 non-diabetic subjects (52 males and 72 females) with culture positive UTI were studied. As shown in this study there were no clinical significant differences among the clinical symptoms between the diabetic and non-diabetic group. Our present study did although find clinical significant difference in symptoms of per urethral discharge, vomiting and lower abdominal tenderness. Their study also showed a past history of UTI being common in 27 % of diabetics vs 18 % of nondiabetics, whereas our current study showed the difference of presence of a previous episode of UTI to be significant among the diabetics as compared to the non-diabetics (28% vs 10.7% respectively).

A study was conducted by Mehvish Saleem, Betty Daniel et al to find out the prevalence of Urinary tract infection among patients with diabetes in the city of Bangalore, from July 2005 – 2009<sup>10</sup> and their comparison with the non-diabetic controls. This spectrum of microbes was almost comparable with our current study, where even our diabetic population had E. coli (54.7%), Klebsiella (17.4%) being the most common followed by staph (8%), pseudomonas (6.7%) and then enterococci (5.3%). And the non-diabetics harbouring E. coli (48%), Klebsiella (14.6%), staph (14.6%) and pseudomonas (5.3%). Even like this study, our current observations revealed that the organisms seen in both diabetics and non-diabetics are similar. Although occurring in different numbers the comparison amongst the two groups wasn't really significant.

As our current study found a significant difference between the diabetics and non-diabetics in the symptomatology, Kim Y, Wie SH, Chang UI, Kim J, Ki M et al published a study done to compare clinical characteristics revealed a completely different picture where patients of pyelonephritis with diabetes had fewer of prominent clinical symptoms when compared to the non-diabetics<sup>11</sup>. Their study also had a high incidence of azotemia / acute kidney injury in the diabetics when compare to the nondiabetics (29.3% vs 13.4 %, p < 0.001) as similar to our present study which also showed increased blood urea concentrations amongst the diabetics than non-diabetics (63.51% vs 41.30%, p value 0.002).

As our current study of pattern of antibiotic sensitivity reveals that only few percentage of microbes isolated among both the groups are sensitive to the cephalosporins and Fluoroquinolones, more importantly around 76% of isolates among the Diabetics and 72% isolates in the Non-diabetics are sensitive to the drug Nitrofurantoin (NFT). This observation is similar to what was shown in the following study described by Tasbakan MI, Pullukcu H, Sipahi OR, Yamazhan T, Ulusoy S<sup>12</sup> to see the effect of nitrofurantoin (NFT) in extended-spectrum β-lactamase (ESBL)-producing Escherichia coli-related lower urinary tract infection.

**CONCLUSION**

Following are the major conclusions that could be drawn from the limited sample size and study duration :-

The most common age group of presentation of UTI in diabetics was 41-60yrs and that in the Non-diabetics was 31-50years. Female population with UTI was more than the males in the Non-diabetic group, whereas males predominated the Diabetic population. Among the clinical features, lower urinary tract infection symptoms were significantly higher among the diabetics. And same goes with the increased white blood cell counts were seen in a larger proportion of diabetic cases. Owing to the underlying disease and more complications, there was a significantly higher incidence of azotaemia (uraemia) amongst the Diabetic when compared to the Non-diabetics. So also the occurrence of complicated UTI, complicated cystitis, pyelonephritis, renal abscesses and urosepsis were found significantly more number among the Diabetic. There was significantly higher percentage of Glycosuria, Ketonuria and Proteinuria (both microalbuminuria and macroalbuminuria) and also urine

microscopy revealed a higher number of leucocytes per high power field among the Diabetics. Most common microorganism isolated in urine culture was E.coli both among diabetics and non-diabetics. The other uropathogens cultured were by Klebsiella spp, Proteus spp, Staph aureus, Pseudomonas, Enterococci and Coagulase negative staphylococcus as per descending order of percentage. The isolates from the Diabetics exhibited significantly higher degree of resistance when compared to the isolates from Non-diabetics against the most commonly used antibiotics like ceftriaxone, ciprofloxacin, norfloxacin, cotrimoxazole and amikacin. And when the same organisms isolated from the Diabetics and Non-diabetics were compared, the ones from Diabetics exhibited high resistance to ciprofloxacin, norfloxacin, cotrimoxazole, ceftriaxone, amikacin, piperacillin tazobactam.

**SUMMARY**

This study finally brings us to three important points.

- aggressive measures must be applied to prevent infection in diabetes.
- prevention of diabetes related complications (CVD mostly) might reduce the risk of fatal infection.
- there is still far more scope for further studies to ascertain the mechanisms underlying the relationship between diabetes and infections.

**LIMITATIONS OF STUDY :**

1. A larger sample size would provide more significance to the results observed.
2. Inclusive of Asymptomatic bacteriuria among diabetes and non-diabetes and their comparison would give more detailed information of the microbiological profile.
3. The study didn't include patients with other risk factors like Calculi, BPH, Chronic kidney disease or any other obstructive pathology which would help us assess a more broad spectrum of microorganisms causing urinary tract infections.
4. The population included under study belonged to only a few sections of society, the middle class and the lower middle class majorly coming from the rural areas. Hence the results observed here depicts the UTI profile of a certain section of people only and cannot be extrapolated to a larger group.
5. As the patients especially the female subgroup, here were hesitant and reserve enough to reveal accurately regarding their sexual history and use of contraceptives, the exact correlation of the different microorganisms causing UTI in such a context among the two groups couldn't be done.
6. Since the MIC (minimum inhibitory concentration) of the antibiotics tested couldn't be calculated for the microorganisms isolated, the decision as to which antibiotics should be preferred as first line drugs and which antibiotics are not to be used for certain uropathogens couldn't be interpreted from the observations.

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