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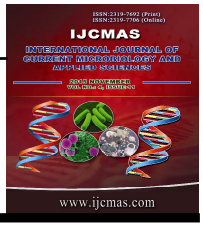

Original Research Article

Prevalence of Uropathogens and their Antibiogram in Diabetic Patients – A Cross Sectional Study

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K e y w o r d s

Diabetes mellitus, Urinary Tract Infection (UTI), *E. coli*

A B S T R A C T

Diabetes mellitus is a chronic, progressive metabolic disorder resulting from loss of loss of early insulin secretion and development of early insulin resistance. Higher frequency of UTI and related complications among diabetics may be attributed to different mechanisms including immune function impairments and higher levels of glucose in urine may contribute to growth of pathogens. This study evaluated the uropathogens in diabetic UTI and their antibiogram. The present study was conducted from 1348 patients sample in Central Clinical Microbiology Laboratory of Narayana General and Super Speciality Hospital for a period of 12 months. Patients attending the Department of Urology diagnosed with Urinary Tract Infections (UTI) and known diabetics and newly diagnosed diabetics were also included in the study. 10ml of clean voided mid stream sample was obtained from all included cases after appropriate instructions. Culture method was done by Blood agar, MacConkey agar plates. Anti microbial susceptibility testing was performed for the isolates by Kirby-Bauer disc diffusion method to different anti-microbial agents. *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923 were used as control organisms. The results were interpreted as per CLSI guidelines. SPSS version 14.0 was used for analysis of data. Escherichia coli was the major uropathogen (27.79%) followed in order by *Klebsiella pneumoniae* (16.00%), *Pseudomonas aeruginosa* (13.43%), *Staphylococcus aureus* (12.00%) and other uropathogens were *Proteus* sp (6%), *Acinetobacter* sp (6.36%), *Citrobacter* sp (3.86%), *Serratia* sp (0.71%), *Staphylococcus saprophyticus* (7.29%), *Enterococci* sp (3.86%). *C. albicans* (2.71%) was the only fungal pathogen isolated in the study. *Escherichia coli* the major pathogen exhibited maximum sensitivity to carbapenems (98%) followed by piperacillin+tazobactum (91%), and maximum resistance was noted to ampicillin (88%) and moderate degree of sensitivity to cefixime, ofloxacin and amikacin (>80%). Almost similar degree of sensitivity was noted among other uropathogens exhibiting maximum sensitivity to carbapenems, *Serratia* sp exhibited maximum sensitivity to all antibiotics (>95%) except trimethoprim +sulphomethoxazole and ampicillin. Among Gram positive pathogens 100% sensitivity was noted to vancomycin and linezolid and maximum resistance noted to Ampicillin. Amikacin and piperacillin+tazobactum exhibited >90% sensitivity to all gram positive pathogens. The prevalence of UTI and ASB was high among diabetic females than in males. Females and males more than 50 years of age post menopausal age were at more risk of acquiring UTI than in young adults. *E. coli* was the most common isolate in ASB cases and maximum sensitive to carbapenems. *S. aureus* was common among gram positive pathogens with maximum sensitivity to vancomycin and linezolid.

Introduction

Diabetes mellitus is a chronic, progressive metabolic disorder resulting from loss of loss of early insulin secretion and development of early insulin resistance (De Fronzo, 1999). It is also considered as an immunocompromised state and is a known risk factor for many diseases (Muller *et al.,* 2005; Shah and Hux, 2003). Asymptomatic Bacteruria (ASB) and Urinary Tract Infections (UTI) are said to be more common in diabetic patients than in general population (Hoepelman *et al.,* 2003; Ronald and Ludwig, 2001). Higher frequency of UTI and related complications among diabetics may be attributed to different mechanisms including immune function impairments and higher levels of glucose in urine may contribute to growth of pathogens (Chen *et al.,* 2009; Mnif et al 2013). The association of UTI in diabetics is more common in females than males because of risk factors like Pregnancy, frequent sexual intercourse, shorter urethra and perineal colonization of common pathogens like *Escherichia coli* and *S. aureus* (Pargavi *et al.,* 2011). UTI complications like bacteraemia, renal abscess and papillary necrosis are more common in diabetics, it is important to recognise the risk factors in diabetic patients. Therefore screening of diabetic individuals for is very important to prevent the complications and cause severe renal damage and failure (Kunin, 1987). Patient related factors like age, metabolic control and duration of diabetes have also been suggested as an increasing risk in acquiring UTI (Turan *et al.,* 2008). The successful management of UTI in diabetics depends on proper identification of bacterial agent and selection of appropriate antibiotic among them. The emergence of resistant bacterial strains due to indiscriminate usage of antibiotics results in increased resistance to commonly used antimicrobials.

The present study was done to evaluate the possible risk factors and the prevalence of ASB and UTI in diabetic patients. This study also evaluated the Uropathogens in diabetic UTI their antibiotic profile which helps to treat the UTI promptly preventing the development of UTI related severe complications which will guide for further management in future. Updated knowledge of the uropathogens and their antibiotic sensitivity helps to mange any kind of emergency in diabetic UTI complications.

Materials and Methods

The present study was conducted at Narayana General and Super Speciality Hospital for a period of 12 months from January 2014 to December 2014.All the patients who attended the OPD of Dept of Endocrinology and General Medicine and all the inpatients diagnosed with diabetes and admitted for various reasons were included in the study. Patients attending the Dept of Urology, diagnosed with Urinary tract Infections (UTI) and known diabetics and newly diagnosed diabetics were also included in the study. The Institutional Ethical committee clearance was obtained for the study.

Inclusion criteria: All the age group individuals who were known diabetic and newly diagnosed cases of diabetes. Diagnosis of diabetes according to WHO guidelines include symptoms of plus random blood glucose concentration equal or more than 11.1mmol/l (200mg %) or fasting plasma glucose equal or more than 7.0mmol/l (126mg %) were considered. All diagnosed cases of UTI. Patients with UTI were diagnosed by having one or more of the following symptoms: frequency, urgency, supra pubic discomfort, dysuria and flank pain. The demographic data like age, duration of diabetes, type of medication

were obtained from each patient. The purpose of the study was explained to the patient or to the care taker and consent was obtained before collection of urine samples.

Exclusion criteria: Patient with H/O of administration of antibiotics for UTI before collection of urine sample or 2 weeks prior were not included in the study.

Sample collection: Blood sample was collected from the included cases for estimation of Hb1Ac. The specimen was centrifuged and serum sample collected and estimation of HbA1c (Glycated haemoglobin) was done by HPLC (Biorad D 100) and the values were noted. Patients with good glycaemic control [HbA1c <8.0% (64 mmol/mol)], [HbA1c range: 8.0–9.0% (64–75 mmol/mol)] moderate control and [HbA1c- 9.0% (75 mmol/mol)] poor control were taken as cut off values and indicators.

Urine specimen: About 10ml of clean voided mid stream sample was obtained from all included cases after appropriate instructions. Female patients were advised to wash the labia before collection of sample. The sterile collected containers were transported immediately to microbiology laboratory for processing.

Processing: Using calibrated loops (10^{-3} ml, Himedialabs), urine specimens were plated on blood agar, MacConkey agar plates and incubated at 37°C for 18–24 hrs. The number of c.f.u/ml (Colony forming units) was counted on Blood agar and c.f.u $>10^5$ /ml were considered significant (Wilson and Gaido, 2004). Isolated colonies were identified and processed and isolates were identified by standard procedures and biochemical reactions (Collee *et al.,* 1989). The specimen was also plated on SDA (Sabourads Dextrose Agar) for growth of *Candida* sp and incubated at 37°C for 18–24 hr and *C. albicans* identified by germ tube test (Koneman *et al.,* 1997). Anti microbial susceptibility testing was performed for the isolates by Kirby-Bauer disc diffusion method to different anti-microbial agents. Escherichia coli ATCC 25922 and Staphylococcus aureus ATCC 25923 were used as control organisms. The results were interpreted as per CLSI guidelines (CLSI, 2005). SPSS version 14.0 was used for analysis of data.

Results and Discussion

The present study was conducted in Central clinical Microbiology laboratory of Narayana General and Super Speciality Hospital for a period of 12 months. The baseline characteristics of the patients included in the study according to age, sex, duration of diabetes, type of medication and glycaemic control based on Hb1Ac is summarised in table 1.

A total of 1348 patients were included of which 526 (526/1348, 39.02%) were males and 822 (822/1348, 60.98%) are females. Out of 968 culture positive cases (71.81%), females outnumbered (584/968, 60.33%) males were 384 (384/968, 39.67%). 380 of the cases showed no growth (380/1348, 28.19%) of which 142 are males (142/380, 37.37%) and 238 were females (238/380, 62.63%).

Out of total 968 culture positive cases 756 (756/968,78.1%) showed symptomatic bacteruria and 212 (212/968,21.90%) demonstrated Asymptomatic bacteruria (ASB). The criteria for defining Asymptomatic bacteruria was defined as the presence of at least 10^5 c.f.u/ml in culture of clean, voided mid stream urine sample.

Out of total 1348 cases, 870(64.54%) had poor glycaemic control as estimated by

Hb1Ac levels and 478 (35.46%) had good glycaemic control. 554 cases (41.10%) were on insulin, 514 (38.13%) were on oral hypoglycaemic agents and 280 (20.77%) were on both. Duration of diabetes was <1 year among 241 (17.88%) cases, >10 years in 421 (31.23%) and maximum 686 (50.89%) falling between >1 year and <10 years. The age distribution of cases in the study is summarised in table 2 with maximum number of cases in the age group of >50 years (57.12%). Females outnumbered in the study with 822 (822/1348, 60.98%) and males 526 (526/1348, 39.02%).

In the present study of all the 1400 total isolates, 463 (33.07%) were isolated from cases of ASB and 937(66.93%) from symptomatic UTI. *Escherichia coli* was the major uropathogen (27.79%) followed in order by *Klebsiella pneumoniae* (16.00%), *Pseudomonas aeruginosa* (13.43%), *Staphylococcus aureus* (12.00%) and other uropathogens were *Proteus* sp(6%), *Acinetobacter* sp(6.36%), *Citrobacter* sp(3.86%), *Serratia* sp(0.71%), *Staphylococcus saprophyticus*(7.29%), *Enterococci* sp (3.86%). *C. albicans* (2.71%) was the only fungal pathogen isolated in the study (Table 3).

The antibiotic sensitivity of the uropathogens is summarised in table 4. A total of 10 antibiotics were chosen and tested against the gram negative isolates and vancomycin, linezolid were tested in additional for gram positive pathogens. *Escherichia coli* the major pathogen exhibited maximum sensitivity to carbapenems (98%) followed by piperacillin+tazobactum (91%), and maximum resistance was noted to ampicillin (88%) and moderate degree of sensitivity to cefixime, ofloxacin and amikacin (>80%). Almost similar degree of sensitivity was noted among other uropathogens exhibiting maximum sensitivity to carbapenems, *Serratia* sp exhibited maximum sensitivity to all antibiotics (>95%) except trimethoprim + sulphomethoxazole and ampicillin.

Among Gram positive pathogens 100% sensitivity was noted to vancomycin and linezolid and maximum resistance noted to ampicillin. Amikacin and piperacillin+tazobactum exhibited >90% sensitivity to all gram positive pathogens.

The present study clearly indicated that UTI in females outnumbered the males as indicated in many literatures all over the world (Bonadio *et al.,* 2006; Jha and Bapat, 2005). The prevalence of UTI in females in our study was 60.32% and males were 39.68%. However prevalence of UTI among diabetic females in studies by Huvos and Rocha (1959) was 41%, Geerlings and colleagues (2000) was 26%. These findings are in contrast to our study, however factors like race, ethnicity, and geographical variation may contribute to differences in results. The prevalence of ASB among diabetics in our study was 21.9% with females accounting to 60.38% and males 39.62% which coincides with the studies of Zhanel *et al.* (1995), Hooton *et al.* (1995). However findings in our study were in contrast to studies of Turan *et al.* (2008) 17.8% and Zamand *et al.* 20%. The reported prevalence of ASB in diabetics has been 10% or less (Zhanel *et al.,* 1995; Hooton *et al.,* 1996; Schmitt *et al.,* 1986). The most common age group was >50 years in both males and females (57.12%) indicating that post menopausal age in females and prostatic hyperplasia in males are one among many factors for UTI in this age group. This is in accordance with studies of Adeyaba *et al.* (2007), Patil *et al.* (2012). Active sexual intercourse during adult age

and increasing diabetic age make them more vulnerable for UTI.

There was high prevalence of UTI in cases with duration more than 1year and less than 10 years (50.89%) which coincides with the findings of Schmitt and colleagues (1986).This study has found that UTI were common in diabetics on insulin than on OHA or both. These findings are in concordance with findings of Turner *et al.* (1999).

Table.1 Baseline characteristics of enrolled cases

	DM		
	Male (No & %)	**Female (No & %)**	**TOTAL**
NO	526(39.02%)	822(60.98%)	1348
CULTURE POSITIVE	384(39.67%)	584(60.33%)	968(71.81%)
CULTURE NEGATIVE	142(37.37%)	238(62.63%)	380(28.19%)
ASB	84(39.62%)	128(60.38%)	212(21.90%)
UTI	300(39.68%)	456(60.32%)	756 (78.1%)
Duration			
<1 year	133(25.29%)	108(13.14%)	241(17.88%)
>1 year- <10 yeras	248(47.15%)	438(52.28%)	686(50.89%)
> 10 years	145(27.57%)	276(33.58%)	421(31.23%)
Medication			
oral	236(45.91)	278(54.09%)	514(38.13%)
Insulin	150(27.08%)	404(72.92%)	554(41.10%)
Both	128(45.71%)	152(54.29%)	280(20.77%)
Hb1Ac			
Normal	228(47.70%)	250(52.30%)	478(35.46%)
Abnormal	298(34.26%)	572(65.74%)	870(64.54%)

Table.2 Age distribution of cases

AGE	**NO OF CASES**		**TOTAL (No &%)**
	MALE (No &%)	**FEMALE (No& %)**	
<15 YEARS	28 (5.32%)	38 (4.62%)	66 (4.9%)
16 -30 YRS	62 (11.79%)	78 (9.49%)	140 (10.39%)
31- 50 YEARS	168 (31.94%)	204 (24.82%)	372 (27.60%)
>50 YEARS	268 (50.95%)	502 (61.07%)	770 (57.12%)
TOTAL	**526(39.02%)**	**822(60.98%)**	**1348**

Table.3 Uropathogens isolated

NAME	ASB	UTI	Total No	%
Escherichia coli	*123*	*266*	389	27.79
Klebsiella pneumoniae	*94*	*130*	224	16.00
Proteus mirabilis	*8*	*38*	46	3.29
Proteus vulgaris	*4*	*34*	38	2.71
Citrobacter freundii	*24*	*30*	54	3.86
Serratia sp	*6*	*4*	10	0.71
Pseudomonas aeruginosa	*22*	*166*	188	13.43
Acinetobacter sp	*18*	*71*	89	6.36
S. aureus	*46*	*122*	168	12.00
Enterococci sp	*28*	*26*	54	3.86
S. saprophyticus	*68*	*34*	102	7.29
Candida albicans	*22*	*16*	38	2.71
Total (No& %)	**463 (33.07%)**	**937(66.93%)**	**1400**	

Chart.1

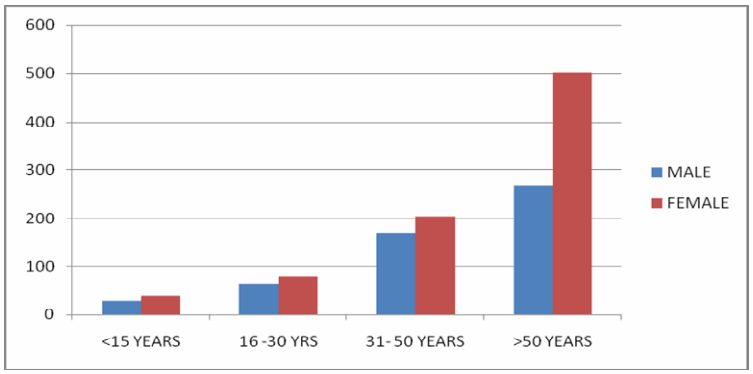

Chart.2

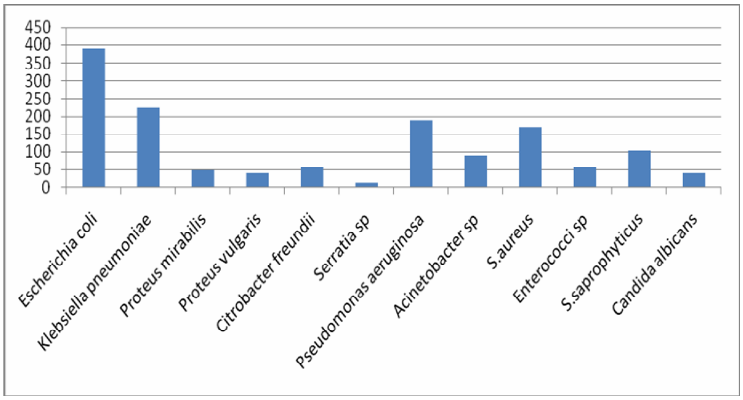

Table.4 Sensitivity % of uropathogens

UROPATHOGEN	AMP	AMX+CV	CTX	CFX	PIP+TZM	OFX	AKN	TMP+SM	IPM	MPM	VAN	LZD
Escherichia coli	22	78	77	81	91	88	86	68	98	98	**	**
Klebsiella pneumoniae	26	81	81	87	93	87	90	72	97	100	**	**
Proteus mirabilis	18	84	79	89	93	84	92	77	99	100	**	**
Proteus vulgaris	26	80	81	88	94	84	94	77	100	99	**	**
Citrobacter freundii	38	85	81	84	94	90	98	82	100	100	**	**
Serratia sp	68	91	92	92	95	91	100	88	100	100	**	**
Pseudomonas aeruginosa	**	72	77	82	89	80	94	**	96	100	**	**
Acinetobacter sp	**	76	72	74	88	83	92	**	95	100	**	**
S. aureus	36	82	80	79	90	87	92	81	**	**	100	100
Enterococci sp	38	80	83	82	90	88	90	**	**	**	100	100
S. saprophyticus	40	92	88	89	94	92	93	84	**	**	100	100

AMP: Ampicillin; AMX+CV: Amoxycillin Clavulanic acid; CTX: Cefotaxime; CFX: Cefixime; PIP+TZM: Piperacillin+Tazobactam; OFX:Ofloxacin; AKN: Amikacin; TMP+SM: Trimethoprin+Sulphomethoxazole; IPM: Imipenum; MPM: Meropenem; VAN: Vancomycin; LZD: Linezolid **-- Not done

In our study 60.98% of cases with poor glycaemic control as shown by Hb1Ac estimation had UTI when compared with 39.02% in cases with good glycaemic control. However studied on this criteria are limited.

As indicated in literatures worldwide and findings of studies Escherichia coli was the predominat pathogen (27.79%) (Bonadio *et al.,* 1999). Several other also reported the occurrence of *Klebsiella pneumoniae* as the next common pathogen (Ludwig, 2000) Literatures in many studies show that *E. coli* may account to 90% of UTI in diabetics. Some of the studies state that the prevalence of *E. coli* as pathogen in DM and Non diabetics is not that significant (Nicolle, 2001). The antibiotic sensitivity pattern of the majority of the isolates were similar to most of the studies reported previously (Hansen *et al.,* 1998; Stapleton, 2002; Boroumand *et al.,* 2006). Carbapenems (Imipenem and meropenems) exhibited maximum sensitivity to most of the gram negative pathogens followed by Piperacillin+tazobactam. Vancomycin, linezolid exhibited 100% sensitivity to *S. aureus*, *Enterococci* sp and *S. saprophyticus* which is similar to studies of Mario *et al.* (2006). All the isolates of the study exhibited maximum resistance to ampicillin.

To conclude in our study the prevalence of UTI and ASB was high among diabetic females than in males. Females and males more than 50 years of age post menopausal age were at more risk of acquiring UTI than in young adults. Diabetics with>1 year and <10 year duration, on insulin therapy and poor glycaemic control are more prone to develop UTI than On OHA or both. Prevalence of ASB was common in female diabetics than males. *E. coli* was the most common isolate in ASB cases and maximum sensitive to carbapenems. *S. aureus* was common among gram positive pathogens with maximum sensitivity to vancomycin and linezolid.

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