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Microbiological Profile and Antibiotic Resistance Pattern of Uropathogens in Diabetic and Non-Diabetic Patients

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Abstract

***Background & Aims*:** Urinary tract infection (UTI) is one of the most common human infections which is more prevalent especially in patients with diabetes mellitus. The aim of this study was to compare the uropathogens isolated from the urine culture of diabetic and non-diabetic patients and their antibiotic resistance pattern in patients admitted to Imam Khomeini Hospital in Ardabil from 2012 to 2013.

Materials & Methods: In this descriptive cross-sectional study, the medical records of all patients admitted to Imam Khomeini University Hospital in Ardabil province from the beginning of 2012 to the end of 2014 were reviewed and the required information including age, sex, or the absence of diabetes was recorded.

Results: *E. coli* was the most common uropathogens isolated from both diabetic (58.1%) and non-diabetic (53.6%) patients followed by yeast (19.4%) in both groups. Other common organisms in diabetic and non-diabetic patients were *Staphylococcus aureus* (8.4%) and coagulase negative *Staphylococcus* (7.1%), respectively. Among diabetic patients, *E. coli* had the highest sensitivity to polymyxin (100%), tetracycline (100%), and amikacin (88.9%). In non-diabetic patients, *E. coli* had the highest sensitivity to amikacin (90.4%), nitrofurantoin (86%), cefoxitin (85.3%), and gentamicin (82.1%).

***Conclusion*:** Our findings indicated that susceptibility profiles of uropathogens are different in diabetic and non-diabetic individuals, therefore, empirical treatment for diabetic and non-diabetic patients will be different.

***Keywords*:** hospital, antibiotic, *Escherichia coli, Staphylococcus aureus*

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Introduction

Urinary tract infections (UTIs) are one of the most prevalent microbial infections. According to the last reports, 1 in 5 adult women experience a UTI at some point in time(1). The clinical presentation of UTI is painful, burning sensation when passing urine, a frequent or constant urge to urinate and in some cases fever and hematuria. *E. coli* is the most common cause of UTI, however, other bacteria and fungi may be involved. Female anatomy structure, sexual intercourse, diabetes, obesity, and family history are the most important risk factors. The spectrum of UTI ranges from asymptomatic bacteriuria to serious complications cystitis, pyelonephritis, renal abscesses, and renal papillary necrosis. Different studies showed that the frequency of severe complications in diabetic patients is higher than the normal population. Also, they are more at risk for infection with a resistance pathogen such as extended-spectrum β-lactamase, fluoroquinolone-resistant, carbapenem-resistant Enterobacteriaceae, and vancomycin-resistant *Enterococci* and fungal mainly by *Candida* (2-4). Several studies indicated that the overall incidence rate of different types of UTI is more frequent in diabetic patients compared to normal individuals(5, 6). According to the hypothesis high glucose levels in urine facilitate the growth of the bacteria also another study suggests that cytokine secretion capacity in patients with diabetic asymptomatic bacteriuria (ABS) is significantly lower than non-diabetic bacteriuric subjects(7).

Control of glycaemia, accurate screening along with identifying microbiological infection features and their antibiotic susceptibility profiles will be critical to treat and prevent the related complications in diabetic patients. Also, the resistance rate of uropathogens to different antibiotics may vary in different geographical locations. In this regard, the present work aimed to assess the frequency of isolated microbes in diabetic and non-diabetic patients and evaluate antimicrobial drug susceptibility patterns of isolates(8, 9).

Materials and Methods

The present work was a descriptive cross-sectional study conducted at Imami Khomain University Hospital in Ardabil province. The purpose of the current study was to compare the uropathogens isolated from the urine culture of diabetic and non-diabetic patients with urinary tract infections and survey their antibiotic resistance patterns. For this purpose, the medical records of all patients admitted to Imam Khomeini Hospital in Ardabil province from the beginning of 2012 to the end of 2015 were reviewed and the required information including age, sex, or absence of diabetes, the type of isolated uropathogens, and their antibiotic susceptibility pattern was extracted. The most important limitation of the present study was incomplete records which were excluded. A total of 314 patients was studied, of whom 252 patients (80.3 %) were non-diabetic and 62 patients (19.7%) were diabetic with culture-positive UTIs. Information of patients and uropathogens were analyzed using SPSS software version 22.0 (SPSS, Chicago, IL, USA). Student's t-test and K^2 test were used for calculation of variable correlations. The p-value under 0.05 was considered statistically significant.

Results

In the present study 62 diabetic (19.7%) and 252 non-diabetic (80.3%) inpatients were included.

42.9% of non-diabetic patients with UTI were male and 57.1% of them were female. This rate for diabetic patients was 43.5% for males and 56.5% for females, respectively. These two groups were not statistically different with regard to sex.

The mean age of all patients with UTI was 60.2 ± 18.1 years, ranging from 14 to 88 years. The mean age of non-diabetic group was 60 ± 18.8 years and the mean age of diabetic group was 61 ± 14.8 years. The mean age of these two groups were not statistically different (p = 0.691)(Table 1).

Table1: distribution of diabetic and non-diabetic patients by mean age

age	Standard deviation	mean	p-value
Non-Diabetic	18.8	60	0.691
Diabetic	14.8	61	
Total	18.1	60.2	

E. coli was the most prevalent uropathogens isolated from all patients (n=171, 54.5%). The most common uropathogens were yeast (n=61, 19.4%), coagulase negative Staphylococcus (CoNS) (n=21, 6.7%), *Enterococci* (n=20, 6.4%), *Acinetobacter* (n=14, 4.5%), *Klebsiella* (n=12, 3.8%), *Pseudomonas* (n=6, 1.9%), *Staphylococcus aureus* (n=3, 1%), *Staphylococcus epidermidis* (n=3, 1%) , and *Staphylococcus saprophyticus* (n=3, 1%)(Figure1).

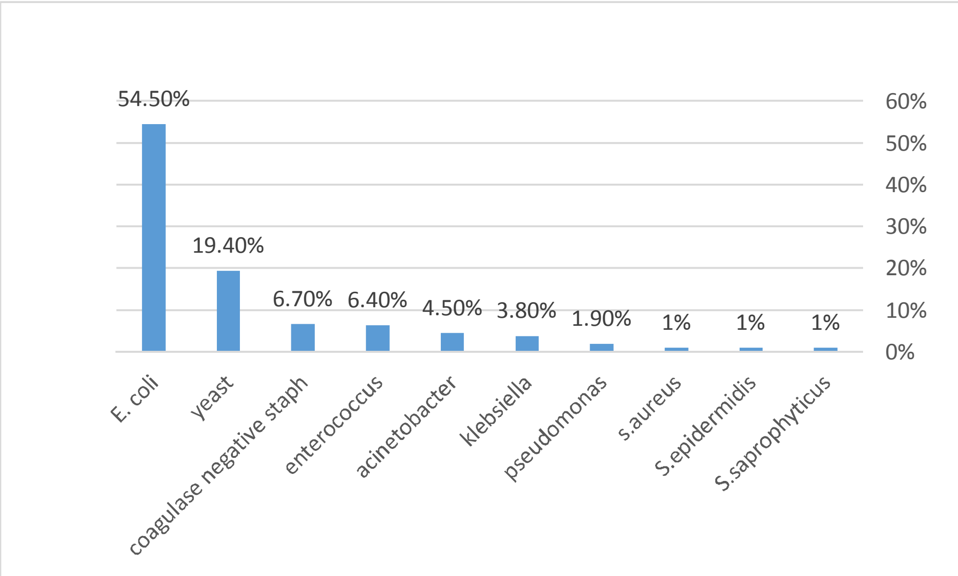

Fig1. Frequency and percentage distribution of uropathogens isolated from all studied patients

As shown in Table 2, *E. coli* was the most common isolate in both diabetic and non-diabetic groups (53.6% in non-diabetics and 58.1% in diabetics) followed by yeast (19.4% in each group). Also, in patients with non-diabetic urinary tract infection, no cases of *S. aureus* and *S. saprophyticus*, and among patients with diabetic urinary tract infection, no cases of *Acinetobacter*, *Klebsiella*, and *S. epidermidis* were observed (Table2).

Table2: Frequency and percentage distribution of isolated uropathogens in accordance with diabetic or non-diabetic patients

uropathogens	Diabetic	Non-Diabetic	Total	p-value
E. coli	(58.1%)36	(53.6%)135	(54.5%)171	0.001>
yeast	(19.4%)12	(19.4%)49	(19.4%)61	
coagulase-negative staphylococci (CoNS)	(4.8%)3	(7.1%)18	(6.7%)21	
enterococcus	(3.2%)2	(7.1%)18	(6.4%)20	
acinetobacter	0	(5.6%) 14	(4.5%)14	
klebsiella	0	(4.8%)12	(3.8%)12	
pseudomonas	(4.8%)3	(1.2%)3	(1.9%)6	
S. aureus	(4.8%)3	0	(1%) 3	

S. epidermidis	0	(1.2%)3	(1%)3
S. saprophyticus	(4.8%)3	0	(1%)3
Total	62	252	314

Table3: Frequency and percentage distribution of isolated uropathogens in non-diabetic and diabetic groups according to Sex

uropathogens	Diabetic			Non-Diabetic		
	male	female	Total	male	female	Total
E. coli	18(66.7%)	18(51.4%)	36(58.1%)	50(46.3%)	85(59%)	135(53.6%)
yeast	6(22.2%)	6(17.1%)	12(19.4%(	22(20.4%)	27(18.8%)	49(19.4%)
coagulase-negative staphylococci (CoNS)	0	3(8.6%)	3(4.8%)	12(11.1%)	6(4.2%)	18(7.1%)
enterococcus	0	2(5.7%)	2(3.2%)	9(8.3%)	9(6.2%)	18(7.1%)
acinetobacter	0	0	0	6(5.6%)	8(5.6%)	14(5.6%)
klebsiella	0	0	0	3(2.8%)	9(6.2%)	12(4.8%)
pseudomonas	3(11.1%)	0	3(4.8%)	3(2.8%)	0	3(1.2%)
S. aureus	0	3(8.6%)	3(4.8%)	0	0	0
S. epidermidis	0	0	0	3(2.8%)	0	3(1.2%)
S. saprophyticus	0	3(8.6%)	3(4.8%)	0	0	0
Total	27	35	62	108	144	252
p-Value	0.031			0.024		

Table 3 shows the frequency of isolated uropathogens in the diabetic and non-diabetic groups by sex. As shown, the most isolated uropathogens among men and women in both diabetic and non-diabetic groups were *E. coli*, and yeast. The frequency of uropathogens causing UTI among males and females in the non-diabetic group (p=0.024) and the diabetic group (p=0.031) were statistically different .

As demonstrated in Figure2, in all patients, the most susceptibility rate was seen to tetracycline, polymyxin, and cefepime (100%) while the highest rate of resistance was observed in afloxacin (100%), cotrimoxazole (77%), amoxicillin (67.8%), cefixime (67.3%), ampicillin (66.4%), and nalidixic acid (66.2%).

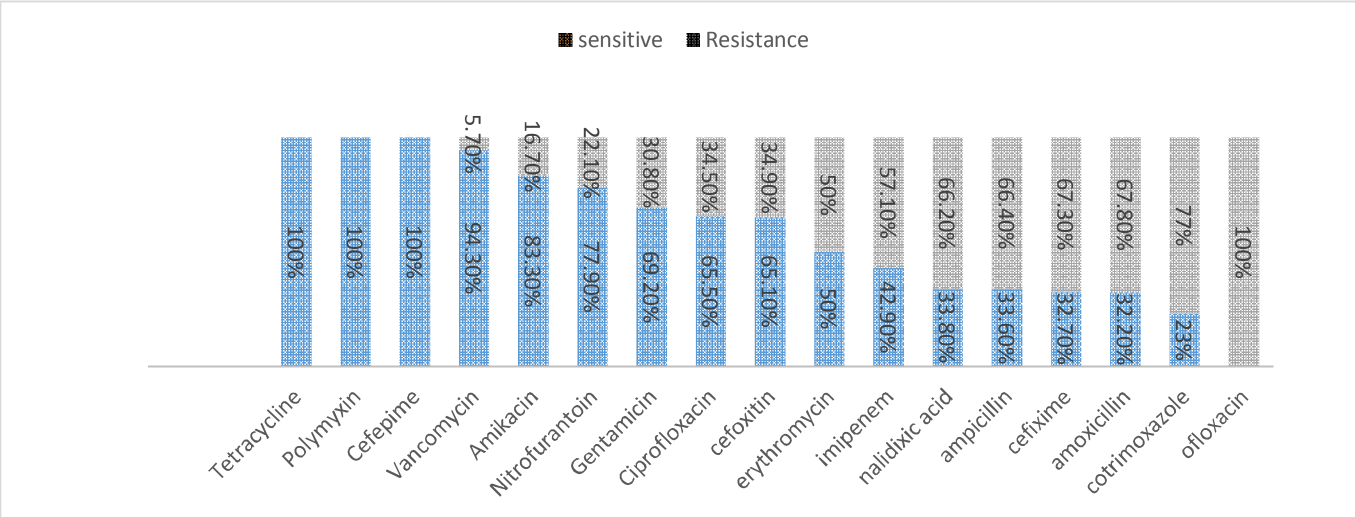

Fig2: Overall susceptibility of uropathogens to antibiotics among all studied patients with UTI

Antibiotic resistance pattern of *E. coli* isolates from diabetic and non- diabetic patients are presented in Table 4.

As it can be seen, among the diabetic patients, the most susceptibility was against polymyxin (100%), tetracycline (100%), and amikacin (88.9%); and the highest resistance to co-trimoxazole (100%), afloxazine (100%), and ampicillin (87.5%). While among non-diabetic patients, the most susceptibility was seen against to amikacin (90.4%), nitrofurantoin (86%), cefoxitin (85.3%), and gentamicin (82.1%), and the most resistance to co-trimoxazole. (75%), amoxicillin (67.3%), and nalidixic acid (64.5%). Also, the resistance rate of *E.coli* isolates taken from diabetic patients to cefoxitin (50% vs. 14.7%, p <0.001), co-trimoxazole (100% vs. 75%, p = 0.004), and ampicillin (87.5% vs. 54.2%; p = 0.004) were significantly higher than non-diabetic patients.

Table4: Susceptibility pattern of *E. coli* isolates, isolated from diabetic and non-diabetic patients with UTI to different antibiotics

		Diabetic	Non-Diabetic	p-Value	Total
cefoxitin	S	18(50%)	99(85.3%)	0.001>0	117(77%)
	R	18(50%)	17(14.7%)		35(23%)
	T	36	116		152
cefixime	S	12(40%)	36(39.6%)	0.966	48(39.7%)
	R	18(60%)	55(60.4%)		73(60.3%)
	T	30	91		121
Nitrofurantoin	S	27(75%)	111(86%)	0.113	138(83.6%)
	R	9(25%)	18(14%)		27(16.4%)
	T	36	۱۲۹ 129		165
cotrimoxazole	S	0	33(25%)	0.004	33(20.8%)
	R	27(100%)	99(75%)		126(79.2%)
	T	27	132		159
Ciprofloxacin	S	21(63.6%)	89(72.4%)	0.329	110(70.5%)

	R	12(36.4%)	34(27.6%)		46(29.5%)
	T	33	123		156
amoxicillin	S	6(28.6%)	33(32.7%)	0.714	39(32%)
	R	15(71.4%)	68(67.3%)		83(68%)
	T	21	101		122
Gentamicin	S	21(70%)	92(82.1%)	0.143	113(79.6%)
	R	9(30%)	20(17.9%)		29(20.4%)
	T	30	112		142
nalidixic acid	S	6(22.2%)	39(35.5%)	0.190	45(32.8%)
	R	21(77.8%)	71(64.5%)		92(67.2%)
	T	27	110		137
amoxicillin	S	24(88.9%)	85(90.4%)	0.729	109(90.1%)
	R	3(11.1%)	9(9.6%)		12(9.9%)
	T	27	94		121
ampicillin	S	3(12.5%)	27(45.8%)	0.004	30(36.1%)
	R	21(87.5%)	32(54.2%)		53(63.9%)
	T	24	59		83
ofloxacin	S	0	-	-	0
	R	6(100%)	-		6(100%)
	T	6	-		6
Polymyxin	S	2(100%)	-	-	2(100%)
	R	0	-		0
	T	2	-		2
Tetracycline	S	2(100%)	-	-	2(100%)
	R	0	-		0
	T	2	-		2
imipenem	S	-	3(42.9%)	-	3(42.9%)
	R	-	4(57.1%)		4(57.1%)
	T	-	7		7

R:
Resistance
T: Total
S: sensitive

The pattern of antimicrobial susceptibility test of coagulase-negative staphylococci (CoNS) isolated from diabetic and non-diabetic patients with UTIs to different antibiotics is shown in Table 6.

Among diabetic patients, the highest rate of susceptibility was seen for gentamicin (100%) and vancomycin (100%); and the highest rate of resistance was observed for cefoxitin (100%), cefixime (100%), ciprofloxazine (100%), and amoxicillin (100%).

Whereas, among non-diabetic patients, the highest rate of susceptibility was observed to vancomycin (100%) and tetracycline (100%); and also, the highest rate of resistance was observed for cefixime (100%), nalidixic acid (100%), afloxacin (100%). Erythromycin (100%), and gentamicin (80%).

These results indicated that sensitivity to gentamicin between diabetic and non-diabetic patients were statistically significant, so that all 3 coagulase-negative staphylococci (CoNS) isolated from diabetic patients were susceptible against gentamicin while Only 20% of isolates taken from non- diabetic patients were gentamicin sensitive (p= 0.025)(Table5).

Table5: Susceptibility Pattern of Coagulase-negative staphylococci (CoNS) isoltes, Isolated from Diabetic and Non-Diabetic Patients with UTI to different types of antibiotics

p-Value	Total	Diabetic	Non-Diabetic		
0.526	6(28.6%)	0	6(33.3%)	S	cefoxitin
	15(71.4%)	3(100%)	12(66.7%)	R	
	21	3	18	T	
-	0	0	0	S	cefixime
	9(100%)	3(100%)	6(100%)	R	
	9	3	6	T	
-	9(60%)	-	9(60%)	S	Nitrofurantoin
	6(40%)	-	6(40%)	R	
	15	-	15	T	
-	9(75%)	-	9(75%)	S	cotrimoxazole
	3(25%)	-	3(25%)	R	
	12	-	12	T	
	3(33.3%)	0	3(50%)	S	Ciprofloxacin
0.464	100(66.7%)	3(100%)	3(50%)	R	
	9	3	6	T	
0.1	3(50%)	0	3(100%)	S	amoxicillin
	3(50%)	3(100%)	0	R	
	6	3	3	T	
0.025	6(33.3%)	3(100%)	3(20%)	S	Gentamicin
	12(66.7%)	0	12(80%)	R	
	18	3	15	T	
-	0	-	0	S	nalidixic acid
	3(100%)	-	3(100%)	R	
	3	-	3	T	
-	6(66.7%)	-	6(66.7%)	S	amikacin
	3(33.3%)	-	3(33.3%)	R	
	9	-	9	T	
-	3(50%)	-	3(50%)	S	ampicillin
	3(50%)	-	3(50%)	R	
	6	-	6	T	
-	18(100%)	3(100%)	15(100%)	S	vancomycin
	0	0	0	R	
	18	3	15	T	

-	0	-	0	S	ofloxacin
	12(100%)	-	12(100%)	R	
	12	-	12	T	
-	0	-	0	S	erythromycin
	6(100%)	-	6(100%)	R	
	6	-	6	T	
-	9(100%)	-	9(100%)	S	Tetracycline
	0	-	0	R	
	100	-	9	T	

S: sensitive

R: Resistance

T: Total

The pattern of susceptibility for *Enterococci* isolates, isolated from diabetic and non-diabetic patients with UTI to different antibiotics is presented in Table 6.

Accordingly, among the diabetic patients, the most susceptibility was seen for nitrofurantoin (100%) and the most resistant rate was observed for co-trimoxazole (100%), ciprofloxacin (100%), gentamicin (100%), and vancomycin (100%).

While among non-diabetic patients, the most susceptibility was observed for amikacin (100%), vancomycin (100%), and erythromycin (100%); and the most resistant rate was observed for cefixime (100%), co-trimoxazole (100%), Ampicillin (100%), and afloxacin (100%).

Also, the two groups , diabetic and non-diabetic patients, were significantly different in terms of vancomycin sensitivity where 2 *Enterococci* isolates from diabetic patients (100%) were resistant to vancomycin while all 9 *Enterococci* isolates from non-diabetic patients (100%) were sensitive to vancomycin (P = 0.018).

Table 6: The susceptibility pattern of Enterococci isolates, derived from diabetic and non-diabetic patients with UTI to different types of antibiotics

p-Value	Total	Diabetic	Non-Diabetic		
-	3(25%)	-	3(25%)	S	cefoxitin
	9(75%)	-	9(75%)	R	
	12	-	12	T	
	-	-	0	S	cefixime
	12(100%)	-	12(100%)	R	
	12	-	12	T	
1	14(82.4%)	2(100%)	12(80%)	S	Nitrofurantoin
	3(17.6%)	0	3(20%)	R	
	17	2	15	T	
0	0	0	0	S	cotrimoxazole
	8(100%)	2(100%)	6(100%)	R	
	8	2	6	T	
0.074	12(100%)	0	12(80%)	S	Ciprofloxacin
	5(100%)	2(100%)	3(20%)	R	

	17	2	15	T	
-	3(50%)	-	3(50%)	S	amoxicillin
	3(50%)	-	3(50%)	R	
	6	-	6	T	
0.515	6(35.3%)	0	6(40%)	S	Gentamicin
	11(64.7%)	2(100%)	9(60%)	R	
	100	100	100	T	
-	6(66.7%)	-	6(66.7%)	S	nalidixic acid
	3(33.3%)	-	3(33.3%)	R	
	9	-	9	T	
-	9(100%)	-	9(100%)	S	amikacin
	0	-	0	R	
	9	-	9	T	
-	0	-	0	S	ampicillin
	9(100%)	-	9(100%)	R	
	9	-	9	T	
0.018	9(81.8%)	0	9(100%)	S	vancomycin
	2(18.2%)	2(100%)	0	R	
	100	2	9	T	
-	0	-	0	S	ofloxacin
	3(100%)	-	3(100%)	R	
	0	-	0	T	
	3(100%)	-	3(100%)	S	erythromycin
	0	-	0	R	
	100	-	100	T	

S: sensitive

R: Resistance

T: Total

In diabetic patients no UTI infection by *Acinetobacter* was seen, and the pattern of susceptibility of *Acinetobacter* isolates derived from non-diabetic patients with UTI to different types of antibiotics are summarized in Table 7. The highest rate of susceptibility of *Acinetobacter* isolates among non-diabetic patients was to polymyxin (100%), tetracycline (100%), and cefepime (100%) and the high rates of resistance were observed for cefixime (100%), ciprofloxazine (100%), amoxicillin (100%), gentamicin (100%), nalidixic acid (100%), amikacin (100%), and ampicillin (100%). %).

Table7: Susceptibility profiles of Acinetobacter isolates obtained from non-diabetic patients with UTI to Different types of Antibiotics

		Non-Diabetic	
		percent	frequency
cefoxitin	S	50%	3
	R	50%	3

	T	6	
cefixime	S	0%	0
	R	100%	8
	T	8	
Nitrofurantoin	S	37.5%	3
	R	62.5%	5
	T	8	
cotrimoxazole	S	0%	0
	R	100%	9
	T	9	
Ciprofloxacin	S	0%	0
	R	100%	14
	T	14	
amoxicillin	S	0%	0
	R	100%	6
	T	6	
Gentamicin	S	0%	0
	R	100%	3
	T	3	
nalidixic acid	S	0%	0
	R	100%	5
	T	5	
amikacin	S	0%	0
	R	100%	8
	T	8	
ampicillin	S	0%	0
	R	100%	3
	T	3	
Polymyxin	S	100%	6
	R	0%	0
	T	6	
Tetracycline	S	100%	3
	R	0%	0
	T	3	
cefepime	S	100%	3
	R	0%	0
	T	3	

S: sensitive

R: Resistance

T: Total

In the case of *pseudomonas*, all of the isolates derived from diabetic patients (100%) were resistant to all three antibiotics, including cefoxitin, ciprofloxazine, and amikacin; however, among non-diabetic patients, the most susceptible antibiotics were gentamicin (100%), and ciprofloxazine (100%). Also, in these patients, isolates were 100% resistant to cefoxitin, cefixime, nitrofurantoin, co-trimoxazole, and amoxicillin.

Table 8: The sensitivity pattern of *pseudomonas* isolates obtained from diabetic and non-diabetic patients with UTI to different types of antibiotics

		Diabetic	Non-Diabetic	Total	p-value
cefoxitin	S	0	0	0	-
	R	3(100%)	3(100%)	6(100%)	
	T	3	3	6	
cefixime	S	-	0	0	-
	R	-	3(100%)	3(100%)	
	T	-	3	3	
Nitrofurantoin	S	-	0	0	-
	R	-	3(100%)	3(100%)	
	T	-	3	3	
cotrimoxazole	S	-	0	0	-
	R	-	3(100%)	3(100%)	
	T	-	3	3	
Ciprofloxacin	S	0	3(100%)	3(50%)	0.1
	R	3(100%)	0	3(50%)	
	T	3	3	6	
Gentamicin	S	-	3	3(100%)	-
	R	-	0	0	
	T	-	3	3	
amikacin	S	0	3(100%)	3(50%)	0.1
	R	3(100%)	0	3(50%)	
	T	3	3	6	

S: sensitive
R: Resistance
T: Total

According to Table 9, the sensitivity rate of *Klebsiella* recovered from non-diabetic patients to amikacin and ampicillin were 100% and 50%, respectively. In diabetic patients no *Klebsiella* isolates were seen.

Table 9: the Susceptibility pattern of *Klebsiella* isolated from non-diabetic patients

		Non-Diabetic	
		percent	frequency
amikacin	S	100%	3
	R	0%	0
	T	3	
ampicillin	S	50%	3
	R	50%	3
	T	6	

S: sensitive
R: Resistance
T: Total

S. aureus as a causative agent of UTI was only identified in diabetic patients. Among them the susceptibility rate to four antibiotic, including co-trimoxazole, ciprofloxazine, vancomycin, and erythromycin was 100%.

Table 10: Drug sensitivity pattern of *S. aureus* isolated from diabetic patients

Diabetic			
100%	3	S	cotrimoxazole
0%	0	R	
3		T	
100%	3	S	Ciprofloxacin
0%	0	R	
3		T	
100%	3	S	Vancomycin
0%	0	R	
3		T	
100%	3	S	erythromycin
0%	0	R	
3		T	

S: sensitive
R: Resistance
T: Total

Drug Sensitivity pattern of *S. epidermidis* isolates from patients with non-diabetic UTI are listed in Table 11(There was no case of *S. epidermidis* in diabetic patients). As shown in Table 11, in non-diabetic patients with UTI, S. epidermidis isolates were fully susceptible to nitrofurantoin and vancomycin antibiotics and also resistant to co-trimoxazole, ciprofloxacin, amoxicillin, and gentamicin.

Table 11: Sensitivity Pattern of *S. epidermidis* isolated from non-diabetic patients with UTI to different antibiotics

Non-Diabetic			
percent	frequency		
100%	3	S	Nitrofurantoin
0%	0	R	
3		T	
0%	0	S	cotrimoxazole
100%	3	R	
3		T	
0%	0	S	Ciprofloxacin
100%	3	R	
3		T	
0%	0	S	amoxicillin
100%	3	R	
3		T	
0%	0	S	Gentamicin
100%	3	R	
3		T	
100%	3	S	Vancomycin
0%	0	R	
3		T	

S: sensitive
R: Resistance
T: Total

Drug Sensitivity pattern of S. saprophyticus isolates from patients with diabetic UTI are listed in Table 12(There was no case of S. saprophyticus in non-diabetic patients). As it can be seen, in diabetic patients with UTI, Staphylococcus saprophyticus isolates were sensitive to 5 antibiotics, including cefoxitin, cefixime, nitrofurantoin, ciprofloxacin, and amoxicillin (100%).

Table 12: Sensitivity Pattern of *S. saprophyticus* isolated from Diabetic Patients with UTI to Different Antibiotics

Diabetic			
percent	frequency		
100%	3	S	cefoxitin
0%	0	R	
3		T	
100%	3	S	cefixime
0%	0	R	
3		T	
100%	3	S	Nitrofurantoin
0%	0	R	
3		T	

100%	3	S	Ciprofloxacin
0%	0	R	
3		T	
100%	3	S	amoxicillin
0%	0	R	
3		T	

S: sensitive

R: Resistance

T: Total

Discussion

Urinary Tract Infection (UTI) is a prevalent infection of the urogenital system and almost 10% of individuals experience this disorder during their lifetime(10).

Several studies indicated that the risk of UTI in diabetic patients is significantly higher than non-diabetic ones. Also, the causative agent and the susceptibility pattern of uropathogens between diabetic and non-diabetic patients are different. A study by Isapour et al., 2015, found that the prevalence of asymptomatic UTI was higher in people with a history of diabetes and those with uncontrolled hyperglycemia(11). Diabetes is reported as a general predisposing factor for common and complicated UTI, catheter-associated UTI, post-renal transplant-recurrent UTI, and fungal UTI especially Candida (12, 13). Also they are also more likely to become infected with antibiotic-resistant strains than the general population. In fact previous studies confirm that several impairments in immune system like reduction in neutrophil responses, decreases of urinary cytokines, and leukocyte concentration in the bladder may all contribute to adhesion of uropathogens to epithelial cells and the development of infection (14, 15). In addition, further studies have shown that other factors such as age, anatomic structure, hyperglycemia, and uncontrolled metabolic disorders enhance the risk for UTI in diabetics(16).

In this regard, this study aimed to identify the frequency of uropathogens among diabetics and non-diabetics and also tried to analyze their antibiotic resistance pattern in order to identify the predominant pathogens in Ardabil region and achieve appropriate empirical treatment. *E.coli*, yeast, and staphylococcus spp were the most common causative agent of UTI in diabetic and non-diabetic patients in Ardabil province, respectively. Although diabetes is a risk factor for fungal infections, no significant difference was found in the rate of infection between diabetic and non-diabetic individuals ($p>0.05$). However, in other similar studies, the rate of yeast infection in diabetics was significantly higher than non- diabetics(17).

In diabetics, the prevalence of UTI, likely to be infected with resistant pathogens, severity of illness and worse outcome in much higher than non- diabetics(15).

The increased risk of UTI among patients with diabetes, increased rate of diabetes worldwide, along with the irrational prescription of antibiotics has become a serious problem that in the near future may lead to the spread of antibiotic-resistant pathogens.

Due to anatomical structure, generally the rate of UTI in women is higher than men, but in this study there was no significant difference in terms of gender among diabetics and non- diabetics(18).

Previous studies indicated that *E. coli* was responsible for about 80 percent of UTI infection and pyelonephritis was 4 times more frequent in diabetic women compared to non-diabetic ones(19, 20). Previous studies that investigated male patients indicated that severe complicated UTI, such as prostatitis, and prostatic abscess are more common in diabetic patients(21).

According to the literature, *E. coli* is the frequently encountered isolate in UTI infection, however the distribution of other uropathogens varies from one region to another. Literature review of other studies and also a systematic review conducted in Iran indicated that *E. coli*, *Candida albicans*, and negative coagulase staphylococcus were the predominant species that cause UTI but their antimicrobial resistance pattern and distribution of other uropathogens vary by region(22-27). The findings of our study showed that *E. coli* was the major cause of infection in diabetics (58.1%) and non-diabetics (53.6%) followed by yeast (19.4%) in Ardabil region.

A study by Shakib et al, 2018, showed that the most common isolates were *E. coli* (61.43%), 119 *K. pneumoniae* (16.10%), 72 *Staphylococcus* 21% (2.2%). 84) *P. aeruginosa* 21, (74.9%) 17.2%) *Streptococcus* 16, (84.2%) Bacterium Coreine 62.1) Proteus 12, (89.1%) Acinetobacter 14, (27.0%) Citrobacter 2 and (8.1%) of *Enterobacter* were (8%). Therefore, *E. coli* and *Klebsiella* were the most common isolated bacteria causing UTIs. Also, in this study, *E. coli* the highest antibiotic resistance was to co-trimoxazole and nalidixic acid and the most susceptibility was to amikacin and in *K. pneumoniae* the highest resistance and susceptibility was co-trimoxazole and amikacin respectively(23).

Maharjan found that *E. coli* was the most common isolated pathogen in diabetic (61.7 %) and non- diabetic patients (67.3%**).** Other causative agents among diabetics were *K. peumoniae* (14.70%), *S. aureus* (11.77%), *S. saprophyticus* (8.82%), and *P. aeruginosa* (2.94%) and other causative agents among non-diabetics were *K. pneumoniae* (5.45%), *C. freundii* (5.45%), *K. oxytoca* (3.63%), *P. mirabilis* (3.63%), *Providencia spp.* (3.63%), *S. aureus* (5.45%), *S. saprophyticus* (1.82%), *P. aeruginosa* (1.82%), and *E. faecalis* (1.82%)(28).

In 2019, Woldemariam et al. Showed the prevalence of uropathogens among diabetics and non-diabetics. In their study, the most common uropathogen isolates were *E. coli* (23.2%), *Coagulase negative Staphylococci* (CONs) (12.5%), *Enterococcus* Spp. (10.7%), *Candida albicans* (17.9%), and Non-*albicans Candida* Spp. (16.1%) (29).

In our study, the most common uropathogen isolates among diabetics and non- dianbetics were *E. coli*(171 cases, /54.5%), yeast(61 cases, 19.4%),Coagulase-negative staphylococci (CoNS)(21 cases, 6.7%), *Enterococcus* (20 cases, 6.4%), *Acinetobacter* (14 cases, 4.5%), *Klebsiella* (12 cases, 3.8%), *Pseudomonas* (6 cases, 1.9%), *S. aureus* (3 cases, 1%), *S. epidermidis* (3 cases, 1%), and *S. saprophyticus* (3 cases, 1%) respectively.

In the present study, among all the isolates, the highest resistance to ofloxacin and cotrimoxazole was observed while a high percentage of isolates were sensitive to tetracycline, polymyxin, and cefepime.

Although cotrimoxazole is widely used for the treatment of UTI, our finding revealed high rates of resistance among isolates to these antibiotics. Therefore, medication with cotrimoxazole should be revised in the study area.

Finally, constant surveillance of uropathogens and their antimicrobial susceptibility profiles will be helpful in rational use of available antibiotics, decreasing the probability of antimicrobial resistance in uropathogens, establishment of infection control strategies in the healthcare setting, and providing an optimal empirical regimen.

Conclusion: UTI is more frequent, severe and caused by more resistant pathogen in diabetic patients compared to non-diabetic patients. Therefore, diabetes is an underlying disease that imposes a great burden on healthcare systems and society. The results of this study will be a basis for proper medication for diabetic and non-diabetic patients in Ardabil region. Incomplete information about some patients and excluding them from the study was the most important limitation of the present study. At the end, further research on diabetic patients with controlled and uncontrolled glycaemia is recommended.

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Disclosure

The authors state that there is no conflict of interest.

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