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Original Research Article

A clinical study of urinary tract infections in diabetics and non-diabetics patients

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ABSTRACT

Background: The main aim of the present study is to investigate the differences in clinical, microbiological, characteristics of Urinary tract infection between diabetic and non-diabetic patients and influence of diabetes on the spectrum of URO pathogens and the antimicrobial resistance in patients with urinary tract infections.
Methods: The present study is conducted from February 2018-April 2019 in Narayana general hospital. A total of 181 diabetics and 124 non-diabetics are included. A thorough history examination investigations done. The final data was analysed using statistical package SPSS. The percentages in different categories were compared using chi square test and means were compared using student 't' test.
Results: The mean age among diabetic and non-diabetic patients was 60.2+/-13.79 years and 53.47+/-18.56 years. Fever is the most common presenting symptom. BPH was the most common predisposing factor in both diabetes and non-diabetes followed by indwelling catherization but there was no statistically significant difference. Diabetics with UTI majority (87.14%) had glyco HBA1C >6.5% with p<0.001. The prevalence of recurrent UTI is higher in diabetics compared to non-diabetics however difference was not statistically significant. Recurrent UTI is higher in females in both diabetics and non-diabetics. The presence of *E coli* is significantly higher in diabetics compared to non- diabetics. The antimicrobial resistance pattern was similar in both diabetic and no-diabetic subjects in *E coli* with maximum sensitivity to meropenem and least to ampicillin and there is no statistically significant difference.
Conclusion: The host factors found to be associated with UTI are female sex, presence of diabetes, poor glycemic control, presence of fever. No correlation was noted with age, duration of diabetes and type of treatment for diabetes. An elevated HBA1C correlates with occurrence of UTI. *Escherichia coli* (*E. coli*) was the most frequent uropathogen. The resistance of uropathogens to antibiotics are similar in patients with and without diabetes and non-diabetes.

Keywords: Antibiotics, Clinical, Diabetes, Microbial, Predisposing factor, Urinary tract infection

INTRODUCTION

Diabetics are more prone for infections than their nondiabetic counterparts. Infections tend to be more severe and complications are more frequent in diabetics compared to non-diabetics.

Urinary tract infection is the most important and most common site of infection in diabetic patients. Diabetic patients have been found to have 5-fold frequency of acute pyelonephritis at autopsy than non-diabetics.[1] Most of the urinary tract infections in diabetic patients are relatively asymptomatic. The presence of diabetes predisposes to much more severe infections, especially in

patients with poor diabetic control, acute ketoacidosis or diabetic complications such as nephropathy, vasculopathy and neuropathy. This asymptomatic infe3ction can lead to severe kidney damage and cause renal failure.[2]

Bacteriuria is more common in diabetics than in non-diabetics because of a combination of host and local risk factors.[2] A number of uncommon urinary tract infection complications occur more frequently in diabetics, such as emphysematous pyelonephritis and emphysematous cystitis.[2]

Different disturbances (low complement factor 4, decreased cytokine response after stimulation) in humoral innate immunity have been described in diabetic patients.[(3)] However, the clinical relevance of these findings is not clear. Concerning cellular innate immunity most studies show decreased functions (chemotaxis, phagocytosis, killing) of diabetic polymorphonuclear cells and diabetic monocytes/macrophages compared to cells of control. In general, a better regulation of diabetes mellitus leads to an improvement of these cellular functions.

Furthermore, some microorganisms become more virulent in a high glucose environment.[3] Another mechanism which can lead to the increased prevalence of infections in diabetic patients is an increased adherence of microorganisms to diabetic compared to non-diabetic cells. this has been described for candida albicans. Possibly the carbohydrate composition of the receptor plays a role in this phenomenon.[3]

In wheat's review of the issue of infections and diabetes from 1980, 72% of 22 patients with emphysematous pyelonephritis, 80% of 19 patients with emphysematous cystitis, 57% of 250 patients with papillary necrosis, 36% of patients with prenephrotic abscess and 10% of 130 patients with metastatic infection had diabetes.[4]

Therefore, investigation of bacteriuria in diabetic patients by screening for urinary tract infection is very important to enable it to be properly treated to prevent the development of renal complications of diabetes and eventually severe renal damage and failure.

However, controversies do exist with respect to incidence, prevalence and microbiological features between diabetic and non-diabetic patients. The prevalence of bacteriuria as well as bacterial virulence and host factors were studies in 514 diabetic outpatients and 405 nondiabetic controls. Studied the prevalence of bacteriuria was not significantly higher in diabetic women (15/239, 6.3%) than in age matched nondiabetic women (8/236, 3.4%).[5] In diabetic and non-diabetic men, the prevalence was also similar but lower than in women

Hence the study was planned to compare clinical, microbiological and predisposing features of UTI in diabetics and non-diabetics

METHODS

This Prospective study duration February 2018 – April 2019. Detailed history including age, sex, occupation and symptomatology were taken. Detailed general and systemic clinical examination was done. 181 diabetics (98 females and 83 males) and 124 nondiabetics (72 females and 52 males) admitted in Narayana general hospital were studied randomly.

All proven diabetics (fasting venous glucose > 126 mg/dl and postprandial (2 hr.) venous glucose >200 mg/dl were included in the study irrespective of reason for admission. All patients with history of diabetes and those who are on treatment were also eligible for admission.

Inclusion criteria

Culture positive urinary tract infections

Exclusion criteria

Culture negative urinary tract infections, Age <18 years, Patients.

Controls were taken from patients admitted in hospital with comparable age and sex who were proven not be diabetic (absence of history of diabetes and anti-diabetic drugs and fasting blood sugar <110 mg/dl).

Investigation done in all patients included hemoglobin, total WBC count, differential count, ESR, urine for protein, sugar, ketones and microscopy.

A fasting, post prandial sugar and glycosylated hemoglobin was done for all diabetics. Diabetes was diagnosed by history of diabetes, intake of anti-diabetic drugs and newly detected diabetics

Urine culture and gram stain done using Blood agar plate, MacConkey agar plate (MAC) (or another selective/ differential media), anaerobic blood agar plate (for suprapubic, cystoscopy and nephrostomy specimens)

Patients with positive urine cultures underwent appropriate investigations in the form of ultrasound abdomen, x ray, and CT abdomen to look for the predisposing conditions and to aid in the clinical management

Data analysis

Data was analyzed using statistical package SPSS. The percentages in different categories were compared using chi square test and means were compared using student 't' test. A p value less than 0.05 was considered significant.

RESULTS

The study included 181 diabetics (83 males and 98 females) and 124 Non-diabetics (52 male and 72 female) (Figure 1).

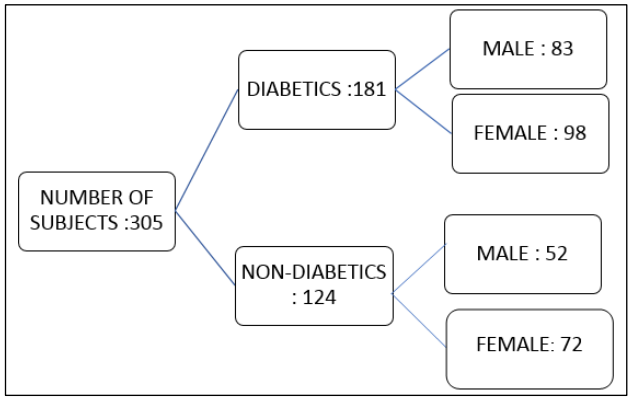

Figure 1: Distribution of diabetics and non-diabetics among subjects.

The mean age among diabetic and non-diabetic patients was 60.2+/- 13.79 years and 53.47+/-18.56 years. Among 18-29 years there are 3(1.7%) diabetics and 16(12.9%) non diabetics, 30-39 years there are 9(5.0%) diabetics and 17(13.6%) non diabetics, 40-49 years there are 24(13.3%) diabetics and 18(14.5%) non diabetics, 50-59 years there are 48(26.5%) diabetics and 18(14.5%) non diabetics, 60-69 years there are 45(24.9%) diabetics and 31(25%) non diabetics, 70-79 years there are 42(23.2%) diabetics and 19(15.3%) non diabetics, among more than 80 years there are 10(5.3%) diabetics and 5(4.8%) non diabetics (Table 1).

Table 1: Age distribution among diabetics and non-diabetics.

Age distribution	Diabetics	Non-Diabetics
18-29 years	3(1.7%)	16(12.9%)
30-39 years	9(5.0%)	17(13.6%)
40-49 years	24(13.3%)	18(14.5%)
50-59 years	48(26.5%)	18(14.5%)
60-69 years	45(24.9%)	31(25%)
70-79 years	42(23.2%)	19(15.3%)
>80 years	10(5.5%)	5(4.8%)
Total	181	124

A Total of 124 non diabetes, 164 type 2 diabetes, 4 type 1 diabetes, 13 gestational diabetes Mellitus (Figure 2). Fever is the most common presenting symptom. Fever is seen among 104 (57.4%) cases of diabetics and 81(65.3%) cases of non-diabetics, dysuria in 74(41.4%) of diabetics and 55(44.3 Authors would like to %) of non-diabetics, increased frequency among 43(23.7%) diabetics and 38(30.8%) of non-diabetics, abdominal pain among 35 (19.3%) diabetics and 34(27.4%) of non-diabetics, vomiting among 44(24.3%) of diabetics and 23(18.3%) of non-diabetics, hematuria among 8(4.4%) of diabetics and 4(3.2%) of non-diabetics, pyuria among 7(3.8%) of diabetics and 3 (2.4%) of non-diabetics, urinary incontinence among 26(14.4%) of diabetics and 15 (12.09%) of non-diabetics, urinary retention among 5(2.7%) of diabetics and 5(4.03%) of non-diabetics. There was no statistically significant difference (p>0.05) between symptoms among diabetes and non-diabetes (Table 2).

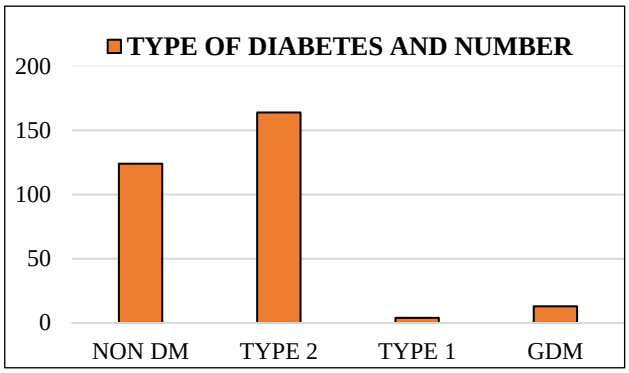

Figure 2: Distribution of different types of diabetics among patients.

Table 2: Symptoms among diabetics and non-diabetics.

Symptoms	Diabetes	Non diabetes	p-value
Fever	104(57.4%)	81(65.3%)	0.94
dysuria	75(41.4%)	55(44.3%)	0.83
frequency	43(23.7%)	38(30.8%)	0.52
Abdominal pain	35(19.3%)	34(27.4%)	0.84
vomiting	44(24.3%)	23(18.3%)	0.24
hematuria	8(4.4%)	4(3.2%)	-
pyuria	7(3.8%)	3(2.4%)	-
incontinence	26(14.4%)	15(12.09%)	0.18
retention	5(2.7%)	5(4.03%)	-

BPH was the most common predisposing factor in both diabetes and non-diabetes followed by indwelling catherization but there was no statistically significant difference. BPH was seen among 32(38.5%) of diabetics males and 21(40.3%) of non-diabetics females, indwelling catheter as predisposing factor seen among 31(37.3%) of male diabetics, 33(33.6%) of female diabetics, 23(44.2%) of non-diabetics males and 22(30.5%) of non-diabetic females, hydronephrosis as a predisposing factor is seen among 8(9.6%) of diabetic males, 7(7.14%) of diabetic females, 8(15.38%) of non-diabetics males and 6(8.33%) among non-diabetic females, calculi as predisposing factor is seen among 5(6.02%) diabetic males, 3(3.06%) o diabetic females, 4(7.6%) of non-diabetic males and 1(1.38%) of non-diabetic females, stricture urethra as a predisposing factor is seen among 7(8.4%) of diabetic males and 5(9.6%) of non-diabetic males, phimosis as a predisposing factor is

seen among 3(3.6%) of diabetic males and 2(3.8%) of non-diabetic males, recent surgery or instrumentation as a predisposing factors is seen among 6(7.2%) of diabetic males and 4(7.6%) of non-diabetic males, balanoposthitis and neurogenic bladder as predisposing factors has been observed in diabetic males, meatal stenosis is seen among 2(2.04%) of diabetic females and 1(1.38%) of non-diabetic females, gynecological disorders predisposing to UTI is seen among 6(6.12%) of diabetics females and 8(11.11%) of non-diabetics females, pregnancy as a predisposing factor 13(13.26%) of diabetic females and 6(8.33%) of non-diabetic females. (Table 3,4).

Table 3: Predisposing conditions for UTI in males.

	Diabetes	Non-diabetes	p- values
Benign prostatic hypertrophy	32 (38.5%)	21 (40.3%)	0.92
Indwelling catheter	31 (37.3%)	23 (44.2%)	0.43
Hydroureteronephrosis	8(9.6%)	8(15.38%)	-
Stricture urethra	7(8.4%)	5(9.6%)	-
phimosis	3(3.6%)	2(3.8%)	-
calculi	5(6.02%)	4(7.6%)	-
Recent Genito-urinary surgery/instrumentation	6(7.2%)	4 (7.6%)	-
balanoposthitis	1(1.2%)	0	-
Neurogenic bladder	3(3.6%)	0	-

Table 4: Predisposing conditions for UTI in females.

Predisposing Condition	Diabetes	Non-Diabetes	p-value
Indwelling catheter	33 (33.6%)	22 (30.5%)	P -0.83
hydroureteronephrosis	7 (7.14%)	6 (8.33%)	-
calculi	3 (3.06%)	1 (1.38%)	-
Meatal stenosis	2 (2.04%)	1 (1.38%)	-
Gynecological disorders	6 (6.12%)	8(11.11%)	-
pregnancy	13(13.26%)	6(8.33%)	-

The presence of HBA1C <6.5% significantly decreased the risk of UTI irrespective of whether there was an underlying predisposing factor.

Among HBA1c of <6.5 21 are with predisposing factors and 3 are without predisposing factors, among 6.5-8.0 39 are with predisposing factors and 16 are without predisposing factors and >8.0 61 are with predisposing factors and 41 are without predisposing factors.(Table 5).

Table 5: Glycemic control and UTI.

HBA1C	With predsposing factors	No predisposing factors	p-Value
<6.5	21(17.02%)	3(4.3%)	0.026
6.5-8.0	39(31.9%)	16(26.08%)	NS
>8.0	61(51.06%)	41(69.57%)	NS

The prevalence of recurrent UTI is higher in diabetics compared to non-diabetics however difference was not statistically significant. Recurrent UTI is higher in females in both diabetics and non-diabetics.

The presence of *E. coli* is significantly higher in diabetics compared to non- diabetics *E. coli* is seen among 117 diabetic patients and 73 among non diabetic patients, *klebsiella* is seen among 22 diabetics and 18 non diabetics, enterococcus is seen among 18 diabetics and 10 non diabetics, pseudomonas is seen among 3 diabetics and 15 non diabetics, *Acinetobacter* is seen among 3 diabetics and 0 non diabetics, *Citrobacter* is seen among 3 diabetics and 2 non diabetics, proteus is seen among 3 diabetics and 1 non diabetics, coagulase negative staphylococcus is seen among 3 diabetics and 4 non diabetics, coagulase positive staphylococcus is seen among 4 diabetics and 1 non diabetics, candida is seen among 5 diabetic patients (Table 6).

Pseudomonas was found out to be associated more with non- diabetes than diabetes suggesting previous predisposing factors and is statistically significant (Table 6).

AKI as complication is seen among 17.7% of diabetics with 21% among non-diabetics, recurrent UTI is seen among 14.4% of diabetics and 10.5% of non-diabetics, septicemia is seen among 18.8% of diabetics and 21.8% of non-diabetics and renal papillary necrosis is seen

among 0.01% of diabetics and 0 of non-diabetics (Table 7).

Table 6: Isolation of different uropathogens in diabetes and non-diabetes.

Organism	Diabetes	Non-diabetes	p-values
E. coli	117	73	>0.05
Klebsiella	22	18	>0.05
Enterococcus	18	10	>0.05
Pseudomonas	3	15	<0.05
Acinetobacter	3	0	-
Citrobacter	3	2	-
Proteus	3	1	-
Coagulase negative *Staphylococcus*	3	4	-
Coagulase positive *Staphylococcus*	4	1	-
Candida	5	0	-

The antimicrobial resistance pattern was similar in both diabetic and no-diabetic subjects in *E. coli* with maximum sensitivity to meropenem and least to ampicillin and there is no statistically significant difference (Figure 3).

Table 7: Complications of UTI.

Complication	Diabetes	Non-Diabetes	p Value
AKI	17.7%	21%	0.34
Recurrent UTI	14.4%	10.5%	0.53
septicemia	18.8%	21.8%	0.82
Renal papillary necrosis	0.01%	0	-

The antimicrobial resistance pattern was similar in both diabetic and no-diabetic subjects in *Klebsiella* with maximum sensitivity to meropenem and least to ampicillin and there is no statistically significant difference (Figure 4).

The antimicrobial resistance pattern was similar in both diabetes and non-diabetes with maximum susceptibility to linezolid, teicoplanin, vancomycin in *Enterococcus* (Figure 5).

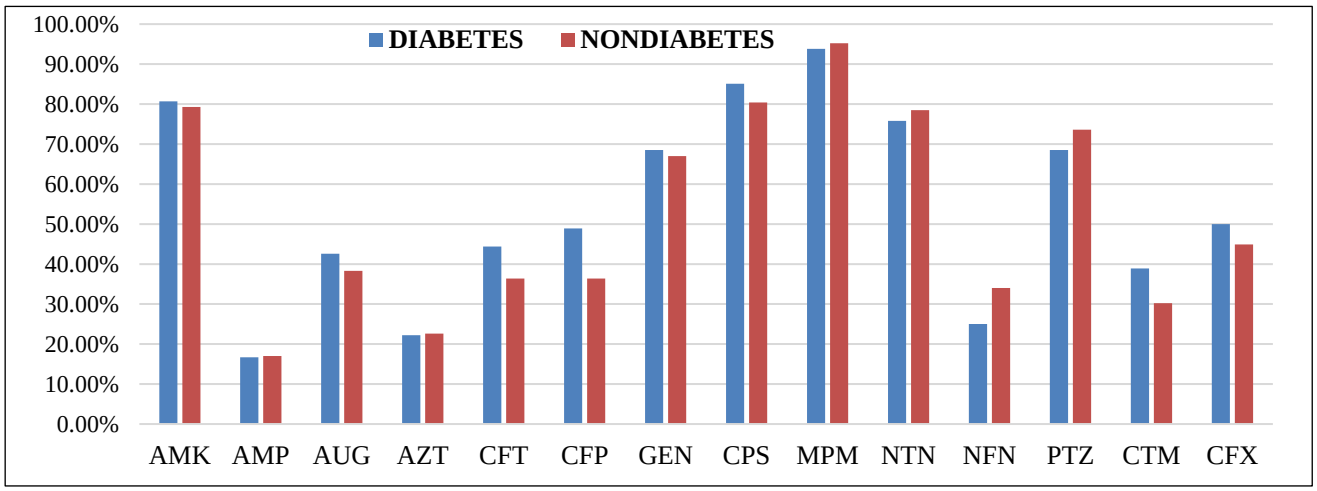

Figure 3: Comparison of antibiotic susceptibility *E. coli*.

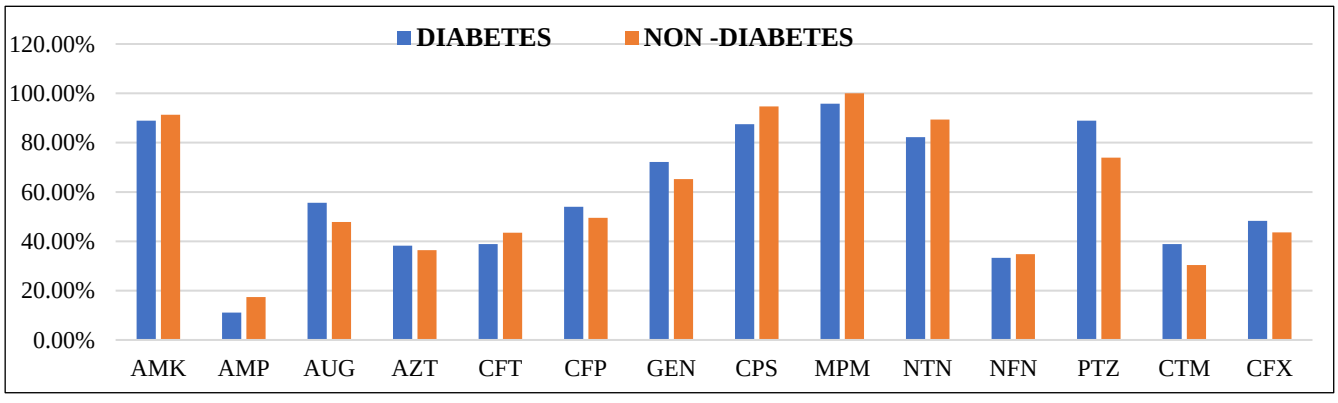

Figure 4: Comparison of antibiotic susceptibility *Klebsiella*.

A higher rate of *Pseudomonas* in non-diabetic than diabetic therefore many of the non-diabetic patients had a history of a previous instrumentation of urinary tract. Amikacin has higher sensitivity among diabetics and netilmycin among non-diabetics for pseudomonas.(Figure 6).

It was shown that aminoglycosides showed a better sensitivity profile than cefoperazone sulbactam in both diabetes and non-diabetes patients however the number of patients were too small to draw conclusion from the above-mentioned observation.

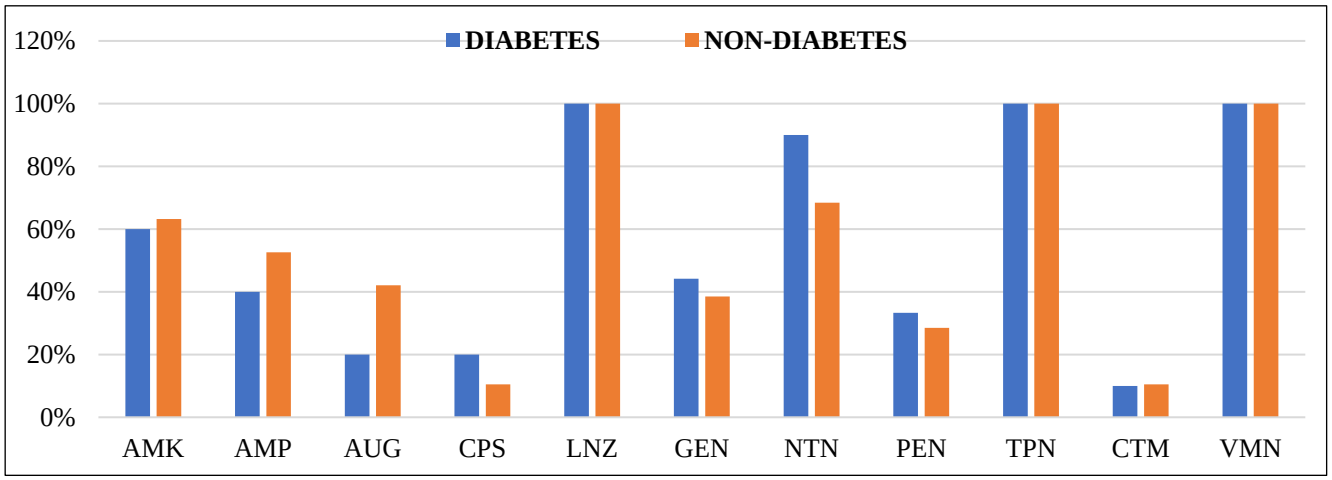

Figure 5: Comparison of antibiotic susceptibility *Enterococcus*.

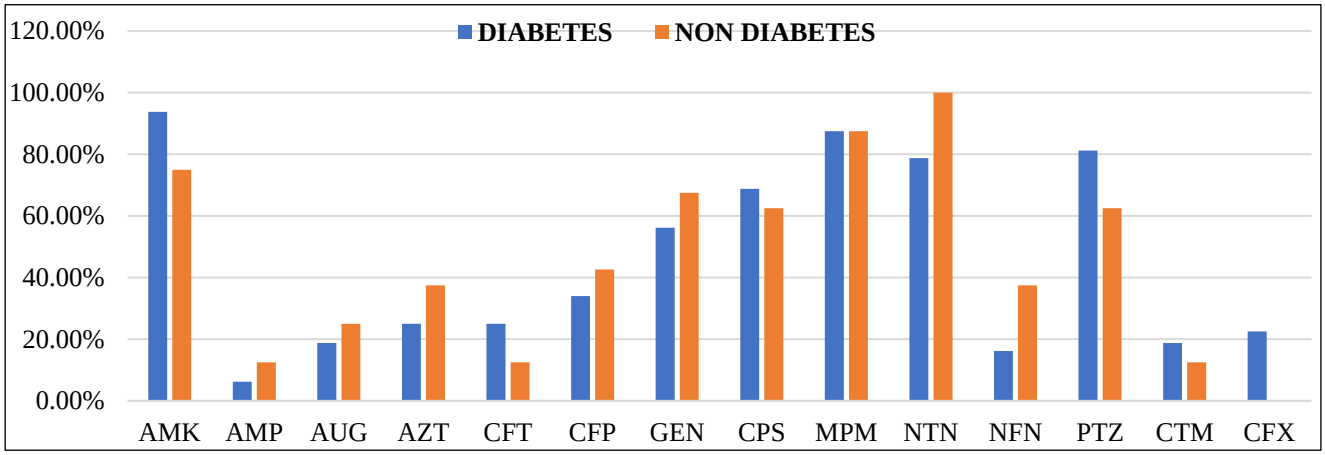

Figure 6: Comparison of antibiotic susceptibility *Pseudomonas*.

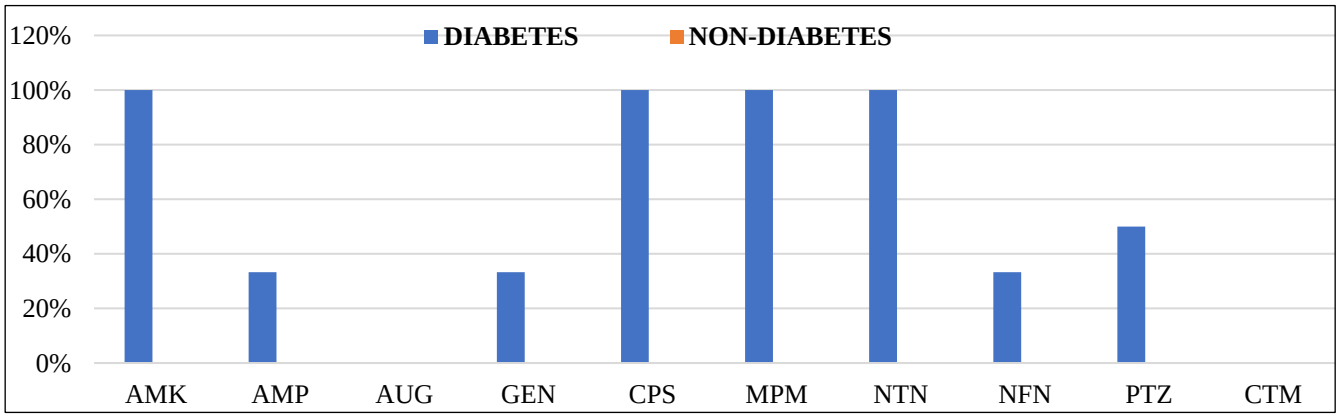

Figure 7: Comparison of antibiotic susceptibility *Acinetobacter*.

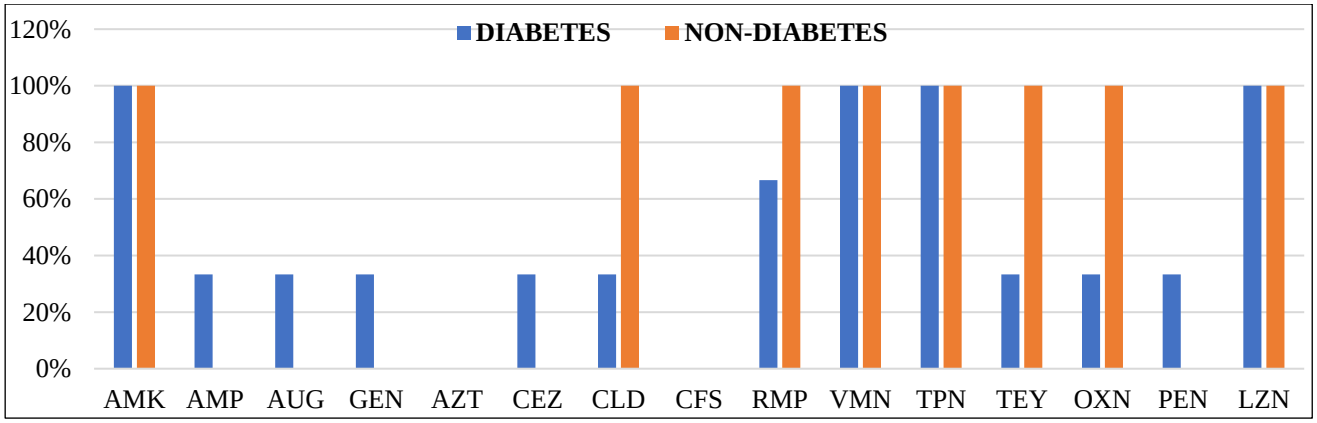

Figure 8: Comparison of antibiotic susceptibility-coagulase positive *Staphylococcus*.

Only 3 cases of *Acinetobacter* were isolated and all of them among diabetic patients and highest sensitivity is noted among cefoperazone sulbactum, meropenem, netilmycin and least sensitivity is for norfloxacin and ampicillin (Figure 7). 5 cases of coagulase positive staphylococcus were isolated. Among them 4 patients were diabetics and 1 patient were non-diabetic. 2 cases are MRSA isolates which are sensitive to vancomycin and linezolid. Among them 1 case was positive for MRSA carrier state (Figure 8). 5 cases of candida species were identified all in diabetes patients.

Bacteria like *Pseudomonas, Acinetobacter, Citrobacter, Proteus, Cons, Coagulase Positive Staphylococcus, Candida* cannot be used for statistical comparison as the proportion of bacteria detected for the sensitivity culture were very low. hence statistical comparison was not possible and only percentages were presented.

Renal papillary necrosis was observed in 2 cases of candida septicemia. Among them one patient was a case of diabetic nephropathy with CKD 5 ESRD on maintenance hemodialysis and the other patient was female who was also diabetic on indwelling catheter in ICU.

DISCUSSION

The present study included 181 diabetic and 124 non-diabetic patients with culture positive urinary tract infections.

In this study, authors have tried to determine whether there are differences in the clinical and microbiological patterns in UTI and the antibiotic sensitivity patterns of the pathogens concerned with diabetic and non-diabetic patients.

Mean age among diabetic and non-diabetic was 60.2±13.76 and 53.47±18.56 years.

There was no significant correlation between age of patient and the incidence of UTI in both diabetic and non-diabetic patients. A similar observation in this study (73.7 years in diabetics vs 72.7 years in non-diabetic subjects).[6]

Of the 181 diabetics, 164 patients were type 2 DM, 13 were GDM and 4 patients were type 1 DM.

Increased prevalence of UTI in type 2 compared to type 1 DM. such conclusion cannot be made from the present study because of the small number of type 1 diabetic patients.[7]

Found significant correlation between duration of diabetes and the prevalence of bacteriuria. The prevalence of bacteriuria increased 1.9-fold for every 10 years of diabetes duration.[8,9] This is probably due to higher prevalence of autonomic neuropathy and subsequent incomplete bladder emptying in longstanding diabetes. However, such a correlation was not observed in our study with maximum number (60%) having diabetes between 1-10 years.

In our study bladder outlet obstruction due to BPH or urethral stricture was the predisposing factor in almost 40% of males with UTI. The presence of underlying autonomic neuropathy in these patients was not investigated.

Fever was the most common symptom associated with UTI in both diabetic and non-diabetic, present in 57.4% of diabetics and 65.1% of non-diabetic subjects.

Diabetes mellitus for a long duration was associated with increased prevalence of bacteriuria compared to non-diabetics.[10,11] in the present study there is not statistically significant diference in prevalence of asymptomatic bacteriuria in females and in males both in diabetics and non-diabetics. This is in agreement with the study conducted (diabetic females 14.97% vs non-diabetic females 13.1%) and (diabetic males 12.76% vs non-

diabetic males 11.4%). However, in the study conducted the prevalence of asymptomatic bacteriuria is higher in women with diabetes than in women without diabetes.[12]

The prevalence of pyelonephritis is significantly higher in diabetics 9.4% vs non-diabetics 3.2% (p-0.04).

The mean HBA1C level of the diabetic patients at the time of admission was 8.42% in our study compared with the mean HBA1C level being 7.8%.

In our study of diabetics with UTI majority (87.14%) had glyco HBA1C >6.5 % with p<0.001. A very high proportion of patients (88.8%) with glycol HBAIC <6.5 and UTI had other underlying factors which are predisposed them to UTI.

The association between Glyco HBA1C and the occurrence of UTI has been investigated in various studies. Analysed the correlation between asymptomatic bacteriuria and glycosylated Hb and did not find any statistically significant association between the degrees of glycemic control and the UTI. He postulated a higher incidence of glucose in patients with UTI; but did not attribute the elevated blood glucose as a predisposing factor for UTI.[13]

Study on factors predisposing to *E. coli* UTI in diabetic population have noted that HBA1C >8.1% was associated with an increased risk for UTI. Our study supports the findings of chung.[14] 26 out of 181 diabetics (14.4%) and 13(10.5%) out of 124 non-diabetic subjects had recurrent UTI. In the study conducted relapses and reinfections were reported in 7.1% and 15.9% of women with diabetes versus 2.0% and 4.1% of women without diabetes.

Concluded that there was an independent higher risk of recurrent UTI in women with diabetes compared with women without diabetes.

E. coli was the most frequent uropathogen isolated, responsible for UTI in 60.2% and 65.3% of diabetic males and females and 50% and 51.4% of non-diabetic males and females. In the study conducted by Mario the isolation rates of ECOLI were, diabetics (males 32.5% vs females 54.1%) and non- diabetics (males 31.4% vs 58.2%).[6]

The prevalence of *E. coli* ESBL is significantly higher in diabetics (78.6%) vs non-diabetics (45.2%). The isolation rates of ECOLI was higher in both diabetics and non-diabetics in our hospital compared to study conducted by in diabetics (50.6%) vs non-diabetics (9.5%).[16]

The prevalence of fungal UTI in diabetic population varies depending on the patient subset under study being more common in patients with prolonged hospital stay, catheterization and prolonged parenteral antibiotic use.[17]

Regarding the antimicrobial resistance profile of the uropathogens, we observed that the isolated *E. coli* strain were resistant at similar rates to ampicillin, cotrimoxazole, norfloxacin and cephalosporin in both diabetic and non-diabetic patients which is in comparison.[6]

Considering the antimicrobial susceptibility, ECOLI has maximum sensitivity to carbapenams in both diabetics (93.8%) and non-diabetics (95.1%). This is comparable to which showed that *E. coli* sensitivity 100% in both diabetic and non-diabetic subjects.

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