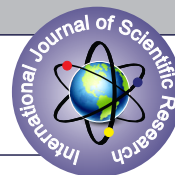


A STUDY OF ETIOLOGICAL AGENTS CAUSING URINARY TRACT INFECTION IN DIABETIC OR NON-DIABETIC PATIENTS IN NORTH INDIA.



Microbiology

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ABSTRACT

Background: Burden of the urinary tract infections (UTIs) is common in both diabetic and non diabetic patients. Since the types of microorganisms causing UTI different in their susceptibility to antimicrobials from place to place and time to time, hence constant screening of trends and susceptibility pattern of predominant organisms against antimicrobials is essential.

Methods: A prospective cross sectional study was conducted during period of January 2019 to June 2019. Among 375 isolates from Urine culture in UTI patients with Diabetic and Non-diabetic attending NIMS Hospital, Jaipur Rajasthan. All samples and isolates were investigated by standard laboratory procedures.

Result: A total number of 375 isolates from Urine culture in UTI patients with Diabetic and Non-diabetic were analyzed. Among the samples, males 145 (38.67%) were 89(39.73%) & 56(37.08%) and females 230 (61.33%) were 135(60.27%) & 95(62.92%), diabetic and non diabetic patients respectively. *Escherichia coli* was the most frequent organism followed by *Pseudomonas spp.* Meropenem was found to be highly sensitive to Gram-Negative Bacilli isolated patients antimicrobials followed by Imipenem, and Nitrofurantoin. Vancomycin and Linezolid were the most sensitive drugs to Gram-positive cocci isolated patients antimicrobials followed by Nitrofurantoin and Teicoplanin. Penicillin was the most sensitive drugs to *Enterococcus spp.* However, no difference was noted on the sensitivity pattern of the antimicrobials among *Escherichia coli* isolated between diabetic and non diabetic patients.

Conclusion: The significance of the study lies in the determination of common pathogens in diabetic and non diabetic patients with UTI and the susceptibility pattern of antibiotics

KEYWORDS

Urinary Tract Infection, Antibiotics, Diabetes

INTRODUCTION

The urinary tract is a primary site of infection in diabetics¹. Urinary tract infection (UTI) can be classified based on anatomy as upper UTI and lower UTI. Urinary tract infection may be symptomatic or asymptomatic but is well defined as the presence of bacteriuria with a quantitative count of at least more than or equal to 10^5 colony-forming units of bacteria per milliliter². Bacteriuria is most common in diabetics compared to non-diabetics due to a combination of host and local risk factors³. Uncomplicated UTIs occur in sexually active healthy female patients with structurally and functionally normal urinary tracts. Complicated UTIs are those that are associated with co morbid conditions that prolong the need for treatment or increase the chances for therapeutic failure. These conditions include abnormalities of the urinary tract that impede urine flow, the existence of a foreign body (e.g., indwelling catheter, stone), or infection with multidrug-resistant pathogens. UTIs in male patients are considered complicated. Although the involvement of the upper urinary tract, pyelonephritis can be considered uncomplicated when it occurs in a healthy patient^{2,3}. Various microorganisms become more virulent in a high glucose environment. Therefore, screening for UTI in diabetic patients is very important to enable bacteriuria to be properly treated⁴. The most common causative pathogen for both uncomplicated and complicated UTIs is *Escherichia coli*⁵. Other organisms that cause UTI are *Klebsiella pneumoniae*, *Staphylococcus saprophyticus*, *Proteus mirabilis*, *Enterococcus faecalis*, group B *Streptococcus*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, and *Candida spp.*⁶.

There is a significant correlation between the duration of diabetes and UTI⁷. Changes in host defense mechanisms, the presence of diabetic cystopathy and of microvascular disease in the kidneys may play a role in the higher incidence of UTI in diabetic patients. As diabetics are more prone to UTI, it is necessary to pay special attention to early diagnosis and treatment⁸. Diabetes mellitus is a group of metabolic disorders classified by high blood sugar levels over an overlong period. Diabetes mellitus is classified as type I or type II based on the pathology. Type I results due to the failure of the pancreas to produce insulin, while type II is the resistance of insulin by the cells of the body⁹. Both types of Diabetes mellitus can have acute and chronic complications. Some acute ones include hyperosmolar hyperglycemia, diabetic ketoacidosis, coma or death, and chronic ones

are nephropathy, ophthalmopathy, foot ulcers, and cardiovascular diseases^{7,8}.

Material & Methods:-The present study was carried out from January 2019 to June 2019 at the department of microbiology, National institute of medical science and research Hospital, Jaipur, Rajasthan. The study included 375 patients with positive urinary tract infection these patients were divided into 2 groups (diabetic or Non- diabetic). Information on patients, age, gender, Diabetic and history of urinary frequency was collected at the time of sample collection.

Urine collection and processing: clean voided midstream urine samples were collected in sterile containers with the assistant of trained lab staff at NIMS before sample collection, each patient was instructed how to collect a correct midstream urine sample to avoid contamination. All urine samples were inoculated with an inoculating loop on three types of media CLED agar, Blood agar & MacConkey agar. All plates were incubated at 37° C for 18- 24 hrs for visible growth.

Identification of Isolated microorganism:-urine samples showing a colony count of more than 10^5 /ml CFU were considered to be positive for UTI. UTI isolates were identified following standard biochemical tests.

Susceptibility testing:-susceptibilities of the isolated bacteria to the selected microbial agent were examined. Antimicrobial susceptibility testing of all isolates was performed on Muller Hinton agar plate according to the Kirby-Bauer method following the Clinical and Laboratory Standards Institute (CLSI)⁹. Bacterial inoculums were prepared by suspending the freshly grown bacteria in 2 ml sterile peptone water. A sterile cotton swab was used to strike the surface on the Muller Hinton agar plate. Antimicrobial disks containing a designated concentration of the Antimicrobial drugs obtained from Himedia were used. The antimicrobial drugs which used for susceptibility testing are given below were Imipenem(10mcg), Meropenem(10mcg), Gentamicin(30mcg), Ceftazidime(30mcg), Ceftriaxone(30mcg), Cefotaxime(30mcg), Piperacillin/Tazobactam (100/10µg), Norfloxacin(10mcg), Nitrofurantoin(300µg), Amikacin (30mcg), Ciprofloxacin (10mcg), Aztreonam(30mcg), Ampicillin

(10mcg), Tobramycin(10mcg), Penicillin-G(10units), Teicoplanin (30mcg), Vancomycin(30mcg), Linezolid(30mcg), Cefoxitin (30mcg), Clindamycin (2mcg), and Erythromycin(15mcg).

Results:- This study was conducted on urine samples from 825 patients. The patients (diabetic or non diabetic both) received at Nims hospital during the period between January 2019 to June 2019. Among the 825 analyzed samples, 450(54.55%) were sterile urine samples, while 375(45.45%) were positive for UTI(Figure. 1).

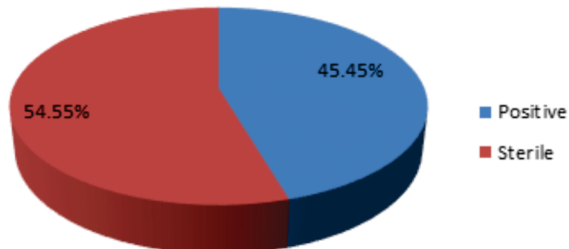


Figure. 1 Culture Positivity Among urine Samples

Among the samples 375 samples, 145 (38.67%) were male patients and 230 (61.33%) were female patients. In males was Diabetic patients 89(39.73%) and 56(37.08%) were Non-diabetic patients. In female was Diabetic patient 135(60.27%) and 95(62.92%) were Non-diabetic patients (Table No:1).

Table 1:- Distribution of male and female in diabetics and non-diabetics patients.

Sex	Diabetic n=224 (59.73%)	Non Diabetic n=151 (40.27%)	Total n=375 (100%)
Male	89 (39.73%)	56 (37.08%)	145 (38.67%)
Female	135 (60.27%)	95 (62.92%)	230 (61.33%)

Table no. 2 show the highest number of cases belong to age group 46-60 years in diabetic patients while highest number of cases belong to age group 16 to 30 and 31 to 45.

Table 2:- Distribution of Age wise (male and female) in diabetics and non-diabetics patients.

Age groups	Diabetic n= 224(59.73%)		Non Diabetic n= 151(40.27%)	
	Male n= 89	Female n= 135	Male n=56	Female n=95
0-15	0	0	2 (1.32%)	5 (3.31%)
16-30	8 (3.57%)	12 (5.37%)	13 (8.61%)	27 (17.88%)
31-45	24 (10.71%)	35 (15.63%)	11 (7.28%)	30 (19.87%)
46-60	33 (14.73%)	58 (25.89%)	18 (11.92%)	25 (16.56%)
61-75	24 (10.71%)	30 (13.39%)	12 (7.95%)	8 (5.30%)

Escherichia coli 211(56.27%) was the most frequent organism isolated in UTI patients accounting 55.35% in diabetic and 57.61% non-diabetic patients followed by *Pseudomonas spp.* 34 (9.06%) accounting 11.16% in diabetic and 5.96% in non diabetic. The pattern of all the organisms isolated from patients with both diabetic and non-diabetic (Table 3).

Table 3:- Distribution of organism isolated from diabetics and non-diabetic.

Organisms	Total no=375 (100%)	Diabetic n=224 (59.72%)	Non Diabetic n=151 (40.28%)
<i>Escherichia coli</i>	211 (56.27%)	124 (55.35%)	87 (57.61%)
<i>Pseudomonas spp.</i>	34 (9.06%)	25 (11.16%)	09 (5.96%)
<i>Candida spp.</i>	36 (9.60%)	23 (10.27%)	13 (8.61%)
<i>Klebsiella Spp.</i>	28 (7.47%)	16 (7.14%)	12 (7.95%)
<i>Acinetobacter spp.</i>	04 (1.06%)	03 (1.35%)	01 (0.67%)
<i>Enterococcus spp.</i>	14 (3.73%)	07 (3.12%)	07 (4.63%)
MSSA	18 (4.8%)	10 (4.46%)	08 (5.30%)
MRSA	12 (3.3%)	06 (2.69%)	06 (3.97%)
CoNS	18 (4.8%)	10 (4.46%)	08 (5.30%)

Meropenem was found to be highly sensitive to Gram-Negative Bacilli isolated in diabetic and non-Diabetic patients antimicrobials followed by Imipenem, Nitrofurantoin, and Gentamicin. However, we found no

difference in the sensitivity pattern of the antimicrobials GNB isolated between diabetic and non-diabetic patients (Table 4).

Table 4:- Antimicrobial sensitivity pattern of Gram Negative Bacilli in patients with and without diabetes.

S. No.	Drugs	<i>Escherichia coli</i> n=211		<i>Pseudomonas spp.</i> n=34		<i>Klebsiella spp.</i> n=28		<i>Acinetobacter spp.</i> n=4	
		Diabetic n=124	Non Diabetic n=87	Diabetic n=25	Non Diabetic n=9	Diabetic n=16	Non Diabetic n=12	Diabetic n=3	Non Diabetic n=1
1	Imipenem	87.90%	86.21%	80%	77.77%	81.25%	75%	66.66%	100%
2	Meropenem	91.93%	94.25%	88%	88.88%	93.75%	91.67%	100%	100%
3	Gentamicin	81.45%	79.31%	72%	66.67%	75%	66.66%	100%	100%
4	Ceftazidime	73.39%	68.96%	60%	66.67%	62.5%	58.33%	66.66%	100%
5	Ceftriaxone	48.39%	62.07%	0	0	56.25%	50%	33.33%	0
6	Cefotaxime	44.35%	65.52%	0	0	43.75%	41.67%	33.33%	0
7	Piperacillin-Tazo	ND	ND	80%	77.77%	ND	ND	ND	ND
8	Norfloxacin	76.61%	70.11%	60%	66.66%	62.5%	66.66%	66.66%	100%
9	Nitrofurantoin	88.71%	81.61%	72%	77.77%	87.5%	83.33%	100%	100%
10	Amikacin	79.84%	78.16%	76%	77.77%	75%	75%	66.66%	100%
11	Ciprofloxacin	58.87%	63.21%	60%	66.66%	62.5%	41.67%	66.66%	0
12	Aztreonam	40.74%	45.98%	0	0	43.75%	41.67%	0	0
13	Ampicillin	62.90%	77.01%	0	0	0	0	0	0
14	Tobramycin	ND	ND	84%	88.88%	ND	ND	ND	ND

Vancomycin and Linezolid were the most sensitive drugs to Gram-positive cocci isolated in diabetic and non-Diabetic patients antimicrobials followed by Nitrofurantoin and Teicoplanin. Penicillin was the most sensitive drugs to *Enterococcus spp.* in diabetic and non-diabetic patients. However, we found no difference in the sensitivity pattern of the antimicrobials GPC isolated between diabetic and non-diabetic patients (Table 5).

Table 5:- Antimicrobial sensitivity pattern of Gram Positive cocci in patients with and without diabetes.

S. No	DRUGS	MRSA n= 12		MSSA n=18		Enterococcus spp. n=14		CONS n=18	
		Diabetic n= 6	Non Diabetic n= 6	Diabetic n=10	Non Diabetic n=8	Diabetic n=7	Non Diabetic n=7	Diabetic n= 10	Non Diabetic n= 8
1	Penicillin	33.33%	33.33%	30%	37.5%	85.71%	71.43%	40%	62.5%
2	Ampicillin	50%	33.33%	40%	50%	71.43%	71.43%	50%	50%
3	Teicoplanin	66.66%	66.66%	70%	100%	71.43%	85.71%	50%	100%
4	Vancomycin	100%	100%	100%	100%	100%	100%	100%	100%
5	Linezolid	100%	100%	100%	100%	100%	100%	100%	100%
6	Norfloxacin	66.66%	66.66%	50%	75%	71.43%	85.71%	50%	87.5%
7	Nitrofurantoin	83.33%	83.33%	70%	100%	71.43%	100%	60%	87.5%
8	Cefoxitin	0	0	100%	100%	0	0	60%	75%
9	Gentamicin	50%	66.66%	60%	75%	0	0	50%	50%
10	Amikacin	50%	50%	50%	62.5%	57.14%	85.71%	50%	50%
11	Clindamycin	50%	66.66%	70%	87.5%	0	0	60%	87.5%
12	Erythromycin	33.33%	50%	50%	62.5%	57.14%	57.14%	60%	75%

DISCUSSION

Diabetic patients have a higher risk of UTI particular in women. The present study is investigated the possible impact of diabetes control on the UTI prevalence, type of strains and their antimicrobial drug susceptibility in diabetic and non-diabetic patients.

Our main findings are followings:-

There is a much higher prevalence of UTI in diabetic patients in comparison to non-diabetic patients. Diabetes does affect the distribution of the UTI according to age and gender.

The etiology of the isolated strains and their antimicrobial susceptibility pattern does not differ between diabetic and non-diabetic patients.

Analysis of our results showed that among the 825 patients 45.45% were positive for uropathogens. This prevalence is lower than a study conducted by Satish Kumar Legha *et al*¹⁰ in Jaipur, Rajasthan. This might be due to the fact that most of our subjects were not diabetic for long periods (less than 3 to 5 years)

In the total number of UTI, patients are reported 59.73% of patients with diabetic and 40.27% non-diabetic. A study conducted by Acharya D *et al*¹¹ in Katmandu supports our findings.

In the present study, most of the affected age group in diabetic patients was from 45 to 60 years in diabetic patients and non-diabetic patients both. These findings supported by a study conducted by Jagadeeswaran G1 *et al*¹² & R. Simkhada *et al*¹³.

The rate of *Escherichia coli* isolation we found in both diabetic and non-diabetic patients are almost similar, which predominant organism is constituted 56.27% and 55.35% among diabetic and non-diabetic patients respectively. It was a similar study done in Katmandu by Acharya D *et al*¹¹.

In our study *Pseudomonas spp.* and *Klebsiella spp.* 9.06% & 7.47% and their similar result in a study done in Turkey by Demiss Nigussie *et al*¹⁴.

In our study, *Acinetobacter spp.* was found 1.06% and the same study done in Andhra Pradesh by C. Sayee Sankar Vinod *et al*¹⁵.

In our study, *Enterococcus spp.* was 3.73% and their similar study was done in Katmandu by Acharya D *et al*¹¹.

In our study were MSSA, MRSA, CoNS 4.8%, 3.3%, and 4.8% respectively. Which study similar results to a study by Jagadeeswaran G1 *et al*¹² and the same study done in Andhra Pradesh by C. Sayee Sankar Vinod *et al*¹⁵.

Meropenem (88% to 100%) 91.93% was found to be highly sensitive to Gram-Negative Bacilli isolated in diabetic and non-Diabetic patients. This was nearly similar to a study by Jagadeeswaran G1 *et al*¹² & and the same study done in Andhra Pradesh by C. Sayee Sankar Vinod *et al*¹⁵.

In our finding, nitrofurantoin (81% to 100%) was found to be highly sensitive to Gram-Negative Bacilli isolated in diabetic and non-Diabetic patients. similar to as seen by PK Jha *et al*¹⁶ and Jagadeeswaran G1 *et al*¹².

In our findings, Gram-positive isolates have shown 100% sensitivity to Vancomycin and Linezolid in diabetic and non-Diabetic patients antimicrobials followed by Nitrofurantoin and Teicoplanin. Similar to as seen by Jagadeeswaran G1 *et al*¹² while an article from south India by Abdulla MC *et al*¹⁷ shows 81% and 94% susceptibility respectively by *Enterococcus* and *Staphylococcus*.

CONCLUSION

The significance of the study lies in the determination of common pathogens in diabetic and non-diabetic patients with UTI and the susceptibility pattern of antibiotics so that the clinicians get useful information regarding the use of antibiotics in diabetes patients to treat UTI. Further validation is hence anticipated in a larger diabetic population study. The study also gives evidence of differences in the etiological agents in Rajasthan as compared to other regions which highlight the need for proper use of antibiotics in diabetic patients, particularly.

The current study, however, has some limitations including the small number of diabetic patients analyzed and the lack of historical information on the non-UTI diabetic patients with and without UTI in relation to glycemic control help in reducing the occurrence of UTI.

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