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Comparative Study of Isolates Associated With Urinary Tract Infection among Diabetic and Non-Diabetic Patients Attending Tertiary Care Hospital, Chitwan, Nepal

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Abstract

➢ ***Introduction:***

Diabetes causes several abnormalities of the host defense system that might result in a higher risk of certain infections, including UTI. Furthermore, when diabetic patients acquire UTIs, it is more likely to be caused by unusual pathogens and antibiotic-resistant organisms.

➢ ***Aim of the Study:***

The present study was undertaken to determine types of isolates and microbial profile of UTI among diabetic and non-diabetic patients, Multidrug-resistant (MDR) producing bacterial isolates and to determine statistical significance between them by a recommended method.

➢ ***Methods:***

A prospective study was conducted from 13th February 2016 to 13th May 2016 in the CMCTH; Semi-quantitative cultures of Urine samples were performed with the threshold defined by Kass, 1960. The presence or absence of diabetes was confirmed after measuring blood sugar level by standard method.

➢ ***Results:***

Most of the cases of UTI in both groups were caused by gram-negative which accounts for 93.81% in diabetic and 95.74% in non-diabetic patients. UTI caused by Candida albicans and Proteus mirabilis was higher in diabetic patients. PIT was the most effective antibiotic in both groups (83.87% sensitive in diabetic whereas 87.78% sensitive in non-diabetic patients). A/S was least effective in both groups with a sensitive rate of less than 10.0% in both groups. Among 124 MDR isolates, 73 (31.06%) were from non-diabetic patients whereas 51 (52.57%) were from diabetic patients.

➢ ***Conclusion:***

Gram-negative bacilli were predominant uropathogen in both diabetic and non-diabetic patients. Quinolone and sulfonamides resistance gram-negative bacteria were higher in diabetic patients. The association of having UTI and being diabetic or non-diabetic was statistically significant (P<0.05).UTI in diabetic patients has a high rate of MDR pathogens.

Keywords:- *Urinary Tract Infection, UTI, Uropathogen, MDR, Diabetic , Non Diabetic*

I. INTRODUCTION

Urinary tract infection (UTI) simply defines as presence of microbial pathogens within the urinary tract. UTI is defined as the microbial invasion of any tissue of the urinary tract, extending from the urethral meatus to the renal cortex. It is a condition where one or more part of urinary systems become infected.[1] UTI is also defined as the presence of at least 100,000 organisms per milliliter of urine in an asymptomatic patient, or as more than 100 organisms/mL of urine with accompanying pyuria (>5 WBCs/mL) in a symptomatic patient.[2] Asymptomatic bacteriuria (ASB) is defined as the presence of $>10^5$ colony-forming units (CFU) per milliliter of one or two of the same microorganisms in a culture of clean-voided midstream urine from a patient without fever or symptoms of a UTI. Particularly in asymptomatic patients, a diagnosis of UTI should be supported by a positive culture for a uropathogen.[3]

Diabetes mellitus is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both.[4] Diabetes was defined according to the World Health Organization's criteria as a fasting plasma glucose ≥7.0 mmol/l (126 mg/dl) or a 2-h plasma glucose ≥11.1 mmol/l (200 mg/dl) during an OGTT.[5,6] It has been estimated that 347 million people all over the world have diabetes, and Nepal with the mortality rate of about 300.[4,7]Diabetes mellitus (DM) is a worldwide health problem, with an expected prevalence of 593 million by 2035.[8] According to WHO, diabetes mellitus is the ninth leading cause of death worldwide. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction, and failure of different organs particularly the eyes, genitourinary system, nerves, heart, and veins.[9]Diabetes is associated with many complications and major effects on the genitourinary system which makes diabetic patients more vulnerable to UTI, particularly to upper urinary tract infections.[10] Diabetes causes several

abnormalities of the host defense system that might result in a higher risk of certain infections, including UTI.[11]

In both diabetic and non-diabetic patient screening for UTI is very important to enable it to be properly treated and to prevent the development of possible complications. This study aimed to find the prevalence of culture positive UTI, their clinical presentation and pattern of antibiotic sensitivity in our setting. This will guide for further management of patients in future.

To the best of our knowledge, there are no published data regarding the epidemiology of UTI among diabetic and non-diabetic patients in Chitwan and its surrounding areas. No sufficient studies have been carried out making a comparison between UTI in diabetics and non diabetics. Clinical information on the relationship of diabetes mellitus with regular diseases are essentially missing, not definitive and frequently biased. The prevalence of UTI in both non-diabetic and diabetic population is increasing worldwide and the emergence of multi-drug-resistant (MDR) strains is escalating; hence, determining the prevalence of UTI among both diabetic and non-diabetic patients and investigating the sensitivity of bacterial isolates to antimicrobial agents is important for the epidemiologist, scientist, health planner, and clinician. It is essential that the clinician be aware of the local pathogen and susceptibility pattern to decide on the most appropriate antibiotic for empirical treatment to reduce the incidence of antimicrobial resistance and life threatening septicemia. The fact that antibiotic sensitivity changes with time;[12,13] therefore knowledge of common bacteria involved and their current sensitivity pattern will help us not only in providing the best initial empirical therapy but also in preventing the long-term morbidity. This will have favorable effect on patient outcome and health related expenditures.

II. METHODS

This was a prospective, cross-sectional comparative study conducted at the Laboratory department, Chitwan Medical College Teaching Hospital, Chitwan, Nepal. The study was carried out from February 2016 to May 2016. Patients with negative culture, not willing to participate, age <10 yrs of old, pregnant women, impaired glucose tolerance test, patients with chronic kidney disease were excluded.

- *Laboratory Procedure*

Both Midstream Clean Catch specimen and bladder catheterization specimen were accepted. The samples were cultured in Cystine Lactose Electrolyte Deficient (CLED) agar and Blood agar and incubated at 37°C overnight for visible growth. The isolated organisms were identified with the appropriate count. Antimicrobial susceptibility of isolates was tested by disc diffusion. All patients with urine sample, blood sample were also collected and were tested for their blood glucose level and renal function test. Blood sugar level and renal function test was measured by using a Siemens Dimension RxL automatic analyzer and OGTT test. Patients were then classified as diabetic, non-diabetic and impaired glucose tolerance patients. Impaired glucose tolerance patients were excluded and true diabetic and non-diabetic patients with UTI were categorized and compared.

- *Statistical Analysis*

The collected data were summarized, presented, and analyzed using the software SPSS version 20 (Chicago, USA) and Medcalc version 13.0. Qualitative data were summarized as frequency and percentages. Data were expressed as mean ± SD for quantitative variables. *P*- value less than 0.05 was considered statistically significant.

- *Ethical Considerations*

Consent from the ethical committee (Institutional review committee of CMCTH) and informed consent form the patients or responsible guardians were obtained before carrying out this study.

III. RESULTS

- *Incidence of UTI*

A total of 1417 urine sample were received from suspected patient (age >10 years) in the bacteriology laboratory for culture and sensitivity. Among the total processed samples, insignificant growth of microorganism occurred in 81 samples (5.71%), significant growth of bacterial occurred in 328 samples (23.14%), and no growth of microorganism occurred in 1008 samples (71.13%) as shown in Figure 1.

Out of 328 growths, 93 were diabetic patients and 235 were from non-diabetic patients. Growth of multiple organism occurred in 4 samples (1.21%), significant growth of a singular organism that causes UTI was found in 324 samples (98.78%) as show in Table 1.

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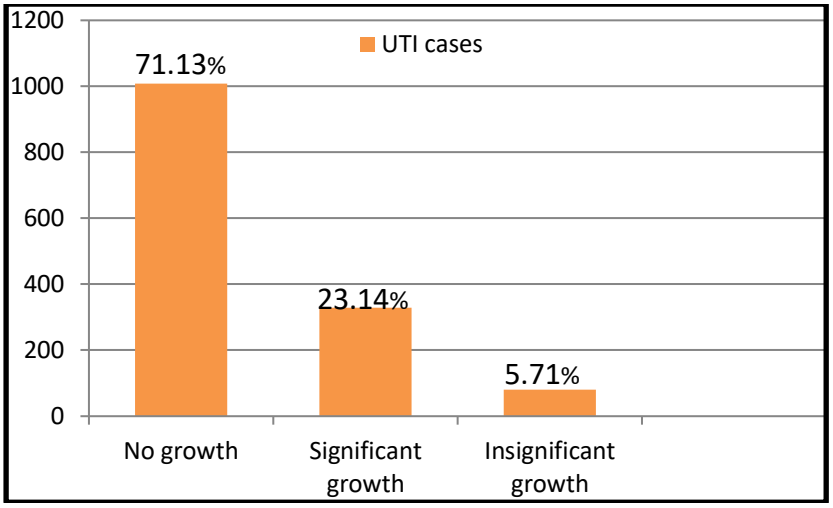

Fig 1:- Urine Culture Result in Suspected Patients.

Types of growth	Diabetic patients	Non-diabetic patients	P-value
Mono-microbial growth	89	235	P=<0.001
Poly-microbial growth	4	0	
Total	93	235	

Table 1:- Pattern of Urine Culture in Diabetic and Non-diabetic Patients.

➢ *Distribution of urine culture isolates*

In diabetic patients, incidence of UTI was seen in increasing order of age whereas in non-diabetic patients, the incidence of UTI was highest in the patients between 21 to 30 years age groups as shown in Table 2. In relation to gender incidence, UTI was more among diabetic females 54.83% and non-diabetic females 80.42% as shown in Table 3.

Age (years)	Diabetic		Non-Diabetic		Total	P- value
	No.	%	No.	%		
11-20	0	0	22	9.36	22	P=<0.001
21-30	2	2.15	110	46.8	112	
31-40	4	4.30	41	17.44	45	
41-50	9	9.67	20	8.51	29	
51-60	17	18.27	20	8.51	37	
61-70	27	29.03	11	4.68	38	
>70	34	36.55	11	4.68	45	
Total	93	100	235	100	328	

Table 2:- Age Wise Distribution of Isolates in Diabetic and Non-diabetic Patients.

Gender	Diabetic		Non-Diabetic		Total	P- value
	No.	%	No.	%		
Male	42	45.16	46	19.57	88	P=<0.001
Female	51	54.83	189	80.42	240	
Total	93	100	235	100	328	

Table 3:- Gender Wise Distribution of Isolates in Diabetic and Non-diabetic Patients.

➢ *Causative Organism of UTI in diabetic and non-diabetic groups.*

Most of cases of UTI in both groups were caused by gram negative which accounts for 93.81% in diabetic and 95.74% in non-diabetic patients. Slightly higher incidence of UTI by gram positive bacteria was seen in non-diabetic patients whereas fungal UTI was seen in only diabetic patients as show in table 4. The commonest causative organism causing UTI was *Escherichia coli* (80.85% in non-diabetic whereas 76.28% in diabetic patients) followed by *Klebsiella pneumonia* (5.53% in non-diabetic whereas 3.09% in diabetic patients), *Pseudomonas aeruginosa* and

Acinetobacter spp. Infection was seen slightly higher in diabetic patients than non-diabetic patients *Staphylococcus aureus* infection was seen only in non-diabetic infection whereas *Candida* infection was seen only in diabetic group. Details of isolates causing UTI in diabetic and non-diabetic patients is shown in Table 5.

Bacteria isolated	Non-diabetic patients		Diabetic patients		P-value
	No.	%	No.	%	
Gram negative	225	95.74	91	93.81	P=0.005
Gram positive	10	4.25	2	2.06	
Candida albicans	0	0	4	4.12	
Total	235	100	97	100	

Table 4:- Pattern of Bacterial Isolates in Diabetic and Non-diabetic Patients.

Bacterial Type	Diabetics		Non diabetics		P value
	No.	%	No.	%	
Escherichia coli	74	76.28	190	80.85	P=0.34
Klebsiella pneumonia	3	3.09	13	5.53	P=0.34
Citrobacter spp.	3	3.09	5	2.12	P=0.60
Enterobacter spp.	1	1.03	5	2.12	P=0.49
Proteus mirabilis	2	2.06	0	0	P=0.02
Pseudomonas aeruginosa	4	4.12	7	2.97	P=0.59
Acinetobacter spp.	4	4.12	5	2.12	P=0.30
Enterococcus faecalis	2	2.06	6	2.55	P=0.79
Staph. Aureus	0	0	2	0.85	P=0.36
Staph. Saprophyticus	0	0	2	0.85	P=0.36
Candida albicans	4	4.12	0	0	P=0.002
Total	97	100	235	100	

Table 5:- Bacteria isolated from diabetic and non-diabetic patients.

➢ *Antimicrobial susceptibility profile*

β-lactams, Sulphanamides, Quinolones, Nitrofurans, Aminiglycosides and Tetracycline groups antibiotics were tested against isolates from diabetic and non-diabetic patients. In addition to these, Glycopeptides, Macrolides and Lincosamides groups antibiotics were tested among *staphylococcus species* isolated from non-diabetic patients. Among β-lactams, Piperacillin/Tazobactam was most effective antibiotics in both group (83.87% sensitive in diabetic whereas 87.78% sensitive in non-diabetic patients). Ampicillin/Sulbactam was least effective with sensitive rate less than 10.0% in both groups. Rest antibiotics of this group were less effective in diabetic patients with sensitive rate less than 36.0% whereas same antibiotics shown sensitive rate more than 55.0% among isolates from non-diabetic patients.

Class of antibiotics	Antibiotic used	Susceptibility pattern			
		Resistant		Sensitive	
		No.	%	No.	%
β-lactams	Ceftriaxone(CTR)	58	64.44	32	35.55
	Cefotaxime (CTX)	55	67.90	26	32.09
	Meropenem(MRP)	33	75	11	25
	Piperacillin/Tazobactam(PIT)	15	16.12	78	83.87
	Ampicillin/Sulbactam(A/S)	47	97.91	1	2.08
	Carbenicillin(CB)	3	75	1	25
	Ceftazidime(CAZ)	4	100	0	0
Sulphanamides	Cotrimoxazole(COT)	59	67.81	28	32.18
Quinolones	Ciprofloxacin(CIP)	34	79.06	9	20.93

	Levofloxacin(LE)	32	59.25	22	40.74
Nitrofurans	Nitrofurantoin (NIT)	26	27.95	67	72.04
Aminoglycosides	Amikacin (AK)	9	9.67	84	90.32
	Gentamicin(GEN)	9	29.03	22	70.96
	Tobramycin(TOB)	1	25	3	75
Tetracycline	Tigecycline(TGC)	0	0	19	100

Table 6:- Antibiotic Susceptibility Pattern of Bacteria Isolated from Diabetic patients.

Class of antibiotics	Antibiotic used	Susceptibility pattern			
		Resistant		Sensitive	
		No.	%	No.	%
β-lactams	Ceftriaxone(CTR)	83	38.07	135	61.92
	Cefotaxime (CTX)	83	41.70	116	58.29
	Meropenem(MRP)	48	44.44	60	55.55
	Piperacillin/Tazobactam(PIT)	27	12.21	194	87.78
	Ampicillin/Sulbactam(A/S)	111	90.98	11	9.01
	Cefoxitin(CX)	1	25	3	75
	Carbenicillin(CB)	2	28.57	5	71.42
	Ceftazidime(CAZ)	5	71.42	2	28.57
Sulphanamides	Cotrimoxazole(COT)	107	48.63	113	51.36
Quinolones	Ciprofloxacin(CIP)	26	56.52	20	43.47
	Levofloxacin(LE)	61	35.26	112	64.73
Nitrofurans	Nitrofurantoin (NIT)	40	17.39	190	82.60
Aminoglycosides	Amikacin (AK)	23	10.40	198	89.59
	Gentamicin(GEN)	17	16.50	86	83.49
	Tobramycin(TOB)	1	14.28	6	85.71
Tetracycline	Tigecycline(TGC)	4	9.52	38	90.47
Glycopeptides	Vancomycin(VA)	0	0	6	100
Macrolides	Erythromycin(E)	2	50	2	50
Lincosamides	Clindamycin(CD)	2	50	2	50

Table 7:- Antibiotic Susceptibility Pattern of Bacteria Isolated from Non-diabetic Patients.

S.N.	Organism Isolated	Antibiotic used	Antibiotic susceptibility test (In diabetic)				Antibiotic susceptibility test (In non-diabetic)			
			Resistant		Sensitive		Resistant		Sensitive	
			No.	%	No.	%	No.	%	No.	%
1	*E. coli*	AK	4	5.40	70	94.59	14	7.95	162	92.04
		GEN	8	27.58	21	72.41	13	15.11	73	84.88
		A/S	37	97.36	1	2.63	96	95.04	5	4.95
		CTR	46	64.78	25	35.21	70	39.77	106	60.22
		CTX	44	68.75	20	31.25	68	43.31	89	56.68
		MRP	22	78.57	6	21.42	38	45.78	45	54.21
		COT	43	61.42	27	38.57	85	47.48	94	52.51
		NIT	12	16.21	62	83.78	22	11.89	163	88.10
		PIT	9	12.16	65	87.83	15	8.42	163	91.57
		CIP	30	88.23	4	11.76	21	58.33	15	41.66
		LE	24	58.53	17	41.46	50	35.46	91	64.53
		TGC	0	0	12	100	1	3.70	26	96.29

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2	*K.pneumonia*	AK	0	0	3	100	1	7.69	12	92.30
		GEN	1	33.33	2	66.66	1	7.69	12	92.30
		A/S	3	100	0	0	8	72.72	3	27.27
		CTR	2	66.66	1	33.33	3	27.27	8	72.72
		CTX	2	66.66	1	33.33	4	36.36	7	63.63
		MRP	3	100	0	0	3	30	7	70
		COT	3	100	0	0	5	38.46	8	61.53
		NIT	2	66.66	1	33.33	8	61.53	5	38.46
		PIT	1	33.33	2	66.66	1	7.69	12	92.30
		CIP	2	66.66	0	33.33	2	100	0	0
		LE	0	0	1	100	2	15.38	11	84.61
		TGC	0	0	2	100	0	0	4	100
3	*Citrobacter sps.*	AK	1	33.33	2	66.66	0	0	5	100
		CTR	2	66.66	1	33.33	2	50	2	50
		CTX	2	66.66	1	33.33	2	40	3	60
		MRP	2	100	0	0	3	100	0	0
		COT	3	100	0	0	5	100	0	0
		NIT	1	33.33	2	66.66	3	60	2	40
		PIT	0	0	3	100	0	0	5	100
		LE	3	100	0	0	4	80	1	20
		TGC	0	0	2	100	0	0	3	100
4	*Enterobacter sps.*	AK	0	0	1	100	1	20	4	80
		CTR	1	100	0	0	0	0	5	100
		CTX	1	100	0	0	0	0	5	100
		PIT	1	100	0	0	1	20	4	80
		COT	1	100	0	0	1	20	4	80
		NIT	1	100	0	0	4	80	1	20
		CIP	0	0	1	100	-	-	-	-
		LE	-	-	-	-	0	0	5	100
5	*Proteus mirabilis*	AK	1	50	1	50	-	-	-	-
		CTR	1	50	1	50	-	-	-	-
		CTX	1	50	1	50	-	-	-	-
		MRP	1	50	1	50	-	-	-	-
		COT	2	100	0	0	-	-	-	-
		NIT	2	100	0	0	-	-	-	-
		PIT	0	0	2	100	-	-	-	-
		LE	0	0	2	100	-	-	-	-
6	*Pseudomonas aeruginosa*	AK	0	0	4	100	0	0	7	100
		A/S	4	100	0	0	2	100	0	0
		TOB	1	25	3	75	4	100	0	0
		CTR	2	50	2	50	3	42.85	4	57.14
		CTX	2	50	2	50	4	57.14	3	42.85
		MRP	2	100	0	0	4	100	0	0
		CB	3	75	1	25	2	28.57	5	71.42
		CAZ	4	100	0	0	5	71.42	2	28.57
		COT	2	100	0	0	3	100	0	0
		NIT	4	100	0	0	7	100	0	0
		PIT	0	0	4	100	2	28.57	5	71.42

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		CIP	1	50	1	50	1	33.33	2	66.66
		LE	1	50	1	50	1	20	4	80
		Polymyxin-B	0	0	4	100	0	0	7	100
7	*Acinetobacter spp.*	AK	3	75	1	25	2	40	3	60
		A/S	3	100	0	0	0	0	3	100
		CTR	3	75	1	25	0	0	5	100
		CTX	2	100	0	0	0	0	5	100
		MRP	3	100	0	0	1	33.33	2	66.66
		COT	4	100	0	0	2	40	3	60
		NIT	4	100	0	0	1	20	4	80
		PIT	3	75	1	25	0	0	5	100
		CIP	0	0	2	100	1	50	1	50
		LE	3	100	0	0	2	66.66	1	33.33
		Polymyxin-B	0	0	4	100	0	0	5	100
		TGC	0	0	3	100	0	0	2	100
8	*Staph. aureus*	AK	-	-	-	-	0	0	2	100
		CD	-	-	-	-	0	0	2	100
		E	-	-	-	-	0	0	2	100
		CX	-	-	-	-	0	0	2	100
		CTR	-	-	-	-	1	50	1	50
		CTX	-	-	-	-	1	50	1	50
		COT	-	-	-	-	0	0	2	100
		NIT	-	-	-	-	1	50	1	50
		LE	-	-	-	-	1	50	1	50
9	*Staph. saprophyticus*	AK	-	-	-	-	0	0	2	100
		CD	-	-	-	-	2	100	0	0
		E	-	-	-	-	2	100	0	0
		CX	-	-	-	-	1	50	1	50
		CTR	-	-	-	-	1	50	1	50
		CTX	-	-	-	-	1	50	1	50
		MRP	-	-	-	-	1	50	1	50
		COT	-	-	-	-	2	100	0	0
		NIT	-	-	-	-	0	0	2	100
		LE	-	-	-	-	1	50	1	50
		PIT	-	-	-	-	0	0	2	100
10	*Enterococcus faecalis*	AK	0	0	2	100	5	83.33	1	16.66
		GEN	-	-	-	-	3	75	1	25
		A/S	-	-	-	-	4	100	0	0
		CTR	1	50	1	50	3	50	3	50
		CTX	1	50	1	50	3	60	2	40
		VA	0	0	2	100	0	0	6	100
		COT	1	50	1	50	4	66.66	2	33.33
		NIT	0	0	2	100	0	0	6	100
		PIT	1	50	1	50	1	16.66	5	83.33
		CIP	1	50	1	50	1	33.33	2	66.66
		LE	1	50	1	50	2	33.33	4	66.66

Table 8:- Antibiotic Susceptibility Pattern of Bacterial Isolated from Diabetic and Non-diabetic Patients.

➢ *Multidrug Resistant*

Overall 124 (37.80%) bacterial isolates were multi drug resistant. Among 124 MDR isolates, 73 (31.06%) were from non-diabetic patients whereas 51 (52.57%) were from diabetic patients. Among 124, 120 (96.77%) gram negative bacterial isolates were found MDR. A high frequency of MDR was found in diabetic patients. *Acinetobacter spp.,Citrobacter spp.* and *Enterobacter spp.* isolated from diabetic patients were 100% multidrug resistant whereas in non-diabetic patients they were 40%, 20%, and 80% multidrug resistant respectively. *Klebsiella pneumoniae* was 66.66% MDR in diabetic isolates and 38.46% MDR in non-diabetic isolates. *Escherichia coli* of diabetic group were 50% MDR and were 29.47% MDR in non-diabetic group respectively. *Pseudomonas aeruginosa* was 50% MDR in diabetic group whereas 28.57% MDR in non-diabetic group. Distribution of MDR strains in diabetic patients and non-diabetic patients is shown in Table 9 and Table 10 and Table 11 respectively.

S.N.	Bacterial isolates	Frequency	Drug resistance in diabetic patients				
			No drugs resistant	1 Drug	2 Drugs	>2Drugs (MDR)	% of MDR
1.	*Escherichia coli*	74	7	7	23	37	50
2.	*Klebsiella pneumonia*	3	0	1	0	2	66.66
3.	*Citrobacter spp.*	3	0	0	0	3	100
4.	*Enterobacter spp.*	1	0	0	0	1	100
5.	*Proteus mirabilis*	2	0	0	1	1	50
6.	*Pseudomonas aeruginosa*	4	0	1	1	2	50
7.	*Acinetobacter spp.*	4	0	0	0	4	100
8.	*Enterococcus faecalis*	2	1	0	0	1	50
9.	*Candida albicans*	4	-	-	-	-	-
	Total	97				51	

Table 9:- Distribution of MDR Strains in Diabetic Patients.

S.N.	Bacterial isolates	Frequency	Drug resistance in diabetic patients				
			No drugs resistant	1 Drug	2 Drugs	>2Drugs (MDR)	% of MDR
1.	*Escherichia coli*	190	28	51	55	56	29.47
2.	*Klebsiella pneumoniae*	13	2	3	3	5	38.46
3.	*Citrobacter spp.*	5	0	4	0	1	20
4.	*Enterobacter spp.*	5	0	1	0	4	80
5.	*Pseudomonas aeruginosa*	7	0	1	4	2	28.57
6.	*Acinetobacter spp.*	5	2	1	0	2	40
7.	*Enterococcus faecalis*	6	1	2	1	2	33.33
8.	*Staph. aureus*	2	0	0	2	0	0
9.	*Staph. saprophyticus*	2	0	0	1	1	50
	Total	235				73	

Table 10:- Distribution of MDR Strains in Non-diabetic Patients.

S.N.	Bacterial isolates	% of MDR isolates		P-value
		Diabetic patients	Non-diabetic patients	
1.	*Escherichia coli*	50	29.47	P=0.0017
2.	*Klebsiella pneumonia*	66.66	38.46	P=0.3902
3.	*Citrobacter spp.*	100	20	P=0.0404
4.	*Enterobacter spp.*	100	80	P=0.65
5.	*Proteus mirabilis*	50	-	-
6.	*Pseudomonas aeruginosa*	50	28.57	P=0.4980
7.	*Acinetobacter spp.*	100	40	P=0.0736
8.	*Enterococcus faecalis*	50	33.33	P=0.6932
9.	*Staph. Aureus*	-	0	-
10.	*Staph. Saprophyticus*	-	50	-

Table 11:- Comparison of MDR Strains in Diabetic and Non-diabetic Patients.

IV. DISCUSSION

In this study we have tried to determine whether there are differences in the microbiological patterns of UTI and in the antibiotic sensitivity patterns of the pathogens concerned with diabetic and non-diabetic patients. Our study had shown that there is significant correlation between the increasing age of patient and the incidence of UTI in both diabetic and non-diabetic patients. Maharjan MN et al. also made a similar observation in his study.[14] It has shown in several studies that women are at increased risk to develop UTI then men.[15, 16, 17] Majority of the culture positive patients in our study were also female (73.17%). Among culture positive UTI, non-diabetic females patients showed a higher rate (80.42%) of UTI compared with males (19.57%), which is in agreement with the various study. [18, 19, 16, 14, 17] Our finding also shows male predominance in diabetic patients with positive cases of UTI which is not in accordance with the results from a study [20, 17] where female were more infected than male among diabetic patients. But Maharjan MN et al. study had shown male predominance in diabetic patients and our finding correlates with it, which is current and Nepali research. The similarities and differences in the distribution of UTI among diabetic male and female may result from different environmental conditions and host factors, and practices such as healthcare and education programmes, socioeconomic standards and hygiene practices in each country.

The bacteria causing UTI in diabetic patients are the similar as in non diabetic patients with only few differences and the predominant of pathogens isolated in our study were gram negative enteric organisms that commonly cause UTI. The uropathogens found in this study are similar to uropathogens identified in other studies conducted in different parts of the World.[15,19,20,16,21,14,17]

Among different uropathogens, the most predominant organism among diabetic and non-diabetic patients was found to be *E. coli* (in diabetic: 76.28% and in non-diabetic: 80.85%) which is confirmatory to the study done by Acharya D et al.[17] and also in study conducted by Daad H. Akbar[15] where the predominant organism was *E.coli*. The dominance of *E. coli* is followed by *Pseudomonas aeruginosa*, *Acinetobacter spp.* and *Candida albicans* with prevalence of 4.12% of each type in diabetic patients whereas *E. coli* is followed by *Klebsiella pneumonia* (5.535%) and then *Pseudomonas aeruginosa* (2.97%) in non-diabetic patients. Bacteria distribution among diabetic and non-diabetic patients in this study more or less resembles to the study done by Muhammad Saqib Ishaq et al.[16] and Saber et al.[20]

Proteus incidence (p=0.03) and *Candida* incidence (p=0.002) was found only among diabetic patients, *Proteus* significant in diabetic patients of our study confirmed the report of Muhammad Saqib Ishaq et al.[16] who also indicated the *Proteus mirabilis* as most common isolate among patients with complicated infections. *Candida* significant in diabetic UTI of our study correlates with study by Debora da Silva Krenke et al.[22] One reason might be that *Proteus* and *Candida* is found in multiple environmental habitats, including long term care facilities and hospitals.[22, 16] Except these two isolates, other type of isolates has no statistical significant among diabetic and non-diabetic patients as shown in Table 5. The differences in prevalence rate of different bacteria may be due to climatic conditions, hospitalization or socio-economic conditions of the patients.

Regarding the antimicrobial susceptibility pattern of the uropathogens, we observed that the isolated gram negative enteric organisms were sensitive at similar rates in both diabetic and non diabetic patients for aminoglycosides, nitrofurans, Tetracycline and Piperacillin/Tazobactam. In our study, a reasonable number of diabetic patients with UTI caused by gram negative bacteria were resistant to quinolones, some of β-lactams drugs and sulphanamides whereas only a minority of the non-diabetic patients had such resistance. The significant differences between diabetic and non diabetic patients to the sensitivity to ciprofloxacin was noted in a study from Bangladesh.[20] Ciprofloxacin resistant *E. coli* was noted significantly higher in diabetic patients than the non-diabetic group in a study done in Iraq.[23] Maharjan MN et al. study also shows different sensitivity rate of isolates from diabetic and non-diabetic patients to quinolones, sulphanamides and some of β-lactams drugs.

Moreover this difference in sensitivity pattern of isolates could be attributed to time difference between the two studies or environment factors such as practices of self medications, the drug abuse and indiscriminate misuse of antibiotics among the general population which has favored the emergence of resistance strains. Antibiotic susceptibility test reveals that higher percentage of susceptibility for Piperacillin/Tazobactam which was most effective antibiotics in both group (83.87% sensitive in diabetic whereas 87.78% sensitive in non-diabetic patients).Ampicillin/Sulbactam was least effective in both group with sensitive rate less than 10.0% in both group. Nitrofurantoin was another most effective antibiotic against isolates from both diabetic and non-diabetic patients (sensitive rate 72.04% in diabetic whereas 82.60% in non-diabetic patients). All aminoglycosides tested i.e. Amikacin, Gentamicin and Tobramycin were effective against isolates from both group with sensitive rate more than 70.0%. Tigecycline was effective for both group with sensitive rate more than 90.0% in both types of patients.

Overall 124 (37.80%) bacterial isolates were multidrug resistant pathogens (MDR). Among 124 MDR isolates, 73 (31.06%) were from non-diabetic patients whereas 51 (52.57%) were from diabetic patients. Among 124, 120 (96.77%) gram negative bacterial isolates were found MDR. A high frequency of MDR was found in diabetic patients. *Acinetobacter spp.,Citrobacter spp.* and *Enterobacter spp*. isolated from diabetic patients were 100% multidrug resistant whereas in non-diabetic patients they were 40%, 20%, and 80% multidrug resistant respectively. *Klebsiella pneumonia* was 66.66% MDR in diabetic isolates and 38.46% MDR in non-diabetic isolates. *Escherichia coli* of diabetic group were 50% MDR and were 29.47% MDR in non-diabetic group respectively. *Pseudomonas aeruginosa* was 50% MDR in diabetic group whereas 28.57% MDR in non-diabetic group. Recent studies have shown the increasing incidence of multidrug resistant pathogens among the UTI patients with diabetes.[14] Statistical significance of MDR isolates among diabetic and non-diabetic patients as show in Table 11 of our study resembles with study by Maharjan MN et al.[14]

The study conducted to focus on the importance of UTI prevention, early detection and eradication of UTI in order to reduce the life threatening consequences of persistent or repetitive infections. Antibiotic therapy is the first & the foremost for UTI in which the invasive agents are controlled. Therefore a correlation between the overuse of antimicrobials & increasing emergence of resistant bacteria seems natural. Incomplete treatment may also be a factor contributing to development of resistance.

V. CONCLUSIONS

We found high proportion of gram negative bacilli with predominant uropathogen being E. coli in both diabetic and non diabetic patients. UTI caused by *Candida albicans* and *Proteus mirabilis* was higher in diabetic patients when compared to non-diabetics. The sensitivity of uropathogens to the antibiotics was similar for some drugs and different for some drugs between two study groups. Another important piece of data was Quinolone and sulfonamides resistance gram negative bacteria, was higher in diabetic patients when compared to non-diabetics UTI in diabetic patients is increasingly associated with MDR pathogens. In our series of patients, diabetes mellitus could be considered as a risk factor for cause of UTI by organisms other than *E.coli* and for higher antibiotics resistance among them. Thus this study should provoke policy makers to formulate an antibiotic policy for rational use of antibiotics. Both diabetic and non diabetic patients are at high risk of development of UTIs, so laboratories should encourage accurate bacteriological record keeping of urinary isolates. Therefore, continued surveillance of sensitivity rates among uropathogens is needed to ensure appropriate recommendations for the treatment of these infections. Knowledge of the susceptibility pattern of the local pathogens should guide the choice of antibiotics, in addition to the likelihood of organisms.

- *Competing Interests*

The author declares that we have no competing interests concerning the information reported in this paper.

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- *Data Availability*

All the data generated and analyzed during this study are included in this published article.

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