Antimicrobial treatment pattern and Medications Adherence among Iraqi T2DM patients with recurrent urinary tract infection in Wasit province

Maher Kadhum Abed*, Manal Khalid Abdulridha*, Hussein Adnan **

** Department of clinical pharmacy/College of Pharmacy/ Al Mustansiriyah university/ Baghdad, Iraq*

*** Department of internal medicine/ College of Medicine / Wasit university / Wasit, Iraq*

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Corresponding Author email:
maherkadhum@uomustansiriyah.edu.iq
Orcid: https://orcid.org/0009-0007-7124-9697

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Abstract:

Background: Recurrent urinary tract infections (rUTIs) are common in type 2 diabetes mellitus (T2DM) patients due to impaired immunity, glycosuria, and chronic comorbidities. Antimicrobial resistance complicates therapy, and inappropriate use further worsens recurrence.

Objective: To evaluate antimicrobial treatment patterns, among T2DM Iraqi patients with rUTIs.

Methods: A prospective, open-label study was conducted at Al-Zahraa Teaching Hospital and private internal medicine clinics in Wasit, Iraq, from October 2024 to June 2025. Ninety-nine patients with rUTIs were enrolled, including 58 of them with T2DM. Patients underwent structured three follow-up visits from day1 to days 7-14. Laboratory testing, urine cultures, antibiotics sensitivity test, antimicrobial prescriptions, and medication adherence (MARS) were assessed.

Results: *E. coli* was the most frequent uropathogen in this study. Fluoroquinolones—including levofloxacin, ciprofloxacin, and norfloxacin beside to Aminoglycoside as amikacin consistently showed the highest activity against most pathogens, particularly *E. coli*, *Enterobacter spp.*, and *Pseudomonas spp.*, with sensitivity rates frequently exceeding 90%. On the contrary, a wide variety of β-lactam antibiotics, including drugs such as cefixime, Augmentin and amoxicillin, show high degrees of resistance among nearly all strains of bacteria, with the percent of resistance often exceeding 90–100%. Although there was generally moderate adherence to medication regimens reported by participants in the MARS surveys,

Conclusion: Fluoroquinolones and aminoglycosides were the most commonly used antimicrobial treatments in Iraqi T2DM patients with rUTIs. Findings were significantly impacted by adherence and glucose levels.

Keywords: Antimicrobial treatment, Medication adherence**,** Recurrent urinary tract infection, Type 2 diabetes mellitus.

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أسلوب العلاج بالمضادات الحيوية والالتزام بالأدوية بين مرضى السكري من النوع الثاني للعراقيين المصابين بعدوى المسالك البولية المتكررة في محافظة واسط

ماهر كاظم عبد *, منال خالد عبد الرضا* ,حسين عدنان محمد**
*فرع الصيدلة السريرية / كلية الصيدلة / الجامعة المستنصرية/ بغداد
** فرع الطب الباطني / كلية الطب / جامعة واسط / واسط

الخلاصة

الخلفية: التهابات المسالك البولية المتكررة شائعة لدى مرضى السكري من النوع الثاني بسبب ضعف المناعة، وجود السكر في البول، والأمراض المصاحبة المزمنة. مقاومة مضادات الميكروبات تعقد العلاج، والاستخدام غير المناسب يزيد من تكرار العدوى.

الطريقه : تم إجراء دراسة مستقبلية مفتوحة في مستشفى الزهراء التعليمي والعيادات الخاصة للطب الباطني في واسط، العراق، من أكتوبر 2024 إلى يونيو 2025. تم تسجيل تسعة وتسعين مريضًا يعانون من التهابات المسالك البولية المتكررة، بما في ذلك 58 منهم يعانون من داء السكري من النوع الثاني. خضع المرضى لثلاث زيارات متابعة منظمة من اليوم الأول إلى الأيام 7-14. تم تقييم الفحوصات المخبرية، وزرع البول، واختبار حساسية المضادات الحيوية، ووصفات الأدوية المضادة للميكروبات، والامتثال للأدوية.

النتائج: كان بكتريا (أي كولاي) الأكثر شيوعًا من مسببات التهاب المسالك البولية في هذه الدراسة. الفلوروكينولونات بما في ذلك ليفوفلوكساسين، سيبروفلوكساسين، ونورفلوكساسين بالإضافة إلى الأمينوغليكوزيد مثل أميكاسين اظهرت باستمرار أعلى نشاط ضد معظم مسببات الأمراض، وخاصة الإشريكية القولونية، الإنتيروبكتير، وسيدومونس، مع معدلات حساسية تتجاوز 90% بشكل متكرر. على العكس من ذلك، تُظهر مجموعة واسعة من المضادات الحيوية، بما في ذلك أدوية مثل سيفيكسيم، أوكمنتين وأموكسيسيلين، درجات عالية من المقاومة بين جميع سلالات البكتيريا تقريبًا، حيث غالبًا ما تتجاوز نسبة المقاومة 90-100%. على الرغم من أن هناك التزامًا معتدلًا ببرامج الأدوية التي أبلغ عنها المشاركون في استطلاعات (المارس).

الاستنتاج: كانت الفلوروكينولونات والأمينوغليكوزايدات أكثر العلاجات المضادة للميكروبات استخدامًا لدى مرضى السكري من النوع الثاني للعراقيين الذين يعانون من التهابات المسالك البولية المتكررة. تأثرت النتائج بشكل كبير بالالتزام ومستويات الجلوكوز.

الكلمات المفتاحية: العلاج المضاد للميكروبات، الالتزام بالعلاج، عدوى المسالك البولية المتكررة، داء السكري من النوع الثاني.

Introduction

Urinary tract infections (UTIs) are among the most common bacterial. infections worldwide and their recurrence are a severe health concern burden. rUTI, described as two or more infections in six months or three or more in a year, is particularly concerning for patients with type 2 diabetes mellitus (T2DM)[1]. The presence of glycosuria, impaired host immunity, autonomic neuropathy, and frequent comorbidities predispose diabetic patients to infection and recurrence[2].

In Iraq and other regions with rising antimicrobial resistance, the selection of appropriate therapy is a challenge[3]. Empirical prescribing without culture guidance contributes to treatment failure and recurrence. Furthermore, medication non-adherence and poor glycemic control further worsen outcomes in diabetic patients In recent years, the etiological agents of bacterial UTIs have gained resistance to most strong antibiotics, complicating the management of UTIs in diabetes patients[4].

A major burden on public health and medical care may result from the increased risk of UTIs in diabetic patients and the rising incidence of DM globally in recent decades. Global reports have documented the isolation of multidrug-resistant uro-pathogens from diabetes individuals[5]. In Iraq, Multi-drug resistance was reported in different studies[6].

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It complicates the process of empirical antibiotic selection as well as highlights the need for effective antimicrobial stewardship. Additionally, research has shown that Extended Course Antibiotic Therapy (i.e., longer than five days) does not necessarily result in decreased recurrence rates. Therefore, it is critical to utilize evidence-based treatment protocols that are tailored to this patient population(7).

One of the major problems associated with chronic disease management is ensuring that patients take their medications as prescribed. According to the WHO (2006), "Patient medication adherence is the extent to which a patient's behavior corresponds with medical advice." Medication adherence helps improve the effectiveness of medications for chronic diseases(8). However, adherence rates are alarmingly low when it comes to long-term therapy: Approximately 50% of patients in developed countries remain compliant; significantly lower compliance has been found in developing nations(9). Patients with Type 2 Diabetes Mellitus are also at greater risk for complications and higher treatment costs due to poor medication adherence. There are multiple factors that contribute to a patient's inability to correctly use their medications (e.g., socioeconomic, forgetfulness, and health system(10).

Despite the known link between T2DM and its elevated risk for UTI, there remains little understanding of the association between UTI and antibiotic treatment as well as adherence among individuals with T2DM and recurrent UTIs. Previous research has explored each of these variables independently, but there is a lack of comprehensive investigations examining how they combine to affect clinical outcomes in this vulnerable population. As such, there is currently no evidence-based approach on how to effectively and safely manage rUTIs among the growing number of individuals with T2DM, due to lack of research in this area. This study aims to investigate antimicrobial treatment regimens used by T2DM patients experiencing recurrent UTIs, as well as adherence to those medications. By clearly defining these variables, it is the hope that this study will provide insight that can help facilitate the development of tailored interventions to improve medication adherence and thus enhance clinical practice and ultimately improve care quality and clinical outcomes for this at-risk population.

Patients and Methods

Study Design and study groups

A prospective, open-label study enrolling T2DM patients with rUTI, divided into two groups and two subgroups as follows: Group 1 include patients presented with rUTI only, Group 2 include T2DM patients presented with rUTI, subdivided into two subgroups: Group 2A include T2DM patients who presented with good glycemic control with rUTI, and Group 2B include T2DM patients presented with poor glycemic control and rUTI. Patients underwent structured 3 visits follow-up at Days 1, Day 3. and Day 7 to 14. Laboratory testing, urine cultures, antibiotics sensitivity test, antimicrobial prescriptions, and medication adherence (MARS) were assessed. Inclusion criteria included patients age greater than 18 years and less than 80 years. Exclusion criteria included Type 1 diabetes, SGLT2 inhibitor drug use, prior antibiotics (within 72h), pregnancy and lactation.

Diabetes diagnosed as patient had a history of T2DM at least 1 year or HBA1c >7% or in a patient with classic symptoms of hyperglycemia and random blood sugar above 200 mg/dl (11.1 mmol/L)(11).

Urine collection and culture

A midstream urine sample was taken in a sterile container, and each patient had a thorough urine examination. When the patients diagnosed with UTI, a urine culture

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and sensitivity test were conducted. A few drops of the urine precipitate were aseptically added to plates of blood agar and MacConkey media, and the plates were then incubated for 48 to 72 hours. Antibiotic sensitivity testing, and the results were interpreted according to the CLSI guidelines. The following antibiotic disks were obtained (from Oxoid, UK) as reference disks with known potency for laboratory use: Amikacin (30 µg), Ciprofloxacin (5 µg), Trimethoprim-sulfamethoxazole (1.25/23.75 µg), Cefixime (5 mg), Norfloxacin (10 µg), Gentamicin (10 µg), Augmentin (20/10 mg), Amoxicillin (25 µg) and Nitrofurantoin (300 µg)[12].

Blood glucose assessment

Fasting blood glucose (FBG) or random blood glucose (RBG) were assessed using an enzyme-driven reaction called enzymatic oxidation of glucose measurement Glycosylated Hemoglobin A1c (HbA1c) level was measured using the Tina- quant Hemoglobin A1c Dx Gen.3 assay.

Assessment of patients Medication Adherence

The medication adherence rating score (MARS) is a validated tool helps to monitor drug adherence consistency. Development and validation of this tool were done by Thompson K et al[13]. Furthermore, the Arabic version of the MARS has been formally validated, demonstrating good construct validity through principal component analysis and acceptable reliability with Cronbach's alpha values ≥0.70 and intraclass correlation coefficients exceeding 0.70[14]. The ten questions in MARS offer insights about medication adherence behavior, beliefs regarding drugs, and undesirable side effects. The questionnaire requires a binary response of yes or no, with non-adherence marked as 0 and adherence coded as 1. Consequently, for questions 1 through 6 and 9 through 10, a "no" the response is allocated a value of 1, whereas for questions 7 and 8, a "yes" the response is allocated a value of 1(reverse response). Total ratings vary from 0 to 10, with scores of 8 or lower signifying medication non-adherence[15].

Ethical Considerations

The Research Ethical Committee of the College of Pharmacy, Mustansiriyah University, examined and authorized this study (approval number: 80; reference number: 180; date: 3 September 2024). An agreement was established with Al-Zahraa Teaching Hospital in Wasit province. Verbal and written agreement was obtained from all participants.

Statistical Analysis

Statistical analysis was conducted utilizing Statistical Package for the Social Sciences (SPSS) software version 25 (IBM Corporation). Categorical variables were expressed as frequencies and percentages. Continuous variables are expressed as (mean ± standard deviation). An ANOVA test was employed to compare the means among three groups. Pearson's Chi-square and Fisher's exact tests were employed to determine the association between categorical variables. $P \leq 0.05$ was regarded as statistically significant.

Results

Sociodemographic Characteristics of Patients

Baseline demographic and clinical characteristics of the study population are presented in Table 1. A statistically significant difference in age was observed between the two groups, with Group 2 being older than Group 1 (55 ± 15 vs. 41 ± 17 years, $p < 0.001$). Similarly, duration of diabetes differed significantly, with Group 2 demonstrating a longer median duration compared to Group 1 (3 years [range 1–17]

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vs. 0 years, $p < 0.001$). These findings suggest that age and chronicity of diabetes may represent important modifying factors when evaluating antimicrobial response and recurrence outcomes. In contrast, no significant differences were detected in anthropometric parameters, including height ($p = 0.563$), weight ($p = 0.159$), or BMI ($p = 0.275$). Distribution across BMI categories (normal weight, overweight, and obese) was also comparable between groups ($p = 0.437$). Sex distribution showed female predominance in both groups (87.8% vs. 75.9%), consistent with the epidemiology of recurrent urinary tract infections; however, the difference was not statistically significant ($p = 0.137$). Smoking status was similar between groups ($p = 0.51$), with very low prevalence overall. Urban–rural residence distribution was nearly identical ($p = 0.993$), indicating comparable socio-demographic backgrounds. Additionally, the prevalence of comorbid conditions, including hypertension and renal failure, did not differ significantly ($p = 0.882$). Overall, except for age and duration of diabetes, baseline characteristics were well balanced between the two groups, suggesting minimal confounding from other demographic or clinical variables.

Age and the length of diabetes were found to be equal among subgroups in Group 2 (Group 2A vs. Group 2B), ruling out these variables as possible causes of intragroup variations. Interestingly, group 2A's mean BMI was significantly higher than Group 2B's (33.99 ± 5.95 vs. 30.47 ± 4.6, $p = 0.017$), but there was no significant difference in the categorical BMI distribution. These findings suggest that age and duration of diabetes differentiate Group 2 from Group 1, whereas variations within Group 2 are more closely linked to BMI. These findings endorse the potential distinct influences of chronic hyperglycemic exposure and obesity-related metabolic stress on the modulation of disease recurrence and antimicrobial response in individuals with type 2 diabetes mellitus.

Table 1. Sociodemographic Characteristics of Patients among study groups

		Group 1 (n=41)		Group 2 (n=58)		P value	Group 2A (n=18)		Group 2B (n=40)		P value
Age	Mean ±SD	41	±17	55	±15	<0.001†	55.22	±15.4	54.72	±15.4	0.909†
Hight	Mean ±SD	161.2	±7.9	162	±10	0.563†	159.11	±13.0	163.7	±7.9	0.180†
Weight	Mean ±SD	79.12	±11.6	83	±13	0.159†	85.56	±14.9	81.53	±12.5	0.288†
BMI	Mean ±SD	30.47	±4.25	31.57	±5.27	0.275†	33.99	±5.95	30.47	±4.6	0.017†
BMI groups	Normal weight	6	14.60%	5	8.60%	0.437‡	1	5.60%	4	10%	0.333‡
	Overweight	10	24.40%	20	34.50%		4	22.20%	16	40%	
	Obese	25	61.00%	33	56.90%		13	72.20%	20	50%	
Sex	Female	36	87.80%	44	75.90%	0.137‡	14	77.80%	30	75%	0.819‡
	Male	5	12.20%	14	24.10%		4	22.20%	10	25%	
smoking status	No	41	100.00%	56	96.60%	0.51*	17	94.40%	39	97.50%	0.528*
	Yes	0	0.00%	2	3.40%		1	5.60%	1	2.50%	
Residence	Urban	24	58.50%	34	58.60%	0.993‡	10	55.60%	24	60%	0.751‡
	Rural	17	41.50%	24	41.40%		8	44.40%	16	40%	
Duration of diabetes	Median (range)	0	0	3	1-17	<0.001▪	2	0-15	3	1-17	0.628▪
Other diseases	None	33	80.50%	47	81.00%	0.882*	13	72.20%	34	85.00%	0.399*
	Hypertension	8	19.50%	10	17.20%		5	27.80%	5	12.50%	
	Renal failure	0	0.00%	1	1.70%		0	0.00%	1	2.50%	

P value using † student tTest, ‡ Chi Square Test,* Fissue exact▪ Mann Whitney test

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Causative uropathogen among the study groups

Regarding causative bacteria, the frequency of *Escherichia coli* infection was higher in Groups 2A and 2B, affecting more than one-third of patients in each group, compared to 26.4% in Group 1, as shown in Table (2) Similarly, *Pseudomonas* infections were more frequent in Group 2A (4 patients, 22.2%) and Group 2B (7 patients, 17.5%) than in Group 1 (14.6%). Notably, bacteria were not isolated in 2 (4.9%) of Group 1 and 2 (11.1%) of Group 2A.

Table 2. Causative bacterial species among study groups

ISO.BACT	Group-1 n=41		Group-2A n=18		Group-2B n=40		P value
No bacteria isolated	2	4.90%	2	11.10%	0	0.00%	0.497
E coli	11	26.80%	6	33.30%	15	37.50%	
Enterobacter spp.	10	24.40%	1	5.60%	4	10.00%	
Pseudomonas spp.	6	14.60%	4	22.20%	7	17.50%	
Proteus spp.	3	7.30%	0	0.00%	4	10.00%	
Staphylococcus spp.	8	19.50%	4	22.20%	8	20.00%	
Others	1	2.40%	1	5.60%	2	5.00%	

Data presented as number (N) and percentage (%), P-value by Fissure's Exact Test. $p \geq 0.05$ is considered non -significant

Prescribed Antimicrobial Protocol for rUTI

Dual antibiotic therapy was relatively more common among diabetic patients, with 83.3% in Group 2A (15 patients) and 87.5% in Group 2B (35 patients), compared to 73.2% in Group 1 (30 patients).

Monotherapy was least frequent in Group 2B (3 patients, 7.5%), compared to 16.7% in Group 2A and 19.5% in Group 1. These differences, however, did not reach statistical significance. The selection of antibiotic classes did not differ significantly among the study groups as shown in Table (3).

Table. 3 Prescribed Antimicrobial according to the study groups

		Group-1 N=41		Group-2 A N=18		Group-2B N=40		p-value
Levofloxacin		11	26.8%	8	44.4%	11	27.5%	0.375
Nitrofurantoin		18	43.9%	8	44.4%	24	60.%	0.314
Amikacin		17	41.5%	8	44.4%	20	50%	0.747
Ciprofloxacin		2	4.90%	0	0.00%	2	5%	1
Norfloxacin		15	36.6%	6	33.3%	14	35%	1
Amoxicillin		5	12.2%	0	0.00%	4	10%	0.43
Cefixime		2	4.90%	1	5.60%	0	0.00%	0.399
Trimethoprim		0	0.00%	1	5.60%	1	2.50%	0.18
Augmentin		4	9.80%	0	0.00%	2	5.00%	0.555
Gentamicin		1	2.40%	0	0.00%	0	0.00%	1
Antimicrobial Combinations	Single	8	19.5%	3	16.7%	3	7.5%	0.422
	Two drugs	30	73.2%	15	83.3%	35	87.5%	
	Three drugs	3	7.3%	0	0	2	5%	

Data presented as number (N) and percentage (%), P-value by Chi Square Test or Fisher's exact. $p \geq 0.05$ is considered non –significant

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Antibacterial Susceptibility Across Study Groups

The antibacterial susceptibility tests showed identical antibiotic resistance and sensitivity results between all research participants without any meaningful differences between groups ($p > 0.05$). Table 4 show that the sensitivity tests revealed amikacin as the most effective antibiotic against Groups 1,2A and 2B because it showed 84.6%, 100% and 92.5% effectiveness respectively. Fluroquinolone as ciprofloxacin together with levofloxacin demonstrated strong effectiveness in the tests. The antibiotic Nitrofurantoin showed moderate sensitivity levels between 71% and 75% while maintaining lower resistance rates than most β-lactam antibiotics. The resistance rates for cefixime and amoxicillin and amoxicillin–clavulanate and trimethoprim- sulphamethaxazol and gentamicin exceeded 85% in all groups. The susceptibility patterns as in Figure 1 showed identical patterns between different groups while the sensitivity and resistance distribution charts provided visual evidence.

Table 4: Antibacterial sensitivity across study groups

Antibacterial sensitivity		Group 1		Group 2A		Group 2B		P value
		No.	%	No.	%	No.	%	
Levofloxacin	Not tested	7	17.90%	1	6.30%	6	15.00%	0.863
	Sensitive	29	74.40%	14	87.50%	32	80.00%	
	Resistance	3	7.70%	1	6.30%	2	5.00%	
Nitrofurantoin	Not tested	1	2.60%	1	6.30%	2	5.00%	0.874
	Sensitive	28	71.80%	12	75.00%	29	72.50%	
	Intermediate	2	5.10%	0	0.00%	0	0.00%	
	Resistance	8	20.50%	3	18.80%	9	22.50%	
Amikacin	Not tested	3	7.70%	0	0.00%	1	2.50%	0.871
	Sensitive	33	84.60%	16	100.00%	37	92.50%	
	Intermediate	2	5.10%	0	0.00%	1	2.50%	
	Resistance	1	2.60%	0	0.00%	1	2.50%	
ciprofloxacin	Not tested	1	2.60%	0	0.00%	0	0.00%	0.869
	Sensitive	33	84.60%	15	93.80%	37	92.50%	
	Intermediate	1	2.60%	0	0.00%	0	0.00%	
	Resistance	4	10.30%	1	6.30%	3	7.50%	
norfloxacin	Not tested	11	28.20%	3	18.80%	8	20.00%	0.598
	Sensitive	25	64.10%	13	81.30%	31	77.50%	
	Resistance	3	7.70%	0	0.00%	1	2.50%	
Cefixime	Not tested	7	17.90%	1	6.30%	3	7.90%	0.438
	Sensitive	1	2.60%	0	0.00%	0	0.00%	
	Resistance	31	79.50%	15	93.80%	35	92.10%	
Methoprim	Not tested	2	5.10%	1	6.30%	1	2.50%	0.277
	Sensitive	6	15.40%	0	0.00%	2	5.00%	
	Resistance	31	79.50%	15	93.80%	37	92.50%	
Augmentin	Not tested	1	2.60%	1	6.30%	1	2.50%	0.878
	Sensitive	3	7.90%	1	6.30%	1	2.50%	
	Intermediate	1	2.60%	0	0.00%	1	2.50%	
	Resistance	33	86.80%	14	87.50%	37	92.50%	

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Gentamicin	Not tested	0	0.00%	0	0.00%	1	2.50%	0.635
	Sensitive	5	12.80%	1	6.30%	2	5.00%	
	Resistance	34	87.20%	15	93.80%	37	92.50%	
Amoxicillin	Not tested	4	10.50%	1	6.30%	2	5.00%	0.809
	Sensitive	0	0.00%	0	0.00%	1	2.50%	
	Resistance	34	89.50%	15	93.80%	37	92.50%	

Data presented as number (N) and percentage (%), P-value by Chi Square Test.or Fissure's Exact Test $p \geq 0.05$ is considered non -significant $p < 0.01$ is considered significant.

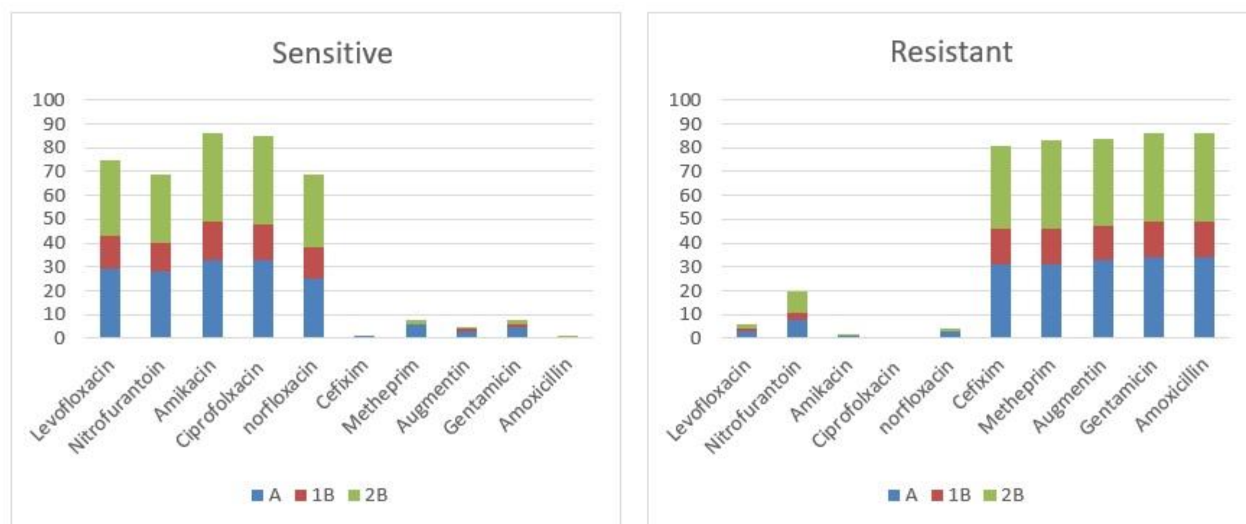

Figure (1): sensitivity and resistance of antibacterial across study groups

Antimicrobial Susceptibility and Resistance Patterns of Isolated Uropathogens

The distribution of antibiotic susceptibility and resistance among various bacterial species isolated from patients with rUTIs. The sensitivity profile (Figure 2) indicates that *E. coli*, *Enterobacter spp*., and *Pseudomonas spp*. demonstrated the highest response rates to fluoroquinolones—specifically levofloxacin, ciprofloxacin, and norfloxacin—as well as to amikacin, with the majority of these antibiotics attaining sensitivity counts in the upper range relative to other drug classes. Nitrofurantoin exhibited considerable sensitivity towards Gram-negative isolates but was much less efficient against *Staphylococcus spp*. and other rare species. On the other end of the spectrum are β-lactams (cefixime, Augmentin, amoxicillin) which show very low levels of susceptibility in nearly all the tested species. This suggests that they have (i) an inherent resistance or (ii) have developed multiple resistances as was the case for most of the other agents tested. The resistance pattern depicted in Figure 3 shows that the levels of resistance for both β-lactam drugs and trimethoprim-sulphamethaxazole remain consistent at very high levels of resistance (in *E.coli*, *Enterobacter* and *Staphylococci*). Very similar conclusions can be drawn regarding the levels of resistance to gentamicin for multiple bacterial species (including *Pseudomonas* and *Staphylococci*). In contrast to Gentamicin, Amikacin and fluoroquinolones overall demonstrate the lowest levels of resistance and exhibit higher levels of susceptibility compared to the other classes of antibiotics we have tested. As a

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result, Amikacin and fluoroquinolones should be considered as having a better therapeutic response against the major uropathogen compared to β-lactam drugs and inhibitors of the folic acid pathway due to the high degree of resistance shown by those classes.

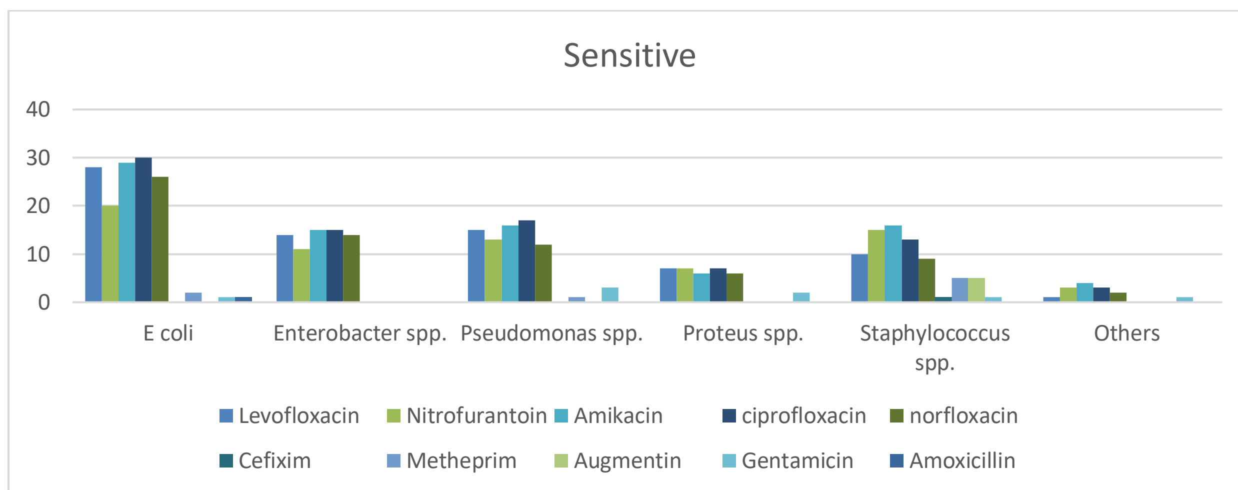

Figure (2) : Sensitivity of bacterial specious to tested antibacterial

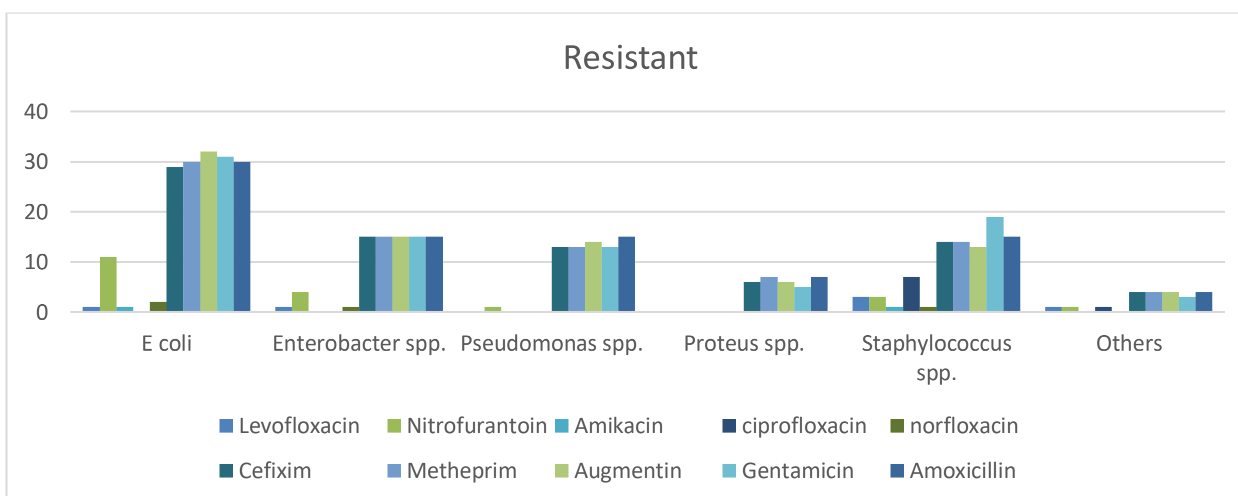

Figure (3): Bacteria associated with antibacterial resistance

Adherence to Medication

Figure (4) displays the replies from every participant regarding the Medication Adherence Report Scale (MARS-10). The outcome was a large section of participants did not follow the daily schedule for taking their antibiotic. More than three-fourths (87.9%) of the participants stated that if their symptoms improved, they would likely stop taking their medication. This suggests that many people are more concerned about symptom management than they are about following their treatment regimen. In addition, more than two-thirds of the responders (73.7%) reported a belief that it is "not natural for the body to be regulated by medicine," which demonstrates how negative beliefs about medication and psychological obstacles to pursuing longer-term pharmacotherapy are significant contributors

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to their lack of adherence. There was some behavioral non-adherence, but to a lesser extent. This encompassed forgetfulness (25.3%) and negligence (9.1%). No respondents indicated that physical side effects, such as fatigue or cognitive impairment, were the reason for noncompliance with the regulations (Q7–Q10, 0%). This indicates that attitudinal and cognitive obstacles, rather than physiological intolerance, are the primary reasons individuals do not adhere to the regulations.

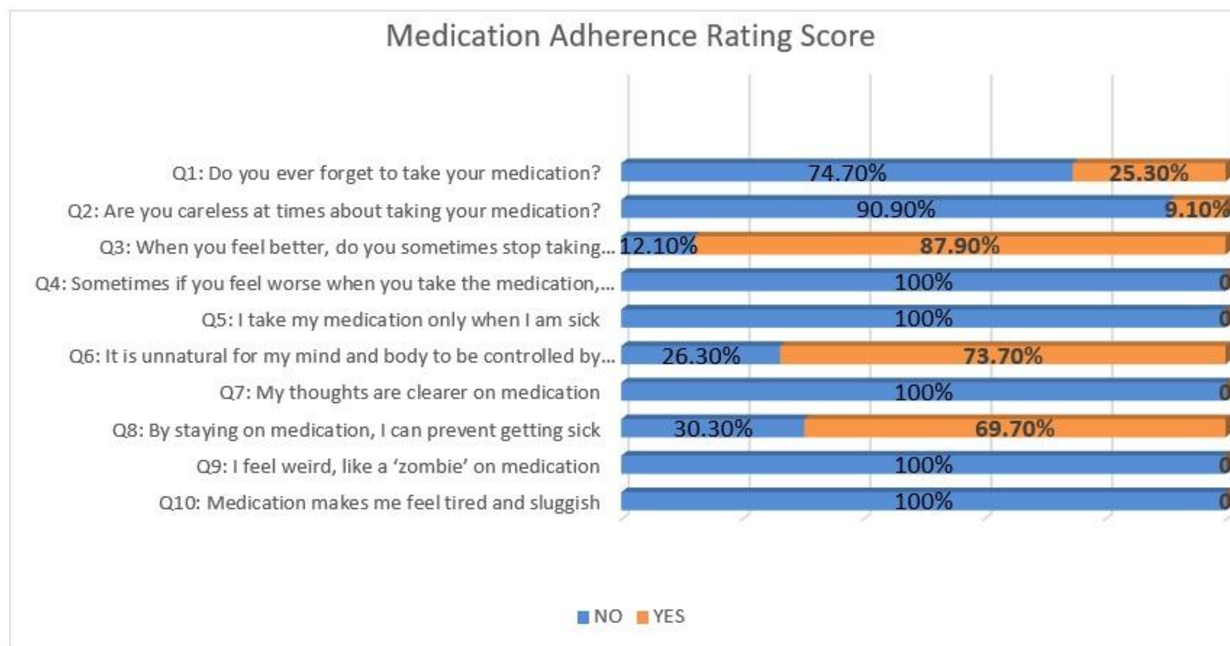

Figure (4): Responses of all patients to the MARS

The total MARS score demonstrated significantly lower medication adherence in Group 2B (5.5±0.88) compared to Group 2A (6 ± 0.59; adjusted post hoc p = 0.028) and Group 1 (5.9 ± 0.35; adjusted post hoc p = 0.041), as illustrated in Figure (5).

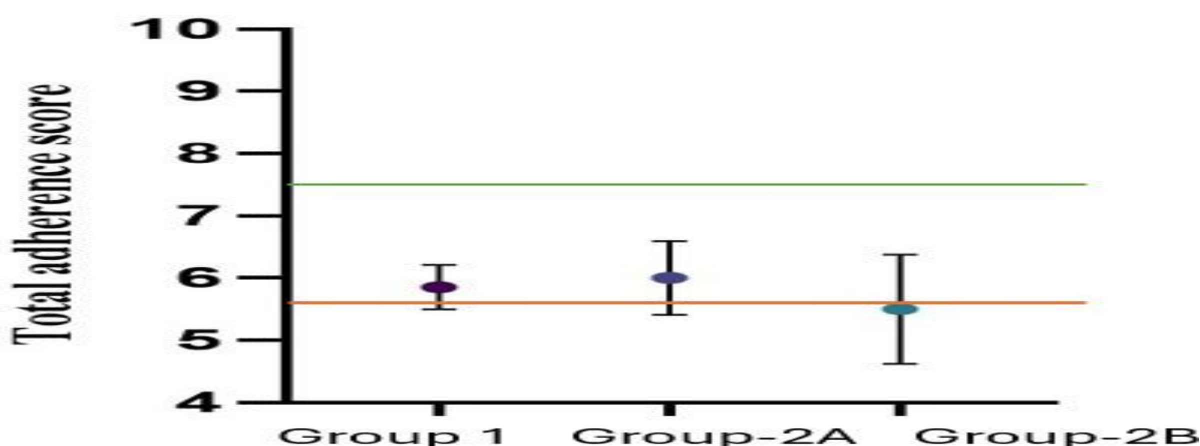

Figure (5): Total MARS score for study groups. Red line is the cutoff for the non-adherence and green line is the cutoff for adherence

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Discussion

This study evaluated the interplay between glycemic control, uropathogen distribution, antimicrobial susceptibility, treatment patterns, and medication adherence among patients with recurrent urinary tract infections (rUTIs), with particular emphasis on type 2 diabetes mellitus (T2DM).

Demographic Data and Disease Characteristics

Demographic characteristics such as sex, place of residence, and smoking history were similar between groups and therefore minimized confounding due to demographic factors. People with T2DM, regardless of the level of glycemic control (i.e., how well they were managing their blood sugar levels), were older than those without T2DM. These findings are consistent with past studies[16] ,indicating that older adults are at greater risk for developing both T2DM and recurrent urinary tract infections because of their weakened immune systems and comorbidity burden. The marked female predominance across all groups aligns with established anatomical and epidemiological data from both global and Iraqi studies[17].This finding supports a recent epidemiological study indicating that advancing age is a substantial risk factor for diabetes and recurrent urinary tract infections, likely attributable to age-related declines in immunological response, hormonal alterations, and increased comorbidity[16].

The global and regional epidemiology of rUTI in Iraq is well-established, as evidenced by the predominance of females across all categories (75–88%). For example, Hasan et al. (2025) reported higher percentages of rUTI infection among females [18]. longer diabetes duration, particularly among poorly controlled patients, was strongly associated with increased rUTI recurrence. Consistent with previous reports, elevated HbA1c was closely linked to bacteriuria, recurrent infections, and poorer treatment outcomes, underscoring HbA1c as both a metabolic and prognostic marker in rUTI management[19]. Additionally, the duration of the disease has been associated with an increase in the colonization of resistant and atypical microorganisms. A previous study has shown that the incidence of rUTI substantially increases after 5–10 years of diabetes as a result of changes in the structure and function of the urinary tract[20]. Furthermore, individuals with inadequate blood glucose control are more susceptible to UTIs and experience more severe and frequent episodes of UTIs than those with adequate blood glucose control. This is because poor glycemic control impairs cytokine response, deranges leukocyte function, and increases bacterial adherence in hyperglycemia[21].

Uropathogen and Antimicrobial Treatment Protocol

During the second clinic visit of patients, the results of the urine culture indicated that *E. coli* was the predominant uropathogen throughout the entire study, with a higher prevalence among T2DM patients in the currently conducted study. These results are consistent with a previous study that identified *E.coli* as the primary etiological agent of both uncomplicated and rUTIs in diabetic and non-diabetic patients[22]. The heightened occurrence of poorly controlled diabetes substantiates the notion that chronic hyperglycemia and glycosuria promote bacterial adherence and colonization, attributed to increased urinary glucose and compromised neutrophil activity. This conclusion corroborates with research suggesting that hyperglycemia facilitates the colonization of more resistant and recurrent infections[23,24].

Every patient in the current study received antibiotic medication based on their urine culture during visit 2. According to the findings, 83.3% and 87.5% of T2DM

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patients, respectively, utilized two drug combinations more frequently than those on a single or triple medication regimen. The therapeutic practice of employing broader antimicrobial coverage of treatment in diabetic patients, particularly in patients with poor glycemic control, was highlighted by the fact that single drug regimens were less common among diabetics.

This clinical practice pattern aligns with prior research indicating an elevated risk of recurring, challenging-to-treat[25]. Consequently, physicians often advocate for multidrug regimens. The results of another longitudinal retrospective study examining antimicrobial resistance in E. coli-induced community-acquired recurrent urinary tract infections were consistent with the current findings, highlighting that the risk of bacteriuria and recurrence was three to four times greater in women with diabetes compared to those without the condition. The utilization of dual therapy among a larger proportion of our diabetic categories is likely associated with both clinical judgment and the severity of the infection[26].

Regarding susceptibility patterns, Amikacin had the highest sensitivity rates across all research groups, achieving total susceptibility in Group 2A and above 90% in Group 2B. This observation aligns with global studies indicating that aminoglycosides retain efficacy owing to their limited use and parenteral delivery[27]. In line with the findings of the current investigation, Mohammad et al. determined that amikacin has strong action against 91% of bacteria, including *Pseudomonas*, Klebsiella, and all other species that cause UTI in Iraqi hospitals(28). The sensitivity of *E. coli* to amikacin was reported to be 90.6% in India, 93.7% in Saudi Arabia, 99.4% in South Korea, and 100% in Taiwan, according to the majority of investigations that produced results similar to the current findings[29]. Similarly, fluoroquinolones, especially ciprofloxacin and levofloxacin, showed relatively high sensitivity, indicating their continued efficacy against dominant uropathogens like *E. coli*, the most commonly isolated organism in the current study. This is consistent with other recent studies that have shown strong sensitivity to fluroquinolones[30].

Nitrofurantoin exhibited considerable sensitivity across all groups, with resistance levels remaining insignificantly low. Topa A et al. stated that nitrofurantoin is the optimal selection for uncomplicated UTI, including in those with diabetes, because to its limited systemic absorption and low propensity for resistance development[31].Conversely, gentamicin exhibited significant resistance across all groups, a result that conflicts with previous reports however corresponds with recent data indicating rising cross-resistance within the aminoglycoside class for example a study in China most *E. coli* isolates resistance to gentamicin (95.1%) was also reported[32] In contrast, significantly higher resistance rates were noted for frequently prescribed oral β-lactam antibiotics, such as cefixime, amoxicillin, amoxicillin–clavulanate, and methoprim. These findings reflect regional resistance patterns observed in Iraq and Saudi Arabia, where widespread empirical prescribing and over-the-counter availability to antibiotics have exacerbated resistance among uropathogen [33].

Assessment of Patients Adherence to Treatment

The therapeutic outcome, particularly rUTI, is significantly impacted by the patients' adherence to or non-adherence to all of their current medications, including both antimicrobial agents and conventional therapy. Current data indicate satisfactory adherence to the antimicrobial therapy advised based on the C/S test; thus, recurrent urinary tract infections may signify inadequate adherence to oral hypoglycemic

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medicines. Patient adherence to prescriptions was evaluated during visit 3, following the completion of the antimicrobial course, utilizing the MARS scoring survey, with a threshold value of less than 8 employed to interpret results related to chronic disease, as referenced in the literature.

In the current investigation, poorly managed diabetes patients showed consistently worse adherence across several categories (scores below 6 on the MARS scale), supporting the known link between poor medication-taking behavior and inadequate glycemic control. Poor glycemic control was significantly associated with "medication forgetfulness and carelessness" when compared to both non-diabetics and well-controlled diabetics. This aligns with recent studies suggesting that T2DM is associated with an increased risk of cognitive dysfunction[34]. Furthermore, the majority of patients concurred with the premature cessation of medication upon symptom amelioration. The premature discontinuation of antimicrobial medication is a recognized contributor to rUTIs, chronic bacteriuria, and antibiotic resistance[34]. When assessing the beliefs about their medication whether totally control their disease “unnatural for my mind” were significantly noticed in poorly controlled diabetics compared with other groups. This is of particular significance due to the fact that medication-related beliefs are well-established predictors of adherence across chronic diseases. Patients with poorly controlled diabetes may believe that their diabetes medications are causing them to be "over-medicated" due to the fact that they are continuing to receive repeat prescriptions for antibiotics for rUTIs, as well as taking multiple medications to regulate their blood sugar and using insulin therapy. This cumulative therapy may result in the belief that medication is the sole necessary component for "body control," which in turn contributes to inadequate adherence to prescribed medications.

Ultimately, these findings indicate that there are various factors contributing to non-adherence to prescribed drugs. The principal elements contributing to this include health attitudes, symptom-driven behaviors, and cognitive influences, rather than pharmaceutical intolerances.

Patients with rUTI and those in the control diabetes group had a moderate level of adherence to their pharmaceutical regimen for managing recurrent UTI episodes. Suboptimal management of T2DM is now evidenced by 55% being categorized as non-adherent according to the MARS. It has been noted that treatment regimens may be influenced by polypharmacy, extended treatment duration, or a perceived improvement in symptoms, leading to premature discontinuation of therapy[35]. Furthermore, inadequate adherence among diabetics correlated with an increased risk of infection recurrence and less severe urinary tract infections, reinforcing the notion that bacteria may persist in the body and reemerge if an antibiotic regimen is not fully finished[36]. Inadequate metabolic management negatively impacts medication adherence by reducing motivation, impairing cognitive function, and increasing treatment weariness. Patients with raised HbA1c levels showed a markedly higher probability of missing antibiotic doses or prematurely terminating treatment[37]. Additional treatment-related concerns pertained to the incorporation of antimicrobial combinations into existing therapies, parenteral administration, or multi-drug regimens like Amikacin, which restrict patient adherence. Almomani et al. (2023) found that poor adherence is prevalent in difficult or extended antibiotic regimens, especially among patients with numerous chronic conditions such as hypertension and diabetes[38].

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Inconsistent or lack of adherence to treatment plans (medications) can result in bacterial infections that do not resolve completely, recurrent infections, and multiple rounds of antibiotics prescribed for the same person, ultimately creating a feedback loop that promotes antimicrobial resistance (AMR) within these specific populations. Studies conducted on Middle Eastern populations demonstrate a high prevalence of individuals with uncontrolled diabetes, low adherence to prescribed medications, and significant hospitalizations due to infection-related complications[39,40].

Conclusion

E. coli was predominant, especially in inadequately managed diabetes highlighting the influence of hyperglycemia on recurrence. Dual antimicrobial regimens were frequently employed, with amikacin, fluoroquinolones, and nitrofurantoin demonstrating great susceptibility, whereas β-lactams and gentamicin displayed significant resistance. Inadequate glycemic control and insufficient adherence, primarily influenced by adverse drug perceptions, were significant predictors of treatment failure and recurrence.

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Conflict of Interest

The authors have declared that no competing interests exist.

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Author contributions

Both authors contributed equally

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