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MICROBIOLOGICAL PROFILE OF URINARY TRACT INFECTION ASSOCIATED WITH TYPE-2 DIABETES

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ABSTRACT

Microbial complication associated with diabetes mellitus is of concern and the Multi drug resistant organisms (MDRO's) prevailing in these infections assumes its significance. The present study aimed to determine the microbial etiology and the drug resistance patterns of the pathogens implicated in urinary tract infections in diabetic patients. Mid- stream urine samples were collected, processed and identified as per CLSI guidelines. Bacterial susceptibility testing was performed by disc diffusion method and *in vitro* presence of Methicillin-resistant Staphylococcus aureus (MRSA) and Extended-spectrum beta-lactamases (ESBL) was confirmed as per CLSI guidelines. The major bacterial pathogens in Urinary Tract Infections (UTI) were *E. coli* followed by *K. pneumoniae* and *S. aureus*. *E. coli,* the predominant isolate of UTI was highly resistant to amoxyclav (27.4%), doxycycline HCl and cefotaxime (20.8%) and least resistant to levofloxacin (4.3%) and imipenin (5.4%). Among the total *E. coli* isolates 30.76% (16 out of 52) were ESBL producers and 44.44% of *K. pneumoniae* (8 out of 18) were ESBL producers. In conclusion, the emergence of multidrug resistant bacterial strains complicates microbial infections. The resistance of ESBL-positive organisms to commonly used antibiotics carries a major concern and limits their usage in treating conditions like UTI in individuals with diabetes.

KEYWORDS: *Urinary Tract Infection; Type 2 Diabetes; Multi Drug Resistant Organisms; Microbial complication; ESBL.*

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INTRODUCTION

Diabetes is a debilitating disease with multiple complications resulting from hyperglycaemia, inflammation and possibly immune dysfunction. Individuals with diabetes are at higher risk for various infections than non-diabetic patients[1-3]due to high glucose levels that adversely affects the phagocytic capabilities of polymorphonuclear leukocytes (PMN), which are the front line of defence against bacterial and fungal infections[4]. Thiscould be attributed mainly to decreased PMN membrane fluidity, which can severely impair processes of migration, chemotaxis and intracellular killing[5]. Thus, the reduced response of the host immune defence mechanism[6] increases the susceptibility to various types of infections. Although these immunologic factors seem to put diabetic subjects at higher risk of infection, only a few infectious diseases have been shown to occur more frequently in diabetic subjects. Urinary tract infection is one such major microbial complication that is commonly encountered and is the leading cause of the hospitalization among diabetic patients[7]. Urinary tract infection (UTI) is responsible for considerable morbidity, when concealed or untreated[8]. Structural or functional abnormality of the genitourinary tract and the presence of underlying disease that interferes with the host defence mechanism increase the risk of acquiring infection[9].Some of the risk factors for UTI are obesity, female sex, and prostate syndrome in men. The incomplete bladder emptying due to neuropathy, glycosuria and low immunity favours the growth of some microorganism[9-10]. The commonly found microorganisms UTI are *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus*[11-13]. The first choice of drugs to combat this condition is the usage of antibiotics and a prolong use of it usually results in resistance to various types of antibiotics. The emergence of multi-drug-resistant (MDR) strains is considerably increasing and there is a dearth of data on the prevalence of MDRO in UTI. Thus, it is of prime importance to analyse the resistance pattern of the isolates for adopting the best suitable therapy[14]. The present study is an attempt towards analyzing the susceptibility profile of the microorganisms isolated from diabetic patients with urinary tract infection and the prevalence of MDROs in these infections.

MATERIALS AND METHODS

Study design and study period

This is a case-series study involving 100 diabeticpatients with UTI for a period of one year from March 2015 to March 2016 at two tertiary care hospitals in Mysuru (KR Hospital and Vikram Hospital). All patients at least 20 years of age and above with diabetic UTI (acute and/or chronic) were screened and enrolled for the study. Each patient's fasting blood glucose concentrationwas measured. Both male and female patients with Type 2 diabetes were approached to participate in the study. Clinical characteristics were recorded using pre-tested questionnaires. Each patient was asked about symptoms suggestive of UTI (urgency, dysuria, urinary frequency, and nausea) and predisposing conditions such as hypertension, menopause, indwelling catheter, pyelonephritis, pregnancy, gynaecological disorders, calculi, benign prostatic hypertrophy, glycosuria, recurrence, hydroureteronephrosis, balanoposthitis. A written consent was obtained from all subjects, and clearance was obtained from the institute's ethics committee (IHEC - UOM No. 109), University of Mysore (Mysuru, India).

Inclusion and Exclusion criteria

Type 2 diabetic patients (men and women) in the age group of 20 and above, with UTI without previous antibiotics therapy (one-week duration) and willing to participate were included. Non-diabetics, type 1 diabetic patients were excluded.

Microbiological Methods

Sample collection and processing

Participants were asked to provide midstream urine according to the clean-catch procedure. Samples were transported in a sterile container to the microbiology laboratory, and processed within an hour of collection. Urine samples were inoculated using a standard quantitative loop (0.001 and 0.01 mL) on Mac-Conkey, Blood agar, Cysteine lactose electrolyte deficient (CLED) agar and Chromogenic UTI agar plates. Significant bacteriuria was defined as urine culture plates showing ≥ 10^5 colony-forming units (CFU)/mL of single bacterial species. All the plates (urine culture) were incubated at 37°C for 24 h and observed for significant growth of the pathogens. Identification of bacteria was done using colony characteristics, Gram's reaction of the organism and biochemical test (catalase test, citrate utilization test, indole production test, methyl red test, nitrate reduction test, oxidase test, starch hydrolysis, triple sugar iron agar test, urease test and voges-proskauer test) following standard procedure[15].

Antimicrobial susceptibility testing

Susceptibility testing was performed as per Clinical and Laboratory Standards Institute (CLSI) guidelines[16]. The media and antibiotic discs were purchased from Hi Media Laboratories, Pvt Ltd Mumbai. The standard antibiotics; amikacin (30 µg), amoxyclav (10 µg), amphotericin-B (100 unit), ampicillin (10 µg), cefotaxime (30 µg), cefoxitin (30 µg), cefuroxime (30 µg), chloramphenicol (30 µg), ciprofloxacin (5 µg), clindamycin (1 µg), clotrimazole (10 µg), co-trimoxazole (25 µg), doxycycline HCl (30 µg), erythromycin (15 µg), fluconazole (25 µg), gentamicin (10 µg), imipenem (10 µg), itraconazole (10 µg), ketoconazole (10 µg), levofloxacin (5 µg), norfloxacin (10 mcg), nystatin (100 unit), oxacillin (1 µg), penicillin-G (10 unit), rifampicin (5 µg), tetracycline (30 µg), vancomycin (30 µg) and linezolid (30 µg) generally used to treat UTI were selected for the disc sensitivity method.

Preparation of inoculum

Stock cultures were maintained at 4°C on slants of nutrient agar. A loopful of stock cultures were transferred to a fresh sterile nutrient broth tubes and incubated for 24 hrs at 37° C. The culture (0.2 mL) was inoculated into 5 mL of nutrient broth and incubated until it reached turbidity equal to a standard 0.5 McFarland solution which is equivalent to 10^6 -10^8 CFU/mL, measured spectrophotometrically at 600 nm.

Antimicrobial susceptibility testing

The disc diffusion method was used to determine the antimicrobial susceptibility pattern of isolates. Colonies were suspended in normal saline and using disposable sterile swabs, the suspensions were inoculated on Muller-Hinton agar and incubated for 18 to 24 hrs. Also, *in vitro* presence of MRSA was done by using cefoxitin (30 µg) disc for a zone of inhibition less than or equal to 21 mm and the presence of ESBL was tested using cefotaxime-clavulanic acid against cefotaxime alone, for an increase in more than 3 mm zone of diameter as per CLSI guidelines.

STATISTICAL METHODS

ANOVA was carried out using predisposing conditions as dependent variable and sugar levels, duration of diabetes, gender, age, and bacteriuria as predictors. Subsequently, bacteriuria as well as duration of diabetes was considered as dependent variables and the remaining parameters as predictors.

RESULTS

A total of 100 diabetic patients were enrolled in this study, Demographic data regarding the age, gender, duration of diabetes andcomplications of UTI is tabulated (Table 1). Among the 100 patients screened UTI, samples from 87 patients were found to be positive for culture with a mean age group 55 yrs and male to female ratio 37:50. In five (5.7%) patients, the duration of diabetes was less than 2 years, 2 to 10 yrs in 57 (65.5%) patients and 10 years and above in 25 (28.7%) patients. Interestingly, we observed female patients be predominant in the study and were much prone to UTI than male subjects.

Table 1
Socio demographic characteristics of study population (n=100).

Clinical Characteristics	Diabetic UTI (n=87)
Age (years)	55.4±12.53
Sex (M/F)	37/50
Duration of diabetes (years)	7.1± 4.1
Blood Glucose (mg/dl)	229.6 ± 54.9
Pre-disposing Conditions in UTI	
Indwelling catheter	32(36.8)
Pyelonephritis	10(11.5)
Menopause	9(10.3)
Pregnancy	4(4.6)
Gynaecological disorders	3(3.4)
Calculi	2(2.3)
Benign prostatic hypertrophy	1(1.14)
Glycosuria recurrence	1(1.14)
Hydroureternephrosis	1(1.14)
Balanoposthitis	1(1.14)

Data are represented asn, n (%), mean ± SD, or median (interquartile range)

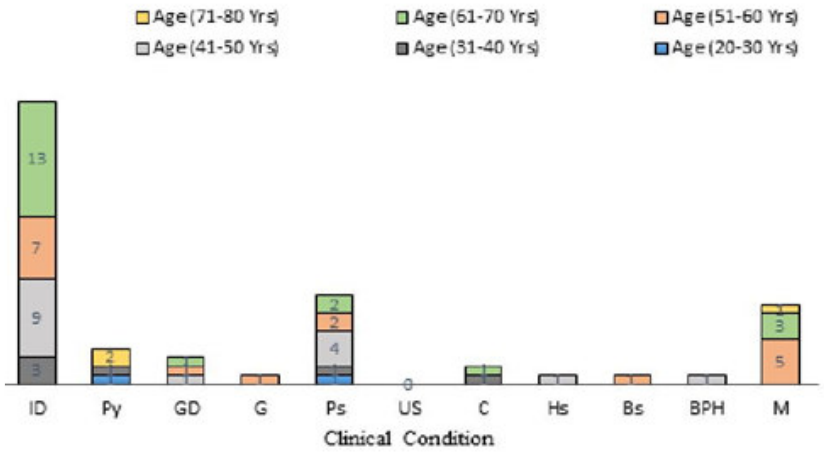

Figure 1
Predisposing clinical conditions associated with urinary tract infection in patients with diabetes.

The conditions represent: ID - Indwelling Catheter; P - Pregnancy; GD- Gynaecological disorder; G- Glycosuria; Ps - Pyelonephritis; US - Urinary surgery; C- Calculi; Hs-Hydroureternephrosis; Bs - Balanoposthitis; BPH - Benign prostatic hyperplasia; M- Menopause. The individual bars in the graph represents total no of patients and within the bar the number represents the patients that fall under different age group. The

predisposing conditions on the basis of age are shown in Figure 1. Thirty-two (36.8%) and 10 (11.5%) had indwelling catheter and pyelonephritis, 9 (10.3%) and 4 (4.6%) had menopause and pregnancy, 3 (3.4%) and 2 (2.3%) had gynaecological disorders and calculi respectively. 1 (1.14%) each had Benign prostatic hypertrophy (BPH), Glycosuria recurrence, Hydroureternephrosis and Balanoposthitis.

Microbiological Surveillance

Sixty-two (71.26%) patients had symptomatic bacteriuria (19 male and 35 female) and twenty-five (28.73%) with asymptomatic bacteriuria (18 male and 15 female). Out of 114 (bacteria) and 11 (fungi) isolates, 91 and 23 isolates were Gram-negative and Gram-positive, respectively. The predominant isolate was *E. coli* (41.6%) followed by *K. pneumoniae* (14.4%), *S. aureus* (11.2%), *P. aeruginosa* (9.6%), *Enterococcus spp* (4.8%), *P. mirabilis* (4%), *Enterobacter spp* (3.2%) and *S. epidermidis* (2.4%). The fungal isolate, *Candida albicans* (8.8%) was less commonly found Table 2.

Table 2
Organisms isolated from urinary tract infections of diabetic patients

Isolates	(%)	20-30 yrs M=0; F=1	31-40 yrs M=3; F=5	41-50 yrs M=9; F=16	51-60 yrs M=9; F=7	61-70 yrs M=14; F=13	71-80 yrs M=4; F=6
Gram negative (n)							
E. coli (52)	41.6	00 (0.0)	07 (5.6)	11 (8.8)	10 (8.0)	19 (15.2)	05 (4.0)
K. pneumoniae (18)	14.4	00 (0.0)	02 (1.6)	08 (6.4)	02 (1.6)	05 (4.0)	01 (0.8)
P. aeruginosa (12)	09.6	00 (0.0)	01 (0.8)	03 (2.4)	04 (3.2)	02 (1.6)	02 (1.6)
P. mirabilis (05)	04.0	00 (0.0)	00 (0.0)	02 (1.6)	00 (0.0)	03 (2.4)	00 (0.0)
Enterobacter spp (04)	03.2	00 (0.0)	01 (0.8)	01 (0.8)	01 (0.8)	00 (0.0)	01 (0.8)
Gram positive (n)							
S. aureus (14)	11.2	00 (0.0)	01 (0.8)	04 (3.2)	04 (3.2)	02 (1.6)	03 (2.4)
Enterococcus spp (06)	04.8	01 (0.8)	00 (0.0)	02 (1.6)	01 (0.8)	02 (1.6)	00 (0.0)
S. epidermidis (03)	02.4	00 (0.0)	00 (0.0)	01 (0.8)	01 (0.8)	01 (0.8)	00 (0.0)
Fungi (n)							
C. albicans (11)	08.8	00 (0.0)	00 (0.0)	03 (2.4)	02 (1.6)	03 (2.4)	03 (2.4)

M-Male; F-Female; n- no of isolates

Table 3
Antimicrobial resistance pattern for the isolates from Urine Samples

Organisms (Total =23)					Organisms (Total =91)						Organisms (Total=11)	
A	**GPB**	***S. e***	***S. a***	***E. f***	**A**	**GNB**	***E.c***	***K. p***	***E. a***	***P.m***	***P. a***	**A**	***C.a***
	n (%)					**n (%)**						**n (%)**	
OX	09(39.1)	01 (04.3)	06 (26.0)	02 (08.6)	**AMC**	41 (45.0)	25 (27.4)	08 (08.7)	01 (01.0)	00 (0.0)	07 (07.6)	**FLC**	05 (45.5)
E	09(39.1)	01 (04.3)	06 (26.0)	02 (08.6)	**DO**	38(41.7)	19 (20.8)	09 (09.8)	02 (02.1)	01 (01.0)	07 (07.6)	**C**	05 (45.5)
P	09(39.1)	00 (0.0)	07 (30.4)	02 (08.6)	**CX**	37(40.6)	18 (19.7)	08 (08.7)	02 (02.1)	02 (02.1)	07 (07.6)	**IT**	05 (45.5)
CD	08 (34.7)	01 (04.3)	05 (21.7)	02 (08.6)	**CTX**	35 (38.4)	19 (20.8)	09 (09.8)	01 (01.0)	00 (0.0)	06 (06.5)	**E**	04 (36.4)
COT	06(26.0)	01(04.3)	05(21.7)	00 (0.0)	**NX**	34 (37.3)	18 (19.7)	09 (09.8)	01 (01.0)	00 (0.0)	06 (06.5)	**KT**	04 (36.4)
TE	08 (34.7)	00 (0.0)	06 (26.0)	02 (08.6)	**GEN**	32 (35.1)	16 (17.5)	07 (07.6)	02 (02.1)	02 (02.1)	05 (05.4)	**LE**	04 (36.4)
GEN	07 (30.4)	01(04.3)	06 (26.0)	00 (0.0)	**COT**	30 (32.9)	18 (19.7)	07 (07.6)	01 (01.0)	00 (0.0)	04 (04.3)	**KAN**	03 (27.3)
CIP	07 (30.4)	01(04.3)	06 (26.0)	00 (0.0)	**CXM**	29 (31.8)	16 (17.5)	06 (06.5)	01 (01.0)	00 (0.0)	06 (06.5)	**AP**	03 (27.3)
C	05 (21.7)	00 (0.0)	05(21.7)	00 (0.0)	**C**	17 (18.6)	08 (08.7)	06 (06.5)	00 (0.0)	00 (0.0)	03 (03.2)	**NX**	03 (27.3)
CTX	03 (13.0)	00 (0.0)	03 (13.0)	00 (0.0)	**AK**	14 (15.3)	06 (06.5)	00 (0.0)	00 (0.0)	02 (02.1)	06 (06.5)	**OX**	02 (18.2)
VA	00 (0.0)	00 (0.0)	00 (0.0)	00 (0.0)	**LE**	14 (15.3)	04 (04.3)	08 (08.7)	01 (01.0)	01 (01.0)	00 (0.00)	**CC**	02 (18.2)
LZ	00 (0.0)	00 (0.0)	00 (0.0)	00 (0.0)	**IMP**	10 (10.9)	05 (05.4)	00 (0.0)	00 (0.0)	00 (0.0)	05 (05.4)	**RIF**	00 (0.00)

OX, Oxacillin; E, Erythromycin; P, Penicillin G; CD, Clindamycin; TE, Tetracycline; CIP, Ciprofloxacin, VA, Vancomycin; LZ, Linezolid; CXM, Cefuroxime; CX, Cefoxitin, DO, Doxycycline HCl; CTX, Cefotaxime; GEN, Gentamycin; AMC, Amoxyclav; NX, Norfloxacin; LE, Levofloxacin; COT, Co-Trimoxazole; AK, Amikacin; C, Chloramphenicol; IMP, Imipenem; AP, Amphotericin-B; CC, Clotrimazole; FLC, Fluconazole; IT, Itraconazole; KT, Ketoconazole; NS, Nystatin; RIF, Rifampicin; KAN, Kanamycin

A, Antibiotics; S.a, Staphylococcus aureus; S.e, Staphylococcus epidermidis; E spp,Enterococcus spp; P.a, Pseudomonas aeruginosa; K.p, Klebsiellapneumoniae; E spp, Enterobacterspp; E.c, Escherichia coli; P.m, Protues mirabilis; C.a, Candida albicans.

The antimicrobial pattern for the UTI isolates is shown in Table 3. A majority of the Gram-positive isolates were resistant to chloramphenicol (39.13%) and penicillin (39.13%). One hundred percent susceptibility was recorded for vancomycin and linezolid. *Staphylococcus aureus*, was found to be predominant isolate among the Gram positives. The resistance pattern of *S. aureus* for penicillin, oxacillin, chloramphenicol, gentamicin, clindamycin and cefotaxime was 26 % and 21.7% for ciprofloxacin. While, the Gram- negative isolates were found to be more resistant to amoxyclav (45%) and doxycycline HCl (41.76%). *E. coli,* the predominant isolate was highly resistant to amoxyclav (27.4%), doxycycline HCl and cefotaxime (20.8%) and low resistant to levofloxacin (4.3%) and imipenin (5.4%). Among the ESBL producers, the percentage of *E. coli* isolates was found to be 30.76% (16 out of 52). While it was interesting to note that 44.44% (8 out of 18) of *Klebsiella pneumoniae* isolates were also positive. *Candida albicans* was found highly resistant to amphotericin- B, erythromycin and chloramphenicol (45.5%) and low resistant to levofloxacin. The results were analysed statistically to find any association between diabetes and UTI. The ANOVA results are tabulated in (Table 4.1 & 4.2), When predisposing conditions were used as dependent variable, bacteriuria appeared as a predictor. When bacteriuria was used as a dependent variable, sugar levels appeared as a significant (P < 0.002) predictor.

Table 4.1
Significance of gender and bacteriuria ANOVA

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	318.922	5	63.784	3.974	**0.003**[b]
	Residual	1508.788	94	16.051		
	Total	1827.710	99			

Dependent Variable: Predisposing conditions for UTI
Predictors: (Constant), Sugar level (mg/dL), Duration of Diabetes (yrs), Gender, Age (yrs), Bacteriuria df-degree of freedom; F-f statistic; Sig- Sigma

Coefficients[a]

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	SE	β		
1	(Constant)	4.686	3.417		1.371	0.174
	Gender	-1.888	0.824	-0.219	-2.290	0.024
	Age (yrs)	-0.017	0.033	-0.052	-0.528	0.599
	Duration of Diabetes (yrs)	0.114	0.099	0.113	1.153	0.252
	Bacteriuria	2.231	0.659	0.338	3.383	0.001
	Sugar level (mg/dL)	0.000	0.007	0.005	0.054	0.957

b- unstandardized beta co-efficients; t- t statistic; SE- Standard error; β- Standardized beta co-efficients; Sig -Sigma

Table 4.2
Significant difference of predisposing conditions of UTI and blood sugar level

ANOVA

Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	9.096	5	1.819	5.197	0.000[b]
	Residual	32.904	94	0.350		
	Total	42.000	99			

Dependent Variable: Bacteriuria
Predictors: (Constant), Sugar level (mg/dL), Duration of Diabetes (yrs), Gender, Predisposing conditions for UTI, Age (yrs) df-degree of freedom; F-f statistic; Sig- Sigma

Coefficients

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		b	SE	B		
1	(Constant)	2.166	0.458		4.728	0.000
	Gender	0.141	0.124	0.108	1.132	0.260
	Age (yrs)	-0.003	0.005	-0.063	-0.661	0.511
	Duration of Diabetes (yrs)	0.006	0.015	0.037	0.383	0.703
	Predisposing conditions for UTI	0.049	0.014	0.321	3.383	0.001
	Sugar level (mg/dL)	-0.003	0.001	-0.295	-3.198	0.002

b- unstandardized beta co-efficients; t- t statistic; SE- Standard error; β-Standardized beta co-efficients; Sig -Sigma

DISCUSSION

With the existing literature, the studies on the microbial complications associated with diabetes are meagre. The results obtained in the present study have shown a varying pattern of microbial distribution and sensitivity based on the severity of an infection. Patients with type 2 diabetes linger with UTI for a long time with the onset of symptoms, where the first sign is the appearance is UTI infections[17-18]. In the present study, an attempt was made to characterize UTI infections using conventional microbiological and biochemical methods of isolation and identification of microbes. Urinary Tract Infection (UTI) is a common condition found associated with diabetes.UTI is one of the most common causes of hospitalization and the symptoms depend on the age and site of infection[19]. The influence of diabetes on the stimulation and development of UTI has been of concern, as the predisposition of the microorganisms involved develops resistance to a routine treatment regimen. In the present study, 91.2% (114 out of 125) isolates in 87 diabetic patients clinically diagnosed with UTI re-emphasizes the fact that regular survey holds a key for the effective treatment especially for people with low-income countries[20]. The prevalence was significantly higher in female patients than male. A significant correlation between the age of the patient, presence of microorganisms and their sugar level has been studied. Mostly female in the age group 61-70 yrs with a mean sugar level of 253 mg/dL were prone to infection; this could be due to a decrease in urinary flow, incomplete bladder emptying after urination and prolapse of the bladder or vagina in women[21]. However, the gender of the patients had no significant influence on the bacterial distribution. The prevalence of UTI increased 1.4-fold for every decade and this observation is in support of earlier studies[22] where they found a significant correlation between duration of diabetes and the prevalence of bacteriuria with a 1.9 fold increase in every 10 years in the duration of diabetes. Such incidence is significantly higher among the rural community due to poor hygiene conditions. The anatomy of the female genitourinary system and immunity in the aged people remains exceptional among factors which dispose people to UTI, especially among those from low socio-economic status. This provides a clue to why female are more prone to UTI than male[23-24]. Our results show that *Escherichia coli* is the most predominant organism isolated in uncomplicated cases of UTI. Whereas in complicated cases, the presence of both Gram-positive and Gram-negative bacteria was observed, this included the multidrug resistant organisms. This is in agreement with the studies reported earlier[25]. *E. coli* caused UTI in 60.91% (53 out of 87) of diabetic patients which is in accordance with the findings of previous studies[26-30]. The overall susceptibility rates to various antibiotics especially for amoxyclav, doxycycline, cefuroxime, cefoxitin, cefotaxime, norfloxacin, gentamycin and chloramphenicol tested among Gram-negative and clindamycin, oxacillin, erythromycin, ciprofloxacin, chloramphenicol and tetracycline among Gram-positive isolates were low. Whilestudies on infections among diabetic subjects have reported high resistance rates to various antibiotics among the tested bacteria (Gram-negative and Gram-positive)[31-33]. A significant number of isolates of *E. coli* (30.76%) and *K. pneumoniae* (44.4%) were ESBL producers. Studies from other investigators have reported similar results (21.4% and 56.2%) when screened for ESBL producing *E. coli* and *K. pneumoniae* in diabetic patients with UTI[34]. The production of ESBL by varying Gram-negative bacteria was earlier reported by Mathur[35]. Treatment of the infection with such MDRO remains a challenge due to the high tendency of the bacteria to develop resistance to conventional antibiotics. The widespread usage of broad spectrum antibiotics leads to selective survival advantage of pathogen[36]. Therefore, antibiotic resistance profile of microbes plays a significant role in determining the phase of infection. Our findings underline the importance of early recognition of the clinical picture of the type of infection and this could be useful in implementing timely therapy. Overall, the blood sugar levels were strong predictors of UTI suggesting that the diabetic condition that leads to elevated blood sugar levels would predispose the individual to infection.

CONCLUSIONS

The present study confirms that presence of MDRO is extremely common in diabetic patients with urine infection and its prevalence is alarming due to prolong usage of various antibiotics that limits the choice of treatment. In view of the emerging resistance amongst the isolates, we must advocate therapy as far as possible, after sensitivity test has been performed. This would facilitate proper treatment to the patients and will also discourage the abrupt use of the antibiotics thereby preventing bacterial drug resistant. The two phenotypic ways to fight bacterial drug resistance would be to reduce the use of antimicrobial drugs so as to decrease the selection of resistant strains, and another way is to improve hygiene to prevent the spread of infections by resistant bacteria. Due to the great resistance offered by these organisms, treatment can be challenging and therefore, demands an effective and alternative treatment that could decrease the incidence of MDRO infection in patients associated with diabetes.

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CONFLICT OF INTEREST

Conflict of interest declared none.

REFERENCES

1. Edwards JE, Tillman DB, Miller ME, Pitchon HE.Infection and diabetes mellitus.West J Med. 1979; 130: 515-521.
2. Wheat LJ. Infection and diabetes mellitus. Diabetes Care.1980; 3: 187-195.
3. Kaslow RA. Infections in diabetics. *Diabetes in America*. Harris MI, Hamman RF, ed. NIH publ; 1985; 85: 1-18.
4. Drachman RH, Root RK, Wood WB. Studies on the effect of experimental nonketotic diabetes on antibacterial defense- I. Demonstration of a defect in phagocytosis. J Exp Med.1966; 124: 227-240.
5. Masuda M, Markami T, Egawa H, Murata K. Decreased fluidity of polymorphonuclear leukocyte membrane in streptozotocin- induced diabetic rats. Diabetes.1990; 39: 466- 470.
6. Peleg AY, Weerarathna T, McCarthy JS, Davis TM. Common infections in diabetes: Pathogenesis, management and relationship to glycaemic control. Diabetes Metab Res Rev. 2007; 23: 3–13.
7. Pappu AK, Sinha A, Johnson A. Microbiological profile of diabetic foot ulcer. Calicut Med Journal 2011; 9(3): 1-4.
8. Schneeberger C, Kazemier BM, Geerlings SE. Asymptomatic bacteriuria and urinary tract infections in special patient groups: women with diabetes mellitus and pregnant women. Curr Opin Infect Dis. 2014; 27(1): 108–114.
9. Nicolle LE. Urinary tract infection in diabetes, Curr Opin Infect Dis. 2005; 18: 49 53.
10. Funfstuck R, Nicolle LE, Hanefeld M, Naber KG. Urinary tract infection in patients with diabetes mellitus. Clin Nephrol. 2012; 77: 40–48.
11. Breen JD, Karchmer AW. *Staphylococcus aureus* infections in diabetic patients. Infect Dis Clin North Am .1995; 9: 11-24.
12. Joshi N, Caputo MG, Weitekamp RM, Karchmer AW. Infections in patients with Diabetes milletus. N Engl J Med .1999; 341: 1906-1912.
13. Das A, Tag H. Ethno-medicinal studies of the khamti tribe of Arunachal Pradesh. Indian J Tradit Know . 2006; 5(3): 317-322.
14. Goldstein EJ, Citron DM, Nesbit CA. Diabetic foot infections: bacteriology and activity of 10 oral antimicrobial agents against bacteria isolated from consecutive cases. Diabetes Care.1996; 19: 638–641.
15. Forbes B A, Sahm DF, Weissfeld AS. Bailey & Scott's Diagnostic Microbiology, 12thedn. St. Louis: Elsevier Science Health Science Division; 2007.
16. CLSI. Performance standards for antimicrobial susceptibility testing. Wayne, PA: Clinical and Laboratory Standards Institute; Approved standard. Document M100 S17; 2007.
17. Carvalho CB, Neto RM, Aragao LP, Oliveira MM, Nogueira MB, Forti AC. Diabetic foot infection. Bacteriologic analysis of 141 patients. Arq Bras Endocrinol Metabol. 2004; 48: 398-405.
18. Pugazhendhi Sugandhi, Durairaj, Arvind Prasanth. Bacteriological profile of Diabetic foot infections. IJIRSET. 2014; 3(7): 14688-14692.
19. Odoki M, Bazira J, Maazam ML, Agwu E. Health point survey of bacteria Urinary tract infections among suspected diabetic patients attending clinincs in Bushenyi district of Uganda. SBPJ. 2015; 1(1): 0005-0009.
20. Agwu E, Ihongbe JC, Inyang NJ. Prevalene of Quinolone Susceptible *Pseudomonas aeruginosa* and *Staphylococcus aureus* in delayed- healing diabetic foot ulcers in Ekpoma Nigeria.Wounds.2010; 4: 100-105.
21. Avril JL, Mesnard R, Roche G, Pouedras P. Place et sensibilite aux antibiotiques des *Enterobacteriaceae* responsables d infections urinaires. Sem Hop Paris. 1993; 69: 81–86.
22. Bahl Al, Chugh, RN, Sharma KB. Asymptomatic bacteremia in diabetes attending a diabetic clinic. Indian J Med Sci. 1970; 24: 1-6.
23. Hummers pradier E, kochen MM. Urinary tract infections in adult general practice patients. Brit J Gepract.2002; 52: 752-761.
24. McLaughlin S.P., Carson, C.C., 2004. Urinary tract infections in women. Med Clin North Am. 88, 417-429.
25. Wagenlehner F, Naber KG. Treatment of Bacterial Urinary Tract Infections: Presence and Future. Europ Urol. 2006; 49: 235-244.
26. Oduyebo OO, Daso MA, Uti RA, Ketiku KK. Prevalence of Urinary tract infection in patients undergoing pelvic radiotherapy at a teaching hospital in lagos, Nigeria. J Nig Infect Con Assoc. 2001; 4: 6-10.
27. TanujaRana, Jasumati, NavroopKaur, Payal Thakur. Isolation, Characterization and antibiotic susceptibility testing of Enteric Bacteria isolated from Urinary tract infection. Int. J. Pharma Bio Sci. 2013; 4(2): 631- 639.
28. Adeyeba OA, Omosighoand PO, Adesiji YO. Bacterial urinary tract infections in patients with diabetes miletus. Int J Trop Med. 2007; 2: 89-92.
29. Bashir MF, Qazi JI, Ahmad N, Riaz S. Diversity of urinary tract pathogens and drug resistant isolates of *Escherichia coli* in different age and gender groups of Pakistanis. Trop J Pharm Res. 2008; 7:1025-1031.
30. Mohammadi M, Ghasemi E, Mokhayeri H, Pournia Y, Borou H. Antimicrobial resistance patterns of *E. coli* detected from hospitalized urine culture samples. Asian J of Biol Sci. 2010; 3: 195-201.
31. Motta RN, Oliveira MM, Magalhães PS, Dias AM, Aragão LP, Forti AC, et al. Plasmid-mediated extended-spectrum beta-lactamase-producing strains of Enterobacteriaceae isolated from diabetes foot infections in a Brazilian diabetic centre. Braz J Infect Dis. 2003; 7:129–34.
32. Varaiya A, Kulkarni M, Bhalekar P, Dogra J. Incidence of metallo-beta-lactamase-producing *Pseudomonas aeruginosa* in diabetes and cancer patients. Indian J Pathol Microbiol. 2008; 51:200–3.
33. Sotto A, Lina G, Richard JL, Combescure C, Bourg G, Vidal L, et al. Virulence potential of *Staphylococcus aureus* strains isolated from diabetic foot ulcers: A new paradigm. Diabetes Care. 2008; 31:2318–24.

34. Mahesh E, Medha Y, Indumathi VA, Prithvi Kumar S, Mohammed Wasim Khan, Punith K. Community acquired UTIin the elderly. Br. J. Med. Pract. 2011; 4(1): a406.
35. Mathur P, Tatman A, Das B, Dhavan B. Prevalence of ESBL Gram negative bacteria in a tertiary care hospital. Indian J of Med Microbiol. 2002; 115: 153- 157.
36. Lidia R, Dominguez MA, Neus R, Miguel V. Relationship between clinical and environmental isolates of *Pseudomonas aeruginosa* in a hospital setting. Arch of Med Res. 2004; 35(3): 251–257.

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