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Original Research Article

Influence of Diabetes Mellitus on the Uropathogens and Antibiotic Sensitivity Pattern in Patients with UTI: A Comparative Study

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Abstract

Aim: To study the influence of diabetes mellitus on the uropathogens and antibiotic sensitivity pattern in patients with UTI.

Material & Method: This was a prospective study conducted at the Department of General medicine, Gouri Devi Institute of Medical Sciences and Hospital, Durgapur, India. The study was carried out over a period of one year. The study included 350 diabetic (167 males and 183 females) and 200 non-diabetic patients (78 males and 122 females) with culture positive UTIs.

Results: There was no significant statistical difference in clinical symptoms between diabetic and non-diabetic subjects. The most common organism isolated being *E. coli.* Aminoglycosides showed a better sensitivity profile than cefoperazone-sulbactum in both diabetics and non diabetics.

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

Diabetes is the most common endocrine disorder in the last century. In developing countries, various factors, including lifestyle changes, have increased the incidence of the disease [1] .There are two main types of diabetes, and type 2 diabetes is more common. Type 2 diabetes is a chronic and progressive metabolic disease involving a heterogeneous group of disorders associated with varying degrees of insulin resistance, insulin secretion disorder, insulin development and persistence, and increased glucose production [2-6].

Bacteriuria is more common in diabetics than in non-diabetics because of a combination of host and local risk factors. [7] 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. [8] However, the clinical relevance of these findings is not clear.

Concerning cellular innate immunity, most studies show decreased function in diabetic polymorphonuclear cells and monocytes/macrophages compared to controls. Improved control of the diabetes mellitus (DM) can lead to an improvement in these cellular functions. As well, some microorganisms become more virulent in a high glucose environment.[8] Therefore, screening for UTI in diabetic patients is very important to enable bacteruria to be properly treated and prevent the development of renal complications of diabetes and eventually severe renal damage and failure. [9] However, controversies exist with respect to incidence, prevalence and microbiological features of UTI between diabetic and non-diabetic patients. [10]

The aim of this study is to study the influence of diabetes mellitus on the uropathogens and antibiotic sensitivity pattern in patients with UTI.

Material & Method:

This was a prospective study conducted at the Department of General medicine, Gouri Devi Institute of Medical Sciences and Hospital, Durgapur, India. The study was carried out over a period of one year. A total of 550 patients were screened, of which 400 patients were included in the study. The study included 350 diabetic (167 males and 183 females) and 200 non-diabetic patients (78 males and 122 females) with culture positive UTIs.

Patients with negative urine culture (n= 70), those diagnosed and treated outside (n= 55), not willing to participate in the study (n= 25) or with an age < 18 years were excluded.

Methodology

The following data including age, sex, occupation and symptomatology were taken and clinical examination was done. All proven diabetics with fasting venous glucose > 126mg/dl and postprandial (2h) venous glucose > 200mg/dl were included in the study irrespective of reason for admission. Patients with a history of diabetes and those who were on treatment for the same were also eligible for admission.

Controls consisted of patients admitted in hospital with comparable age and sex with no history of diabetes and fasting blood sugar < 110mg/dl.

The laboratory tests included complete blood picture, renal and liver function test and urine microscopy including culture. For urine microscopy, 5ml of clean catch midstream urine was centrifuged at 3000 rpm for five minutes and centrifuge was viewed under microscope and more than five WBC per high power field was considered significant. A fasting sugar, postprandial sugar and HbA1c were done for all diabetics.

Statistical analysis

Data was analyzed using statistical package SPSS version 16. The percentages in different categories were compared using Chi square test and means were compared using Student’s t-test. A p-value less than 0.05 were considered significant.

Results:

Table 1 shows the clinical characteristics of the groups. There was no significant statistical difference in clinical symptoms between diabetic and non-diabetic

subjects. Although fever was the most common presenting symptom, almost 35 per cent of the patients (both diabetics and non-diabetics) did not present with any urinary symptoms as shown in Figure 1.

The prevalence of pyelonephritis is significantly higher (p= 0.02) in diabetics (11.3 per cent compared with non-diabetic patients 3.6 per cent (Table 2).

The most common organism isolated being *E. coli* (Table 3).

Benign prostatic hypertrophy (BPH) was the most common predisposing factor in both diabetic (41.3 per cent) and nondiabetic males (49.0 per cent) followed by catheterization in diabetic (38.2 per cent) and non-diabetic (43.9 per cent) subjects (Table 4).

The antimicrobial resistance pattern was similar in both groups with maximum sensitivity to meropenem and least susceptibility to ampicillin as noted in Table 5. Aminoglycosides showed a better sensitivity profile than cefoperazone-sulbactum in both diabetics and nondiabetics; however the number of patients were too small to draw any conclusions from the above mentioned observation. Enterococcus showed maximum susceptibility to linidazole, teicoplanin and vancomycin. Of the five patients with coagulase positive staphylococcus, two cases were MRSA isolates which were sensitive to vancomycin and linidazole.

The micro-organisms isolated from the urine cultures are listed in Table 6. The most common organism isolated among both diabetics and non-diabetics was *E. coli*. When patients with indwelling catheter were considered separately, the isolation rates of different uropathogens significantly differed only for pseudomonas in diabetic and non-diabetic groups (p<0.05). We observed a higher isolation rate of Pseudomonas spp. in non-diabetic males than that in diabetic males (p < 0.05).

Table 1: Clinical characteristics

Symptoms	DM	%	NON-DM	%	p-value
Fever	192	54.86	166	83	0.62
Dysuria	80	22.86	48	24	0.90
Increased frequency	67	19.14	41	20.5	0.77
Abdominal pain	55	15.71	40	20	0.80
Vomiting	62	17.71	38	19	0.56
Haematuria	16	4.571	7	3.5	-
Pyuria	7	2	5	2.5	-
Incontinence	38	10.86	25	12.5	0.10
Retention	8	2.286	7	3.5	-

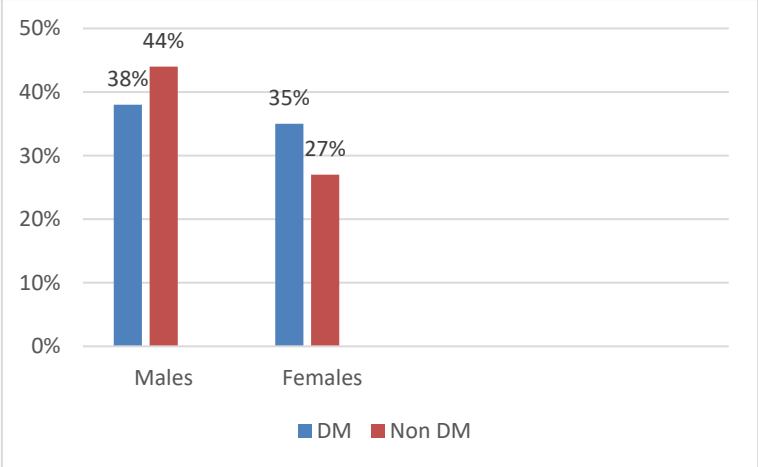

Figure 1: Asymptomatic bacteriuria

Table 2: Pyelonephritis in diabetics

	DM (n=350)	NON-DM (n=200)
Asymptomatic bacteriuria	69	48
Pyelonephritis	22	6

Table 3: Microorganisms causing pyelonephritis

	DM	NON-DM
E. coli	21	5
Klebsiella	7	0
Enterococcus	5	0
Pseudomonas	2	3
Proteus	2	0
Candida	1	0

Table 4: Predisposing conditions for UTI

	DM		NON-DM	
	M	F	M	F
BPH	41.3%	-	49.0%	-
Indwelling catheter	38.2%	38.8%	43.9%	35.8%
Hydroureternephrosis	10.3%	9.2%	18.3%	8.0%
Stricture urethra	9.0%	-	9.8%	-
Phimosis	5.9%	-	4.1%	-
Calculi	8.9%	5 %	8.4%	2.0%
Recent genitourinary surgery/ instrumentation	8.1%		8.7%	-
Balanoposthitis	3.9%	-	0	-
Neurogenic bladder	6.6%	-	0	-
Meatal stenosis	-	2%	-	1.7%

Gynaecological disorders	-	7.2%	-	13.6%
Pregnancy	-	16.5%	-	7.2%

Table 5: Comparison of antimicrobial susceptibility

	***E. coli* sensitivity**		**Klebsiella sensitivity**		**Pseudomonas sensitivity**	
	DM	**NON-DM**	**DM**	**NON-DM**	**DM**	**NON-DM**
Amikacin	85.2%	80.1%	89.0%	91.24%	95.6%	77.2%
Ampicilin	19.1%	15.3%	10.1%	19.2%	8.2%	15.4%
Augmentin	48.4%	40.2%	50.6%	43.1%	19.3%	28.1%
Aztreonam	31.8%	27.1%	39.0%	33.1%	28.3%	38%
Cefotaxime	54.4%	44.1%	40.9%	47.2%	26.9%	11.2%
Cefepime	50.2%	39.2%	58%	51.5%	40%	45.0%
Gentamycin	74.8%	71.8%	74.5%	70%	57.2%	69.0%
Cefoperazone-sulbactum	86.2%	83.6%	89.0%	96%	72.0%	67.5%
Meropenem	91.3%	94.8%	95.0%	100%	90.8%	88.2%
Netilmycin	79.0%	80.3%	85.9%	90.4%	80.2%	100%
Norfloxacin	29.0%	39%	36%	37%	19.2%	40.2%
Piperacillin-Tazobactum	69.0%	75.2%	90.3%	80.2%	81.3%	60%
Cotrimoxazole	44.8%	35%	36%	31.3%	19.6%	12%
Ceftriaxone	59%	47.2%	50.2%	41.3%	20.4%	27.1%

Table 6: Organisms isolated from urine cultures

Organisms	**DM**	**NON-DM**	**p-value**
E. coli	83	79	NS
Klebsiella	24	17	NS
Enterococcus	18	13	NS
Pseudomonas	3	20	<0.05
Acinetobacter	4	0	-
Citrobacter	2	3	-
Proteus	2	2	-
Coag. Negative Staph	3	8	-
Coag. Positive Staph	5	3	-
Candida	6	0	-

Discussion:

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. [11]

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. [12,13] This is probably due to higher prevalence of autonomic neuropathy and subsequent incomplete bladder emptying in longstanding diabetes.

The mean HbA1c level of the diabetic patients at the time of admission was 8.42 per cent ± 2.8 SD in our study compared with Bonadio M et al. (2006) (the mean

HbA1c level being 7.8 per cent ±1.6 SD). [14] Majority of the diabetics with UTI (87.14 per cent) had HbA1c > 6.5 per cent with p <0.001.

Considering the antimicrobial susceptibility, *E. coli* showed an increased sensitivity to carbapenems in both diabetics (93.8 per cent) and non-diabetics (95.1 percent) and decreased susceptibility to ampicillin (diabetics 16.7 per cent vs. non-diabetics 17 per cent). This is comparable to Saber MH et al. (2010) who demonstrated that *E. coli* sensitivity to carbapenems was 100 per cent in both diabetic and non-diabetic subjects. [15]

In people with type 2 diabetes, several different mechanisms may increase the risk of urinary tract infections, including diabetic nephropathy, autonomic neuropathy, immune system disorders, and glucosuria. [16] Diabetic nephropathy leads to disorders such as protein excretion and severe glucosuria. Neurological damage associated with high blood sugar levels can adversely affect the ability of the bladder sensation. Sensory bladder sensory disturbances cause urinary retention and increases urinary tract infections. [8]

Diabetes reduces blood circulation, so as diabetes lengthens, it weakens the immune system, which is reduced by treating certain cytokines such as IL_6 and other anti-inflammatory cytokines in a diabetic patient.

On the other hand, there are abnormal leukocytes. In diabetics and impaired phagocytic function, leukocytes due to high glucose levels in diabetic patients may weaken the immune system of these patients. [17-21] Apart from BMI, UTI is significantly associated with age, sex, recent UTI history and microalbuminuria. [22,23]

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.

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