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A study of microbiological profile of urinary tract infection in diabetic and non-diabetic patients

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Abstract
Background: Diabetes mellitus is a set of metabolic disorder which occurs due to the underutilization of glucose and thus resulting in hyperglycemia. Urinary tract infection (UTI) is a range of diseases which are induced by microbial invasion of genitourinary tract and extending from the renal cortex of kidney to the urethral meatus. In present study, the microorganisms and their antibiotic sensitivity profile were compared in diabetic and non-diabetic patients.
Materials and Method: The study population was selected among patients admitted in the Medicine department, Muzaffarnagar Medical College, Muzaffarnagar. The Pearson's correlation test were used.
Results: The study showed that some of the microorganisms were more common in diabetic group as compared to non-diabetic group. Whereas, few organisms were more common in non-diabetic group.
Conclusion: The present study shows that microorganisms and their antibiotic sensitivity profile differs between both the groups. The glycaemic control has got a strong impact on the UTI patients and UTI is frequently encountered among individuals with poor glycaemic control.

Keywords: diabetes mellitus, urinary tract infection, uropathogens

Introduction

Urinary tract infection (UTI) is a range of diseases which are induced by microbial invasion of genitourinary tract and extending from the renal cortex of kidney to the urethral meatus. Diabetes mellitus is a set of metabolic disorder which occurs due to the under utilization of glucose and thus resulting in hyperglycemia [1]. Currently, the prevalence of diabetes worldwide is estimated to be around 415 million (8.8% of the whole population) and is predicted to reach 642 million by 2040. India has the second highest number of diabetics with estimated prevalence of 69.3 million, which is expected to reach 123.5 million by 2040 [2].

The occurrence of infection is usually higher in diabetes patients including UTI. Diabetes mellitus is also a risk factor for multidrug resistant organisms in UTI patients [3]. The changed host response in diabetes individuals cause expanded attachment of the micro-organisms to the uroepithelial cells. This leads to enhanced susceptibility of these individuals to develop UTI [4, 5]. The reduced neutrophil activity and increased levels of urinary glucose inhibit the phagocytic function of leucocytes and hence, increase the adherance of bacteria to the urothelium.

Diabetes mellitus acts a predisposing factor to much severe infections, particularly in individuals with uncontrolled diabetes, acute diabetic ketoacidosis, or in those with complications i.e. neuropathy, vasculopathy and nephropathy. This asymptomatic infection in such patients can prompt extreme renal damage and eventually causing kidney failure [6].

In women with diabetes, the risk of acute UTI is more common due to presence of shorter urethra allowing easy access of the organisms from vagina and rectum [7, 8].

Kass proposed that individuals with "significant bacteriuria" (urine cultures with at least 10^5 CFU/ml) had a higher probability of true infection as compared to the individuals with "insignificant bacteriuria" (urine cultures with $< 10^5$ CFU/ml) [9, 10].

The common agents causing UTI are bacteria, viruses, fungi, tuberculosis.

E.coli has been considered to be the commonest single bacterial species to cause about more than 95% of urinary tract infections. However, true polymicrobial UTI is not very common and it happens in the clinical situation of long term urinary catheterisation, in patient with stagnant pooling of urine or with foreign body (calculi or necrotic tumors) [11, 12, 13].

Factors influencing the possibility of urinary tract infection to be non-*E.coli* urinary tract infection or antibiotic resistant urinary tract infection are as follows

- If the gastrointestinal tract flora has been modified by previous antimicrobial therapy,
- If urinary tract has been instrumented, or
- If there is any structural or functional urinary tract obstruction

Classification of UTI

According to type of Infection [14, 15, 16]

- Symptomatic UTI
- Asymptomatic UTI
- Acute
- Chronic
- Recurrent
- Complicated
- Uncomplicated

Localisation of UTI [17, 18, 19, 20]

a. Infection of upper urinary tract
- Acute pyelonephritis

- Chronic pyelonephritis

b. Infection of lower urinary tract
- Urethritis
- Cystitis

Kiranmala et al in 2019 conducted a similar study and contrasted the uropathogens and antimicrobial susceptibility of uropathogens causing UTI in patients with and without type II diabetes mellitus. The study showed that the most common cause of UTI is *E. coli* and ceftriaxone is most commonly used in UTI patients in spite of its low sensitivity [21].

Both the duration of diabetes and the presence of associated complications has been related to increased bacteriuria in diabetes [22, 23].

Materials and Method

This prospective observational study entitled "A study of microbiological profile of urinary tract infection in diabetic and non diabetic patients" was conducted after clearance from Board of Studies and Ethical committee in the Department of Medicine, Muzaffar Nagar Medical College, Muzaffar Nagar (U.P.) during the period 2018-2020.

Sample Size

200 patients

Inclusion criteria

Patient of aged more than more than 18 years with positive urine culture either diabetic or non-diabetic were taken for the study.

Exclusion Criteria

1. Gestational Diabetes
2. Less than 18 years of age
3. Bed ridden patients
4. Transplant recipients
5. Patient not giving consent for the study

Study procedure

The target population for the study was the patients admitted in the medicine department of Muzaffarnagar Medical College, Muzaffarnagar. An informed and written consent was taken from all the selected participants.

Statistical analysis

The data was entered into the Microsoft excel and the statistical analysis was performed by statistical software SPSS version 25.0. The Qualitative (Categorical variables) were present in the form of frequency and percentage.

The student t-test was used for comparing the mean values between the 2 groups. The p-value was considered to be significant when less than 0.05.

Results

Out of 200 patients, 116 were kept in diabetic group and 84 were in non-diabetic group. In both the groups, maximum number of patients were in the age group of 61-70 years i.e. 40 (35.1%) in diabetic group and 28 (32.6%) in non-diabetic group.

Table 1: Uropathogens in urine samples of UTI cases

Micro-organisms		Diabetic	Non-Diabetic	Total	p value
E.Coli	N	74	53	127	0.03*
	%	64.9%	61.7%	63.5%	
Enterococcus	N	7	14	21	0.008*
	%	6.1%	16.3%	10.5%	
Klebsiella	N	15	5	20	<0.01*
	%	13.2%	5.8%	10.0%	
Candida spp	N	8	2	10	0.04*
	%	7.02%	2.3%	5.0%	
Pseudomonas	N	4	0	4	<0.01*
	%	3.5%	0.0%	2.0%	
Staph.Aureus	N	3	9	12	0.03*
	%	2.6%	10.5%	6%	
Total	N	114	86	200	
	%	100.0%	100.0%	100.0%	

*: statistically significant

E.Coli was the most common uropathogen found in both diabetic 74 (64.9%) and non-diabetic group 53 (61.7%) respectively (p=0.03). Other gram negative uropathogens found in diabetic and non-diabetic group were Klebsiella 15 (13.2%) vs 5 (5.8%), Pseudomonas 4 (3.5%) vs 0 (0%) respectively. Gram positive uropathogens found in diabetic and non-diabetic group were Enterococcus 7 (6.1%) vs 14 (16.3%) and Staph aureus 3 (2.6%) vs 9 (10.5%) respectively. Candida spp was found in 8 (7.02%) diabetic patients as compare to 2 (2.3%) in non-diabetic patients. The difference between these uropathogens is statistically significant.

Table 2: Antimicrobial sensitivity pattern of E.Coli in UTI cases

Antibiotics	Diabetic (n=74)		Non Diabetic (n=53)	
	No.	%age	No.	%age
Gentamicin	30	40.54	19	35.85
Netilmicin	60	81.08	38	71.70
Amikacin	55	74.32	30	56.60
Nitrofurantoin	70	94.59	45	84.91
Norfloxacin	10	13.51	14	26.42
Cotrimoxazole	9	12.16	3	5.66
Cefotaxime	15	20.27	12	22.64
Cephalexin	15	20.27	12	22.64
Ceftazidime	15	20.27	12	22.64
Ceftriaxone	15	20.27	12	22.64
Cefepime	16	21.62	14	26.42
Nalidixic acid	7	9.46	3	5.66
Piperacillin/ Tazobactam	62	83.78	40	75.47
Cefoperazone/ Sulbactam	62	83.78	42	79.25
Imipenam	74	100	50	94.34
Meropenam	60	81.08	39	73.58
Ertapenam	53	71.62	31	58.49
Polymyxin B	6	8.11	6	11.32
Tigecycline	4	5.41	8	15.09

E.Coli showed more sensitivity to Imipenam in diabetic 74(100%) patients as compared to non-diabetic 50(94.34%) patients. The other antibiotics with decreasing order of sensitivity in diabetic and non-diabetic groups were Nitrofurantoin 70(94.59%) vs 45(84.91%), Piperacillin/ Tazobactam 62(83.78%) vs 40(75.47%), Cefoperazone/ Sulbactam 62(83.78%) vs 42(79.25%), Meropenam 60(81.08%) vs 39(73.58%), Netilimicin 60(81.08%) vs 38(71.70%), Amikacin 55(74.32%) vs 30 (56.60%), Ertapenam 53(71.62%) vs 31(58.49%),

Gentamicin 30(40.54%) vs 19(35.85%), Cefepime 16(21.62%) vs 14(26.42%), Ceftriaxone 15(20.27%) vs 12(22.64%), Ceftazidime 15(20.27%) vs 12(22.64%), Cephalexin 15(20.27%) vs 12(22.64%), Cefotaxime 15(20.27%) vs 12(22.64%), Norfloxacin 10(13.51%) vs 14(26.42%), Cotrimoxazole 9(12.16%) vs 3(5.66%) and Nalidixic acid 7(9.46%) vs 3(5.66%) respectively.

Table 3: Antimicrobial sensitivity pattern of Klebsiella in UTI cases

Antibiotics	Diabetic (n=15)		Non Diabetic (n=5)	
	No.	%age	No.	%age
Gentamicin	3	20	0	0
Netilmicin	10	66.67	5	100
Amikacin	4	26.67	0	0
Nitrofurantoin	12	80	0	0
Norfloxacin	2	13.33	0	0
Cotrimoxazole	2	13.33	0	0
Cefotaxime	2	13.33	0	0
Cephalexin	2	13.33	0	0
Ceftazidime	2	13.33	0	0
Ceftriaxone	2	13.33	0	0
Cefepime	2	13.33	0	0
Nalidixic acid	2	13.33	2	40
Piperacillin/ Tazobactam	10	66.67	5	100
Cefoperazone/ Sulbactam	10	66.67	5	100
Imipenam	15	100	5	100
Meropenam	12	80	3	60
Ertapenam	6	40	2	40

Klebsiella showed 100% sensitivity to Imipenem in both groups followed by Meropenam 12(80%) vs 3(60%), Nitrofurantoin 12 (80%) vs 0 (0%), Netilmicin 10(66.67%) vs 5(100%), Piperacillin/Tazobactam 10(66.67%) vs 5(100%), Cefoperazone/Sulbactam 10(66.67%) vs 5(100%), Amikacin 4(26.67%) vs 0(0%), Norfloxacin 2(13.33%) vs 0(0%), Cotrimoxazole 2(13.33%) vs 0(0%), Cefotaxime 2 (13.33%) vs 0(0%), Cephalexin 2(13.33%) vs 0(0%), Ceftazidime 2(13.33%) vs 0 (0%), Ceftriaxone 2(13.33%) vs 0(0%), Cefepime 2(13.33%) vs 0(0%) and Nalidixic acid 2(13.33%) vs 0(0%) in diabetic and non-diabetic groups respectively.

Table 4: Antimicrobial sensitivity pattern of Staphylococcus aureus in UTI cases

Antibiotics	Diabetic (n=3)		Non Diabetic (n=9)	
	No.	%age	No.	%age
Penicillin	0	0	0	0
Oxacillin	0	0	0	0
Netilmicin	3	100	1	11.11
Nitrofurantoin	3	100	4	44.44
Norfloxacin	3	100	1	11.11
Cotrimoxazole	0	0	4	44.44
Vancomycin	3	100	9	100
Linezolid	3	100	9	100
Teicoplanin	3	100	9	100
Rifampicin	3	100	3	33.33

In diabetic group, Staphylococcus aureus showed 100% sensitivity to Vancomycin, Linezolid, Teicoplanin, Rifampicin whereas in non-diabetic group Staphylococcus aureus showed 100% sensitivity to Vancomycin, Linezolid, Teicoplanin and 33.33% sensitivity to Rifampicin. All the uropathogens were resistant to Penicillin and Oxacillin.

Table 5: Antimicrobial sensitivity pattern of Enterococcus in UTI cases

Antibiotics	Diabetic (n=7)		Non Diabetic (n=14)	
	No.	%age	No.	%age
Penicillin	3	42.86	0	0
Oxacillin	3	42.86	2	14.29
Nitrofurantoin	2	28.57	3	21.43
Norfloxacin	2	28.57	1	7.14
Vancomycin	4	57.14	12	85.71
Linezolid	6	85.71	14	100
Teicoplanin	6	85.71	12	85.71
Rifampicin	3	42.86	4	28.57

For Enterococcus, Linezolid and Teicoplanin have sensitivity of 85.71% in diabetic group whereas it was 100% and 85.71% in non-diabetic group. Vancomycin sensitivity in diabetic group was 57.14% whereas in non-diabetic group it was 85.71%. The other antibiotics with decreasing order of sensitivity in diabetic and non-diabetic group were Rifampicin 3 (42.86%) vs 4 (28.57), Oxacillin 3 (42.86%) vs 2 (14.29%), Nitrofurantoin 2 (28.57%) vs 3 (21.43%), Norfloxacin 2 (28.57%) vs 1 (7.14%) and Penicillin 3 (42.86%) vs 0 (0%), respectively.

Discussion

The mean age in diabetic group was 61.71 years and in non-diabetic was 58.93 years. Female preponderance 60(52.6%) was observed in diabetic group whereas male preponderance 47(54.7%) was observed in non-diabetic group.

The most common uropathogen found was *E. coli* in both diabetic and non-diabetic group, 74 (64.9%) and 53 (61.7%) respectively. The uropathogens like *E.Coli, Candida spp, Klebsiella* and *Pseudomonas* were significantly more common in diabetic group while *Staph.aureus and Enterococcus* were significantly more common in non-diabetic group. Similar observations was made by Krenke DS *el al* [24] which showed *E.coli* being most common microorganism in diabetic and non-diabetic group 31% and 61% respectively. Mario Bonadio *et al* [25] showed most common uropathogen causing UTI in both diabetic and non-diabetic group being *E.coli*. Bonadio *et al* [25] have also shown that E. coli was the most common uropathogen causing UTI in both diabetic and non-diabetic 56.1% vs 56:8% respectively. J.P. Horcajada *et al* [26] have shown that the most common uropathogen was *E. coli*, in both the groups (83% vs 100% respectively). Paget G *et al* [27] had shown that in nosocomial UTI, *E. coli* was the most common uropathogen(50%). The other microorganisms isolated were *S. aureus* (including MRSA), coagulase negative staphylococci, Enterococcus spp. and Pseudomonas aeuroginosa. Krenke DS *et al* [24] had shown that among UTI patients, *Candida albican*s was isolated in 7% diabetic patients and 1% non-diabetic patients (p=0.003). Fluoroquinolone resistance was very commonly seen in diabetic and non diabetic groups being 86% and 24% respectively. Similar observation was made by Akbar DH [28] which showed sensitivity of E. coli in both diabetic and non-diabetic to imipenam (75% vs 70%), amikacin (83% vs 79%), meropenam (75% vs 58%) and gentamicin (75% vs 64%) respectively signifying that if a patient whether having diabetes or not getting admitted with UTI, the initial drug of choice would be aminoglycoside or carbapenam.

The fluoroquinolone resistance among both the groups being 40% in both the groups. This was in contrast to our study which showed higher fluoroquinolone resistance. Spratt BG [29] had shown that factors like overcrowding, poor hygienic practices in low socio-economic population and increasingly mobile population contributed to facilitate the dissemination of antibiotic resistance. Bauza E *et al* [30] had shown that factors leading to resistance include incorrect diagnosis, unnecessary prescription, inadequate use of antibiotics by patients and the use of antibiotics as livestock food additives to promote development. Similar observation was made by Taslima TL *et al* [31] which states that Carbapenam have 100% maximum sensitivity followed by Aminoglycosides.

Fluoroquinolone resistance and probable ESBL production among *E. coli* isolates were 40-50%. This was in accordance with previous studies. The multiple antibiotic resistance among the isolates could be conferred by the plasmid and any other gene transfer method.

Limitations of the study

The present work has several limitations. First, symptomatic patients were admitted in the hospital so it may lead to bias. Second, bed ridden patients and gestational diabetic patients were not included in the study. Lastly, the relationship between microorganisms and diabetes could be very complex, and our study examined only the relationship between few microorganisms and diabetes as a variable to variable relationship.

Conclusion

Our study showed that the uropathogens like E.Coli, Candida spp, Klebsiella and Pseudomonas were significantly more common in diabetic group while Staph.aureus, and Enterococcus were significantly more common in non-diabetic group. The most common uropathogen isolated was E.coli in both the groups. Aminoglycosides and carbapenams are the drug of choice for the UTI patients having growth of *E. coli* in both the groups. Glycaemic control has got a strong impact on UTI and is frequently encountered among individuals with poor glycaemic control.

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