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Original Research Paper

Study on Uropathogens Causing Urinary Tract Infection in Diabetic Patients and Their Susceptibility Pattern

Medical Science

KEYWORDS : Urinary tract infection, Diabetes, Uropathogens

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ABSTRACT

The incidence of diabetes mellitus is increasing markedly throughout the world and is becoming a serious public health threat particularly in developing countries. Diabetes mellitus has long been considered to be a predisposing factor for Urinary Tract Infection (UTI) and the urinary tract is the principle site of infection in diabetic patients with increased risk of complications. Therefore the aim of the current study is to determine the spectrum of uropathogens and their antimicrobial susceptibility pattern in diabetic patients with clinically suspected UTI.Urine samples were collected from 150 diabetic patients with symptoms of UTI attending the Medicine department. The specimens were processed and examined for various uropathogens using the standard microbiological procedures. Antibiotic susceptibility testing was performed and the results were analysed as per CLSI guidelines .Out of the 150 diabetic patients with symptoms of UTI , uropathogens were isolated from 85 (56.7%) patients with females(72.7%) outnumbering males(27.3%). Escherichia coli (42.7%) was the most prevalent uropathogen followed by Enterococcus species (22.9%) Most of the isolates showed moderate to high levels of resistance to one or more antimicrobials commonly used. UTI due to emergence of resistant bacterial strains increases the cost of treatment, morbidity and mortality in diabetics. Therefore regular monitoring is essential to establish reliable information about resistance pattern of urinary pathogens for optimal empirical therapy of diabetic patients with UTI.

INTRODUCTION

Diabetes mellitus (DM) is one of the most challenging health problems of 21st century and is the fifth leading cause of death in developed countries. Asian patients are considered to have a higher risk of developing diabetes and potentially worse prognosis (Ijaz M et al.,2014).The incidence of diabetes is ever-increasing throughout the world and is becoming a serious public health threat particularly in the developing countries (Supriya G .,2016). It is associated with many complications and in the long run it has some major effects on the genitourinary system which makes diabetes patients more vulnerable to Urinary Tract Infection(UTI) , particularly to upper urinary tract infections(Shill MC., 2010).Individuals with diabetes mellitus are reported to have increased risk of UTI both in frequency and severity(Sibi G et al.,2011,Ramana BV et al ., 2012).

Diabetes mellitus causes changes in host defense mechanisms, neuropathy which impair bladder emptying and the presence of diabetic cystopathy and microvascular disease in the kidneys play a significant role in the higher incidence of UTI's in diabetic patients (Ampaire L et al., 2015). The prevalence of DM is increasing worldwide and the emergence of multidrug resistant strains is escalating. The spectrum of organisms causing UTI and their sensitivity patterns have changed over a period of time due to indiscriminate use of antibiotics . A sound knowledge of the current trend helps to initiate an appropriate antibiotic while awaiting culture reports (Kruthika M et al., 2015). The emergence of resistant bacterial strains poses a continued challenge to treat and control the spread of infections. This is a great concern due to the high rates of resistance to antimicrobials used in the treatment of infections caused by uropathogens, particularly in developing countries. UTI due to emergence of resistant bacterial strains increases the cost of treatment, morbidity and mortality in diabetics (Yadav K et al., 2016).Since the microorganisms causing UTI vary in their susceptibility to antimicrobials from place to place and time to time, constant screening of susceptibility pattern of predominant organism against antimicrobials is essential. Therefore the current study was undertaken to determine the organisms causing UTI in diabetic patients and their antibiotic susceptibility pattern.

MATERIALS AND METHODS

The present cross sectional study was conducted in the Department of General Medicine and Department of Microbiology of A.C.S Medical College and Hospital from October 2015 to April 2016.Study group includes 150 diabetic patients presenting with urinary symptoms attending the outpatient and inpatient clinic of Medicine department. The diagnosis of Diabetes was based on WHO-2006 glucose based criteria(WHO 2006).Both males and females above 18 years of age were included in the study. A symptom of UTI is defined as the presence of at least two of the following complaints: dysuria, urgency, frequency, incontinence, supra pubic pain, flank pain or costovertebral angle tenderness, fever and chills (Yismaw G et al.,2016).Exclusion criteria included pregnancy, known underlying renal pathology or chronic renal failure or use of antimicrobial therapy during the previous month. Informed written consent was taken from all the patients included in the study.

Clean voided midstream urine samples were collected in sterile containers after giving proper instructions .The samples were processed in the Microbiology laboratory within 2 hours of collection. Urine cultures were performed using semi-quantitative technique whereby urine samples were inoculated on Cystein-Lactose Electrolyte Deficient (CLED) medium plates with a calibrated loop (0.001ml) and incubated at 37°C for 18-24 hours. Significant bacteriuria was defined as urine culture plates showing more than 10^5 colony-forming units (CFU)/ml of single bacterial species. In case of Staphylococcus aureus, pure growth was considered significant regardless of the CFU's. The presence of yeast in any number was considered to be significant. The pathogens isolated were gram stained and characterized as per the standard microbiological procedures (Colle JG et al.,1996). Antimicrobial susceptibility for bacterial isolates was done by Kirby-Bauer disc diffusion method and the results were interpreted as per CLSI guidelines(CLSI 2012). The data was tabulated and analyzed.

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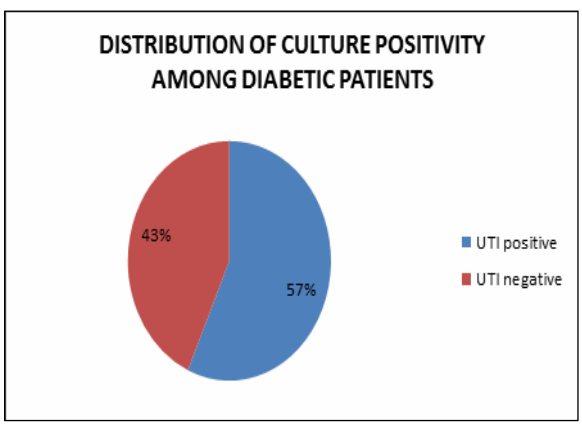
RESULTS

A total of 150 diabetic patients presenting with symptoms of UTI were included in the study. Out of the 150 diabetic patients, 109(72.7%) were females and 41(27.3%) were males. The female patients in our study population were between the age group of 26 -79 years and the males were between the age group of 31 -76 years.

Among the 150 patients, significant bacteriuria was seen in 85 (56.7%) patients, 10(6.7%) patients had an insignificant colony count and no growth was seen in 55 (36.6%) . Patients with significant bacteriuria were considered as culture positive 85(56.7%) for UTI and patients with insignificant colony count and no growth were considered as UTI negative 65(43.3%) as shown in Fig-1.

FIG-1



The overall prevalence of urinary tract infection was found to be 56.7% and analyzing the prevalence with respect to gender, females (61.4%) had a higher prevalence of infection than males (43.9%) .The age and gender distribution of the diabetic patients with UTI is shown in Table-1. In our study, UTI was more prevalent in the age group of 40-60years followed by 21-40 years in both males and females. A total of 96 pathogens were isolated from all patients with significant UTI.

TABLE-1
AGE AND GENDER DISTRIBUTION OF DIABETIC PATIENTS WITH UTI

AGE	MALES			FEMALES		
	Total	UTI POSITIVE	%	Total	UTI POSITIVE	%
21-40	13	08	61.5%	31	19	61.3%
41-60	21	07	33.3%	59	34	57.6%
60-80	07	03	42.9%	19	14	73.6%
Total	41	18	43.9%	109	67	61.4%

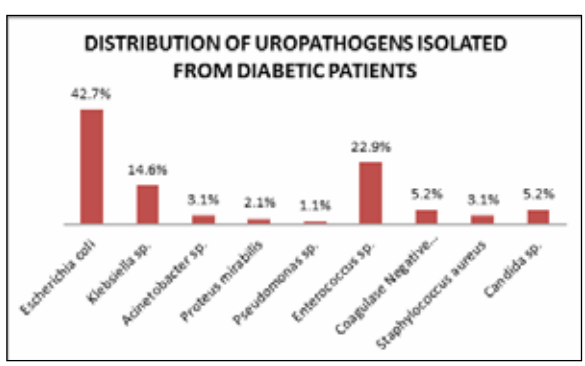
Among the 96 isolated organisms, 61(63.5%) were gram negative isolates followed by 30 (31.3%) gram positive isolates and 5(5.2%) were *Candida* sp. (Table-2)

TABLE-2
DISTRIBUTION OF UROPATHOGENS ISOLATED FROM DIABETIC PATIENTS (n=150)

UROPATHOGENS ISOLATED	NUMBER	%	ORGANISMS ISOLATED	NUMBER	%
GRAM NEGATIVE ISOLATES	61	63.5%	Escherichia coli	41	42.7
			Klebsiella sp.	14	14.6
			Acinetobacter sp.	03	3.1
			Proteus mirabilis	02	2.1
			Pseudomonas sp.	01	1.1
GRAM POSITIVE ISOLATES	30	31.3%	Enterococcus sp.	22	22.9
			Coagulase Negative Staphylococcus	05	5.2
			Staphylococcus aureus	03	3.1
FUNGI	5	5.2%	Candida sp.	05	5.2
TOTAL	96	100	TOTAL	96	100

Escherichia coli was the most frequent uropathogen isolated accounting for 41(42.7%) isolates followed by *Enterococcus* sp. 22(22.9%)and *Klebsiella pneumoniae* 14(14.6%).Among other isolated organisms were *Acinetobacter* sp. 3(3.1%), , *Coagulase Negative Staphylococcus* 5(5.2%), *Staphylococcus aureus* 3(3.1%), *Proteus mirabilis 2* (2.1%), *Pseudomonas* sp.1(1.1%), and *Candida albicans*(5.2%). Distribution of the uropathogens isolated from diabetic patients is shown in FIG-3.

FIG-2



The resistance pattern of the gram negative isolates is shown in Table -3. *E.coli* exihibited high resistance with Ampicillin(80.4%) and Nalidixic acid(80.4%). Cefotaxime (68.3%) and Ciprofloxacin(65.8%) showed moderate resistance against *E.coli* infection. Gentamycin demonstrated only 24.3% resistance while Amikacin and Nitrofurantoin proved to be active against *E.coli* with a resistance of 2.4% and 9.7% respectively.

TABLE-3
ANTIBIOTIC RESISTANCE PATTERN OF GRAM NEGATIVE ISOLATES

Organism	No.	AMP 10 mcg	AK 10 mcg	G 10mcg	CIP 5 mcg	NIT 300mcg	NA 30mcg	CTX 30 mcg
Escherichia coli	41	33 (80.4%)	1 (2.4%)	10 (24.3%)	27 (65.8%)	4 (9.7%)	33 (80.4%)	28 (68.3%)

Klebsiella pneumoniae	14	14 (100%)	2 (14.3%)	3 (21.4%)	07 (50%)	03 (21.4%)	07 (50%)	10 (71.4%)
Acinetobacter sp.	03	2 (66.6%)	1 (33.3%)	2 (66.6%)	1 (33.3%)	ND	1 (33.3%)	2 (66.6%)
Proteus mirabilis	02	2(100%)	0(0%)	1(0%)	1(0%)	ND	1(0%)	1(0%)
Pseudomonas sp	01	1(100%)	0(0%)	1(100%)	0(0%)	ND	ND	0(0%)

AMP- AMPICILLIN, AK-AMIKACIN, G-GENTAMYCIN, CIP-CIPROFLOXACIN, CTX-CEFOTAXIME, NIT – NITROFURANTOIN, NA- NALIDIXIC ACID , ND-NOT DONE

Klebsiella pneumoniae showed 100% resistance with Ampicillin and 71.4% against Cefotaxime. Moderate resistance was observed with Nalidixic acid(50%) and Ciprofloxacin (50%).Lowest resistance was exihibited with Nitrofurantoin (21.4%),Gentamycin(21.4%) and Amikacin(14.3%).Other gram negative isolates also exihibited similar resistance pattern.

Antibiotic resistance pattern of Gram positive isolates were shown in table-4.In the current study, *Enterococcus* sp. was the second common isolate and they have shown a high level of resistance for most of the tested antibiotics, Erythromycin(77.3%), Ampicillin (68.1%) , Ciprofloxacin (59.1%) and Amikacin(40.9%).However they have exihibited low level resistance to Amoxyclav(22.7%) and High level Gentamycin(27.3%). Further all the gram positive isolates have shown 100% susceptibility to Vancomycin and Linezolid.

TABLE-4
ANTIBIOTIC RESISTANCE PATTERN OF GRAM POSITIVE ISOLATES

Organism	No.	AMP 10 mcg	AK 10 mcg	G-10mcg /HLG*-120mcg	CIP 5 mcg	AMC 30mcg	E 15 mcg	VA 30 mcg	LZ 15mcg	CX 30mcg
Enterococcus sp	22	15 (68.1%)	9 (40.9%	06* (27.3%)	13 (59.1%)	5 (22.7%)	17 (77.3%)	0	0	-
Coagulase Negative staphylococcus	05	ND	1 (20%)	02 (40%)	02 (40%)	03 (60%)	02 (40%)	0	0	0
Staphylococcus . aureus	03	ND	0	01 (33.3%)	01 (33.3%)	01 (33.3%)	01 (33.3%)	0	0	0

AMP- AMPICILLIN, AK-AMIKACIN, G-GENTAMYCIN, HLG- HIGH LEVEL GENTAMYCIN ,CIP-CIPROFLOXACIN, AMC-AMOXYCLAV, E-ERYTHROMYCIN, VA-VANCOMYCIN, LZ-LINEZOLID, CX-CEFOXITIN , ND-NOT DONE

DISCUSSION

Urinary tract infection are amongst the most common infections encountered in clinical practice. The urinary tract is the principle site of infection in diabetics with increased risk of complications.

In the current study, among the 150 diabetic patients, the prevalence of UTI was 56.7% which is in good agreement with the finding reported by Ijaz M et al (2014) and Jha PK et al (2014) showing prevalence of UTI to be 51% and 54.7% respectively. The prevalence of UTI among the female diabetic patients was 61.4% which was higher when compared to the prevalence in male. This finding is compatible with the other reports stating high prevalence of UTI in females (Ramana BV et al.,2012, Yadav K et al., 2016,Adeyeba OA et al.,2007). The predominance of female could be explained by its short urethra ,low pH, close proximity of the urethra to anus, teeming of perianal flora, sexual intercourse, favours the infection (Aiyegoro OA et al., 2007).

The predominant number of pathogens isolated in our study were gram negative bacilli. *E.coli* (42.7%) was the most prevalent uropathogen isolated in this study. This is similar with the reports obtained from various other studies where *E.coli* had been the major pathogen (Ramana BV et al ., 2012,Yadav K et al., 2016, Jha PK et al.,2016, Sharma V et al., 2012). The reason for predominant *E. coli* isolation is that it can bind to the glycoconjugate receptor of the epithelial cells of human urinary tract so that it can initiate infection itself. *E.coli* is the most predominant organism to colonize the urethral meatus and perineum before ascending to the bladder. This ability of *E .coli* is the important reason to be the most frequent organism causing UTI in both sexes all over the world (Yadav K et al.,2016). *Klebsiella pneumoniae* was the second most predominant isolate in most of the studies. However current study revealed that the second common pathogen was *Enterococcus* sp..accounting for 22.9%.This result is consistent with the finding of Jha P K et al (2014) in which E.coli (49%) was the most common isolate followed by Enterococcus sp.(35%) In an another study from North India, it was found that *Escherichia coli* was the most commonly grown organism (57.9%) , followed by *Staphylococcus aureus* (21%), *Klebsiella* species (15%) , *Enterococcus* species (2.63%) and *Pseudomonas* sp(2.63%) (Yadav et al., 2015)

Antimicrobial resistance among uropathogens to the commonly used antibiotics is emerging and this makes clinicians to have limited choices of drugs for the treatment of urinary tract infection (Ampaire et al.,2015). In this study , antibiotic susceptibility pattern of the Gram negative pathogens showed that most of the isolates were resistant to Ampicillin , which is relatively a cheaper drug and this finding correlates with other studies(Jha PK et al., 2014,Adeyeba OA et al., 2007).In addition, the most prevalent pathogen , *E.coli* showed high resistance against Nalidixic acid and moderate level against Cefotaxime and Ciprofloxacin. However *E.coli* was highly susceptible to Amikacin and Nitrofurantoin which corrobates with the study done by Jha PK et al(2014). Karlowsky J A et al (2001) detected lowest rates of resistance to Nitrofurantoin among *E.coli* stating that Nitrofurantoin has its potent activity against *E.coli* despite 50 years of use.

In the present study, the most effective antimicrobial agent for Gram negative bacilli were Amikacin and Nitrofurantoin. However in the current study the effect of Nitrofurantoin on *Pseudomonas* sp., *Proteus* sp. and *Acinetobacter* sp. have not been tested as they have intrinsic resistance to Nitrofurantoin (Karlowsky JA et al., 2001). Amikacin has shown to be the most promising antibiotic for UTI in dia-

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betes (Shill MC.,2010). In the present study , Gram positive cocci were sensitive to Linezolid and Vancomycin. However *Enterococcus* sp. have shown a high level resistance to Ampicillin , Amikacin , Erythromycin and Ciprofloxacin and a low level of resistance against Amoxyclav and High Level Gentamycin.

The easy availability and indiscriminate use of commonly used antibiotics may explain the observed increase in resistance since antibiotic resistance has been recognized as the consequence of antibiotic use and abuse (Sharma V et al ., 2012).Therefore early diagnosis and institution of definitive therapy after the sensitivity reports are obtained will not only help in eradication of infection but also prevents the emergence of antimicrobial strains .

CONCLUSION

The study concluded that the prevalence of UTI was higher in females with diabetes than in males. Escherichia coli was the major uropathogen isolated from diabetic patients followed by Enterococcus sp.. Antimicrobial pattern of isolates are very important as it guides the treatment for the clinicians. Most of the isolates showed moderate to high levels of resistance to one or more antimicrobials commonly used. Since the microorganism causing UTI vary in their susceptibility pattern from time to time and place to place , regular monitoring is very essential to establish reliable information about resistance pattern of urinary pathogens for optimal empirical therapy of diabetic patients with UTI.

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