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Evaluation of serum interleukin-6 level in diabetic patients with urinary tract infections

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Abstract

Urinary tract infections (UTIs) are common in type 2 diabetic patients, who have higher risks of mortality and bacteremia. Interleukin-6 (IL-6) plays a dual role: protective at normal levels, but proinflammatory in chronic inflammation. This study aimed to identify the main UTI-causing bacteria in diabetic and non-diabetic individuals, evaluate antibiotic resistance, and assess serum IL-6 levels in both groups. This was a comparative cross-sectional study included 140 patients aged 18–70 years, of both sexes, with and without type 2 diabetes. Patients were divided into four groups, each of 35 patients. Group A (controlled diabetic UTI cases, HbA1c ≤ 7%), Group B (uncontrolled diabetic UTI cases, HbA1c > 7%), Group C (non-diabetic UTI cases, HbA1c < 5.7%), and a normal control group. Urine samples were analyzed by culture, bacterial count, organism identification, and antibiotic sensitivity. Serum IL-6 was measured using an enzyme-linked immunosorbent assay (ELISA. Group B had the highest mean serum IL-6 level (29.60 ± 10.23), followed by Group A (26.42 ± 9.56), while the control group showed the lowest (15.50 ± 5.42). *Candida albicans* was more frequent in Group B (14.29%). Gram-negative bacilli predominated in all groups, especially Group A (91.43%). *Escherichia coli* was the most common bacterial isolate (~50%). Group B had the highest bacterial count (57.89 ± 23.72). Group C showed the highest antibiotic sensitivity, notably to meropenem (91.4%), polymyxin B (82.9%), and amikacin (80.0%). Group B exhibited the highest resistance rates to cefotaxime (79.5%), norfloxacin (61.5%), azithromycin (59%), and cotrimoxazole (56%). In conclusion, diabetic patients, especially those with uncontrolled diabetes, showed higher bacterial loads, more mixed and fungal infections, increased antibiotic resistance, and elevated serum IL-6 levels compared to non-diabetic individuals.

Keywords: Diabetes Mellitus, Urinary Tract Infections, Interleukin-6..

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Introduction

Elevated blood glucose levels cause a variety of symptoms in people with diabetes mellitus (DM), a condition that can progress to both short-term and long-term consequences.[1] In accordance with the most recent International Diabetes Federation (IDF) Diabetes Atlas (2025), 11.1 % or one in nine of the adult population (20-79 years) is currently afflicted with diabetes, with more than four in ten individuals being oblivious of their condition.[2]

Individuals with type-2 diabetes are at increased risk for urinary tract infections (UTIs), which can lead to bacteremia and higher mortality rates.[3] Individuals with type-2 diabetes had an overall prevalence of 11.5 % for UTIs.[4]

Escherichia coli is the most common bacteria in UTIs, followed by *Pseudomonas, Klebsiella* and *Staphylococcus. Citrobacter* is only found in non-diabetic patients, but *Enterococcus* is only found in diabetic patients.[5]

Interleukin-6 (IL-6) is a pleiotropic cytokine that is essential for the regulation of immune and inflammatory responses. It has been the subject of extensive research regarding its role in the development and progression of a variety of diseases, such as UTIs.[6]

Reactive oxygen species (ROS) are produced in DM when glucose is oxidized. The buildup of ROS is the key component of oxidative stress. Inflammation caused by persistent oxidative stress raises cytokine production, which in turn can cause insulin resistance by disrupting insulin signaling and leading to a buildup of inflammatory cells. The insulin's effectiveness will be diminished.[7] The objective of this work was to detect the most common bacteria causing UTI among diabetic and non-diabetic patients, determine the presence of resistant strains and to evaluate the role of serum IL-6 among diabetic and non-diabetic cases.

Patients and Methods

This comparative cross-sectional trail was conducted at the Microbiology and Clinical Pathology laboratories of the Damietta Faculty of Medicine, Al-Azhar University during the period from May 2024 to January 2025. The study included 140 diabetic cases with age ranged from 18 to 70 years old, both sexes, patients suffering from UTI with and without type-2 DM.

Exclusion criteria included chronic diseases as renal failure, liver failure, renal transplantation and immunological diseases, type 1 DM and catheterized patients.

Cases were further separated into four groups based on their clinical and demographic characteristics. Group A: included 35 controlled diabetic cases with UTI (HbA1C ≤ 7%). Group B: included 35 uncontrolled diabetic cases with UTI (HbA1C >7 %). Group C: included 35 non-diabetic cases with UTI (HbA1C < 5.7%). The control group included 35 normal cases.

Laboratory Investigations

The study sample size was calculated using G power software version 3.1.39. Each study subject completed a self-administered structured questionnaire to collect clinical and demographic data.

Urine and blood samples were collected from each patient under complete aseptic condition. For isolation and identification of causative organism: the procedure typically involved collecting a midstream urine sample from each patient in a sterile container. Once collected, the sample was taken to the laboratory where it was subjected to: Direct film, routine urine analysis (If pus cell >10 HPF, bacterial culture and viable count were done).[11]

Bacterial culture: the urine sample was divided in two parts. The first part of the sample was cultured using a sterile calibrated loop (0.1µl) for isolation of the organism.

For Gram -VE: Cysteine-Lactose-Electrolyte-Deficient (CLED) agar and MacConkey agar were used. For Gram +VE: Blood agar and CLED agar were used. For Candida: Sabouraud Dextrose Agar (SDA) was used.

Another part was prepared for colony count by a serial dilution method. The plates were subsequently incubated for 24 to 48 hours at 37°C to facilitate growth. After incubation the

organism was identified by: Gram staining, colony morphology and biochemical reactions.[11]

For Gram -VE: Sugar fermentation (glucose-lactose-maltose-mannite-sucrose), methyl red test, indole test, triple sugar iron (TSI) and citrate utilization test was performed. For Gram +VE: Catalase test and coagulase test were performed. For Candida: Chromogenic agar medium was used.

Antibiotic sensitivity test: It was done by the disc diffusion method, followed by detection of resistant strains12. For bacteria we used 16 antibiotic discs and for Candida we used 3 anti-fungal discs.

Preparation of organism suspension: A culture plate was used to isolate a single, uncontaminated colony of the organism. In order to guarantee a standardized concentration of bacteria, the colony was suspended in sterile saline to obtain a turbidity equivalent to a 0.5 McFarland standard.

Inoculation of agar plates: The medium for testing was Mueller-Hinton agar plates. The standardized organism suspension was evenly applied to the agar surface using a sterile sponge to establish a lawn of growth and allow it to dry.

Placement of antibiotic discs: Antibiotic-impregnated paper discs were placed on the surface of the inoculated agar, ensuring they were spaced adequately apart (at least 24 mm) to avoid overlapping zones of inhibition. Each disc was pressed gently to ensure it makes contact with the agar surface. The plates were incubated at 37 °C for 24 hours, allowing the antibiotics to diffuse into the agar and inhibit bacterial growth.

Measurement of inhibition zones: The diameter of the clear zones surrounding each disc, referred to as zones of inhibition, was determined following incubation. The bacteria's susceptibility or resistance to the specific antibiotics tested is represented by the size of these zones. The Clinical and Laboratory Standards Institute (CLSI) guidelines were employed to interpret the results.[10]

Bacterial viable count: After incubation, the colony-forming unit (CFU)/ml was calculated using the following formula[11]:

CFU/ML = (no. of colonies x dilution factor) / volume of culture plate

The results were interpreted based on the number of colonies present; a count of less than 100,000 colonies per ml indicates non-significant bacteriuria, while higher counts suggest significant bacteriuria.[13]

Blood samples; were collected and subjected to estimation of serum IL-6 by an enzyme-linked immunosorbent assay (ELISA) and estimation of HbA1C.

Human Interleukin 6 (IL-6) was determined by commercial ELISA Kits (Catalog No: DLR-IL6-Hu 96 Tests, Bio Kit Co, China), 14 according to the manufacture guidelines. The final product was measured using a micro plate reader at 450 nm.

Estimation of Hb A1C: Venous blood was typically collected using a sterile 21-gauge needle and K2-EDTA tubes as anticoagulants. Collected blood sample was gently inverted to mix with the anticoagulant and processed within 24 hours to maintain stability. Measurement of glycated hemoglobin (HbA1c) was performed on an automated chemistry analyzer (Cobas c 311 automated chemistry analyzer; Roche Diagnostics, Germany) using the Tina-quant Hemoglobin A1c Gen. 3 assay (Cat. No. 05336163 190, Roche Diagnostics). This method is based on turbid-metric inhibition immunoassay for whole blood with hemolysis and is standardized according to the International Federation of Clinical Chemistry (IFCC) and the National Government Services Portal (NGSP) reference methods.

Statistical Analysis

Data were analyzed utilizing the Statistical Package for the Social Sciences (SPSS) v18. Data are shown quantitatively using means and standard deviations (SD). The Frequency and percentage (%) were used to display the qualitative factors. To ensure that your data are normally distributed we utilized the Shapiro-Wilk test. When testing parametric variables

across more than two groups, the one-way ANOVA test was utilized. For non-parametric variables, the Kruskal-Wallis Test was employed across many groups. Two category variables were compared utilizing the Chi-square test. The significance level was defined at a *p* value of <0.05.

Results

As regarding to demographic data, there were no statistically significant variations in the distribution of age or sex among the research groups (Table 1). As regarding to symptoms in the cases groups, significant variances were observed in symptoms like "bad smell and cloudy urine" and across the groups (Table 2). Regarding the stain results, a significant difference was observed for *Candida*, with group B showing the highest prevalence (14.29%) in contrast to minimal presence in group A (2.86%) and none in group C. No significant distinctions were found for gram-positive cocci bacteria (*p*=0.251) or gram-negative bacilli (*p*=0.329). Gram-negative bacilli were the most prevalent stain in all groups with group A showing the highest rate (91.43%), followed by group C (88.57%) and group B (80.00%) (Table 3).

Table 1. Demographic data of the study groups.

Parameter		Group A (n=35)	Group B (n=35)	Group C (n=35)	Control (n=35)	*p* value
Age (years)	Mean ± SD	47.86 ± 12.96	42.89 ± 12.14	44.46 ± 11.66	47.94 ± 12.34	^{F}NS
	Median (Min-Max)	51.00 (22.00-65.00)	40.00 (26.00-66.00)	45.00 (22.00-67.00)	48.00 (27.00-67.00)	
Sex	Female (F)	25 (71.4%)	26 (74.3%)	25 (71.4%)	22 (62.9%)	$^{X^2}$NS
	Male (M)	10 (28.6%)	9 (25.7%)	10 (28.6%)	13 (37.1%)	

F: One-way ANOVA, X^2: Chi-square test,. $p > 0.05$ is not significant (NS).

Table 2. Clinical symptoms and signs in cases groups.

Symptom	Group A (n=35)	Group B (n=35)	Group C (n=35)	$^{X^2}$*p* value
Frequent urination	35 (100.0%)	35 (100.0%)	35 (100.0%)	NS
Urge	35 (100.0%)	35 (100.0%)	35 (100.0%)	NS
Incontinence	35 (100.0%)	35 (100.0%)	35 (100.0%)	NS
Pelvic pain	34 (97.1%)	35 (100.0%)	35 (100.0%)	NS
Bad smell and cloudy urine	13 (37.1%)	12 (34.3%)	2 (5.7%)	0.004
Burning sensation	34 (97.1%)	32 (91.4%)	32 (91.4%)	NS
Fever	28 (80.0%)	26 (74.3%)	25 (71.4%)	NS
Nocturia	4(11.4%)	5 (14.3%)	4 (11.4%)	NS
Bloody urine	2(5.7%)	1 (2.9%)	6(17.1%)	NS
Renal stone	3(8.6%)	5 (14.3%)	8(22.9%)	NS

X^2: Chi-square test $p > 0.05$ is not significant (NS).

Table 3. Gram stain results in the cases groups.

Stain	Group A (n=35)	Group B (n=35)	Group C (n=35)	*p* value
Number of isolates	40	44	35	-
Mixed infection	5	9	0	-
Gram-positive cocci	7 (20%)	11 (31.43%)	4 (11.43%)	NS
Candida	1 (2.86%)	5 (14.29%)	0 (0%)	0.040
Gram-negative bacilli	32 (91.43%)	28 (80.00%)	31 (88.57%)	NS

X^2: Chi-square test. $p > 0.05$ is not significant (NS).

Regarding bacterial count in the study groups, a significant variation was observed among the groups (p=0.037). Group B had the highest mean bacterial count (57.89 ± 23.72), followed by group A (52.83 ± 25.07), while group C showed the lowest mean count (45.71 ± 24.83) (Table 4).

Table 4. Bacterial count in the cases Groups.

		Group A (n=35)	Group B (n=35)	Group C (n=35)	p value
Bacterial number of isolates		39	39	35	-
Bacterial count	Mean ± SD	52.83 ± 25.07	57.89 ± 23.72	45.71 ± 24.83	^{H}p=0.037
	Median (Min-Max)	44.00 (13.00-104.00)	55.00 (10.00-104.00)	36.00 (10.00-104.00)	

H: Kruskal Wallis test, $p \leq 0.05$ is significant.

Regarding the culture results in the study groups, significant differences were observed for *Staphylococcus aureus* (p=0.007) and *Candida albicans* (p=0.009). *Staphylococcus aureus* was the most prevalent in group B (22.9%), with lower detection in group A (8.6%) and minimal presence in group C (5.7%). Similarly, *Candida albicans* was detected exclusively in group B (14.3%) and in only one in group A (2.9%), with no cases in group C. Group B also showed the highest number of mixed infections (n = 9), compared to group A (n = 5) and none in group C. *E. coli* was the most common isolate across all groups about 50 %. For other organisms such as *Klebsiella pneumoniae*, Coagulase-negative *Staphylococcus*, and *Citrobacter*, no significant distinctions were found among the groups (p>0.05), though agar medium (Table 5). Regarding antibiotic sensitivity, highly sensitive results were observed. Significant differences were observed for meropenem (p=0.01), amoxicillin-clavulanic acid (p<0.001, polymyxin B (p=0.02), cotrimoxazole (p<0.001), cephalexin (p < 0.001), ampicillin-sulbactam (p = 0.01), and amikacin (p=0.04). In contrast, no significant variances were noted for cefoperazone/sulbactam, amikacin, and doxycycline (p>0.05), which showed consistently high sensitivity across all groups (Table 6).

Table 5. Culture results in the cases groups.

Culture Result	Group A (n=35)	Group B (n=35)	Group C (n=35)	X^2 p value
Number of isolates	40	44	35	-
Mixed infection	5	9	0	-
E. Coli	18 (51.4%)	17 (48.6%)	18 (51.42%)	NS
Klebsiella pneumoniae	9 (25.7%)	7 (20.0%)	13 (37.1%)	NS
Staphylococcus aureus	3 (8.6%)	8 (22.9%)	2 (5.7%)	0.007
Coagulase -VE *Staphylococcus*	4 (11.4%)	3 (8.6%)	2 (5.7%)	NS
Citrobacter	5 (14.3%)	4 (11.4%)	0 (0.0%)	NS
Candida albicans	1 (2.9%)	5 (14.3%)	0 (0.0%)	0.009

X^2: Chi-square test. p > 0.05 is not significant (NS).

Table 6. Antibiotic sensitivity (highly sensitive) results in study groups.

Parameter	Group A (n=35)	Group B (n=35)	Group C (n=35)	X^2 *p*-value
Number of isolates	39	39	35	-
MEM (Meropenem)	30 (76.92%)	23 (58.97%)	32 (91.4%)	0.01
AMC (Amoxicillin-Clavulanic Acid)	22 (56.41%)	8 (20.51%)	17 (48.6%)	< 0.001
NOR (Norfloxacin)	13 (33.33%)	6 (15.38%)	13 (37.1%)	NS
AZM (Azithromycin)	11 (28.21%)	7 (17.95%)	15 (42.9%)	NS
PB (Polymyxin B)	31 (79.49%)	22 (56.41%)	29 (82.9%)	0.02
COT (Cotrimoxazole)	19 (48.72%)	8 (20.51%)	20 (57.1%)	< 0.001
AK (Amikacin)	29 (74.36%)	21 (53.85%)	28 (80.0%)	0.04
CAZ (Ceftazidime)	4 (10.26%)	3 (7.69%)	2 (5.7%)	NS
CN (Cephalexin)	21 (53.85%)	6 (15.38%)	15 (42.9%)	< 0.001
CES (Cefoperazone/Sulbactam)	18 (46.15%)	13 (33.33%)	15 (42.9%)	NS
CTX (Cefotaxime)	6 (15.38%)	4 (10.26%)	5 (14.3%)	NS
CEP (Cefoperazone)	20 (51.28%)	12 (30.77%)	17 (48.6%)	NS
A/S (Ampicillin-Sulbactam)	22 (56.41%)	9 (23.08%)	18 (51.4%)	0.01
DO (Doxycycline)	27 (69.23%)	20 (51.28%)	23 (65.7%)	NS
CIP (Ciprofloxacin)	6 (15.38%)	3 (7.69%)	5 (14.3%)	NS
OX (Oxacillin)	2 (5.13%)	7 (17.95%)	2 (5.7%)	NS

X^2: Chi-square test. $p > 0.05$ is not significant (NS).

Regarding moderate sensitivity results, significant differences were detected for meropenem (p=0.03) and norfloxacin (p=0.04). For other antibiotics, including amoxicillin-clavulanic acid, azithromycin, amikacin, and cefoperazone/sulbactam, no significant differences was observed among the study groups ($p > 0.05$) (Table 7). Regarding the antibiotics resistant results, significant differences were observed for several antibiotics, including, amoxicillin-clavulanic acid ($p < 0.001$), norfloxacin ($p < 0.001$), cephalexin ($p < 0.001$), meropenem ($p = 0.01$), amikacin ($p = 0.02$), cefoperazone/sulbactam ($p = 0.01$), and cefoperazone ($p = 0.03$). Group A generally showed lower resistance rates compared to the other groups; however, it demonstrated the highest resistance to oxacillin at 86%, with no notable resistance observed against meropenem. Group B exhibited the highest overall resistance, particularly to cefotaxime (79.5%), norfloxacin (61.5%), azithromycin (59%), cotrimoxazole (56%), and amoxicillin-clavulanic acid (51%). Group C displayed intermediate resistance levels, with the highest resistance observed against ceftazidime at 85.7% (Table 8).

Table 7. Moderate sensitivity for antibiotics in the cases groups.

Parameter	Group A (n=35)	Group B (n=35)	Group C (n=35)	X^2 *p*-value
Number of isolates	39	39	35	-
MS MEM (Meropenem)	9 (23.08%)	9 (23.08%)	1 (2.9%)	0.03
MS AMC (Amoxicillin-Clavulanic Acid)	11 (28.21%)	11 (28.21%)	7 (20.0%)	NS
MS NOR (Norfloxacin)	6 (15.38%)	9 (23.08%)	1 (2.86%)	0.04
MS AZM (Azithromycin)	7 (17.95%)	9 (23.08%)	6 (17.1%)	NS
MS PB (Polymyxin B)	2 (5.13%)	5 (12.82%)	0 (0.00%)	NS
MS COT (Cotrimoxazole)	3 (7.69%)	10 (25.64%)	5 (14.3%)	NS
MS AK (Amikacin)	5 (12.82%)	4 (10.26%)	2 (5.7%)	NS

Table 7. Continued.

Parameter	Group A (n=35)	Group B (n=35)	Group C (n=35)	X^2 *p*-value
MS CAZ (Ceftazidime)	3 (7.69%)	4 (10.26%)	3 (8.6%)	NS
MS CN (Cephalexin)	6 (15.38%)	6 (15.38%)	7 (20.0%)	NS
MS CES (Cefoperazone/Sulbactam)	15 (38.46%)	11 (28.21%)	16 (45.7%)	NS
MS CTX (Cefotaxime)	5 (12.82%)	5 (12.82%)	3 (8.6%)	NS
MS CEP (Cefoperazone)	14 (35.90%)	14 (35.90%)	14 (40.0%)	NS
MS A/S (Ampicillin-Sulbactam)	9 (23.08%)	15 (38.46%)	11 (31.4%)	NS
MS DO (Doxycycline)	6 (15.38%)	10 (25.64%)	6 (17.1%)	NS
MS CIP (Ciprofloxacin)	6 (15.38%)	7 (17.95%)	5 (14.3%)	NS
MS OX (Oxacillin)	3 (7.69%)	4 (10.26%)	3 (8.57%)	NS

X^2: Chi-square test. $p > 0.05$ is not significant (NS).

Table 8. Antibiotics resistant results in the study groups

Parameter	Group A (n=35)	Group B (n=35)	Group C (n=35)	X^2 *p*-value
Number of isolates	39	39	35	-
R MEM (Meropenem)	0 (0.0%)	7 (17.95%)	2 (5.7%)	0.01
R AMC (Amoxicillin-Clavulanic Acid)	6 (15.38%)	20 (51.28%)	11 (31.4%)	< 0.001
R NOR (Norfloxacin)	10 (25.64%)	24 (61.54%)	21 (60.0%)	< 0.001
R AZM (Azithromycin)	21 (53.85%)	23 (58.97%)	14 (40.0%)	NS
R PB (Polymyxin B)	6 (15.38%)	12 (30.77%)	6 (17.1%)	NS
R COT (Cotrimoxazole)	17 (43.59%)	22 (56.41%)	10 (28.6%)	0.05
R AK (Amikacin)	5 (12.82%)	14 (35.90%)	5 (14.3%)	0.02
R CAZ (Ceftazidime)	31 (79.49%)	32 (82.05%)	30 (85.7%)	NS
R CN (Cephalexin)	12 (30.77%)	27 (69.23%)	13 (37.1%)	<0.001
R CES (Cefoperazone/Sulbactam)	6 (15.38%)	15 (38.46%)	4 (11.4%)	0.01
R CTX (Cefotaxime)	28 (71.79%)	31 (79.49%)	27 (77.1%)	NS
R CEP (Cefoperazone)	5 (12.82%)	13 (33.33%)	4 (11.4%)	0.03
R A/S (Ampicillin-Sulbactam)	8 (20.51%)	15 (38.46%)	6 (17.1%)	NS
R DO (Doxycycline)	6 (15.38%)	9 (23.08%)	6 (17.1%)	NS
R CIP (Ciprofloxacin)	27 (69.23%)	28 (71.79%)	25 (71.4%)	NS
R OX (Oxacillin)	34 (87.18%)	28 (71.79%)	30 (85.7%)	NS

X^2: Chi-square test $p > 0.05$ is not significant (NS).

Regarding antifungal sensitivity results, all six isolates (100%) were resistant to itraconazole. However, fluconazole showed full sensitivity (6/6 isolates). For nystatin sensitivity, it showed complete sensitivity in group A (1/1 isolate) and partial sensitivity in group B (5 out of 6 isolates; 83.3%) (Table 9).

Table 9. Antifungal sensitivity results in the diabetic groups.

		Group A (n=35)	Group B (n=35)
	Number of isolates	1	5
Sensitive	FLC (Fluconazole)	1 (100.0%)	4 (80.0%)
	NS (Nystatin)	1 (100.0%)	2 (40.0%)
	IT (Itraconazole)	0 (0.0%)	0 (0.0%)
Moderate sensitivity	MS FLC (Fluconazole)	0 (0.00%)	1 (20.0%)
	MS NS (Nystatin)	0 (0.00%)	2 (40.0%)
	MS IT (Itraconazole)	0 (0.00%)	0 (0.00%)
Resistant	R FLC (Fluconazole)	0 (0.0%)	0 (0.0%)
	R NS (Nystatin)	0 (0.0%)	1 (20.0%)
	R IT (Itraconazole)	1 (100.0%)	5 (100.0%)

Regarding serum IL-6 levels, a significant distinction was observed (p<0.001). Group B exhibited the highest mean IL-6 level (29.60 ± 10.23), followed by group A (26.42 ± 9.56), while the control group demonstrated the lowest mean level (15.50 ± 5.42). These findings indicated elevated serum IL-6 levels in groups A and B compared to the control and group C (Table 10).

Table 10. Serum interleukin-6 (IL-6) levels in study groups.

Parameter		Group A (n=35)	Group B (n=35)	Group C (n=35)	Control (n=35)	p value
IL-6 Level	Mean ± SD	26.42 ± 9.56	29.60 ± 10.23	18.00 ± 7.48	15.50 ± 5.42	^{H}p<0.001*
	Median	26.42	29.60	18.00	15.50	
	(Min-Max)	(10.5–50.0)	(13.0–60.0)	(10.5–45.0)	(10.0–20.0)	

H: Kruskal wallis test, *$p \leq 0.05$ is significant.

Discussion

In the present study there was no significant differences in age or sex distribution among study groups, aligning with findings from Almutawif & Eid, 2023, who reported similar demographic characteristics in their study on bacterial uropathogens.[15] The sex distribution in the current study showed a higher prevalence of females across all groups. This is in line with the observations of Naqid et al., 2020, who found that females are more prone to UTIs because of anatomical and physiological factors.[16] Regarding symptoms in the case groups, the present study revealed significant differences in "bad smell and cloudy urine" with group A and B exhibiting the highest prevalence.

These results correspond with the work of Tegegne et al., 2023, who also identified such symptoms as indicative markers in UTIs among diabetic patients.[17] In contrast Rodríguez et al., 2008, reported that symptom presentation was more variable, possibly due to differences in study populations and inclusion criteria.[18]

In the stain results, a significant presence of gram-positive *Candida albicans* was observed, particularly in group B, which is consistent with a previous research by Gharanfoli et al., 2019.[19] However, the high prevalence of gram-negative bacilli in all groups aligns with findings from the study by Noori et al., 2023, who highlighted the dominance of these organisms in UTIs.[20] And with Majumder et al., 2022, who reported that *E coli* and *Klebsiella* species were the most frequently isolated bacteria overall, in gram-negative organisms in UTI.[21]

Mainly *Staphylococcus aureus*, Gram-positive bacteria were observed in larger proportions in individuals with diabetes, this finding corresponds with previous observations by Ali and Jaafar, 2022, who reported that *Staphylococcus aureus* is more common in

diabetic individuals because the disease is more easily transmitted and the immune systems of persons with diabetes are already compromised.[22]

The current study also indicated significant differences in bacterial count among the groups, with group B having the highest mean bacterial count. This finding corresponds with previous observations by Nagendra et al., 2022, who linked higher bacterial loads with more severe infections.[23] Similarly, the culture results demonstrated notable variations, *Candida albicans* showed significant differences across the groups. These results align with the research of Mishra et al., 2022 and Al-Aameri et al., 2024, who reported higher *Candida albicans* prevalence in diabetic patients with UTIs.[24,25] However, our study disagreed with that of Salehi et al., 2016, who reported a more uniform distribution of *Candida* species across the patient groups, potentially due to differences in antifungal exposure.[26]

Regarding antibiotic sensitivity, our study found significant differences for meropenem, amoxicillin-clavulanic acid, cotrimoxazole, cephalexin, ampicillin-sulbactam, and polymyxin B., where group A and group C exhibited higher sensitivity to these antibiotics than group B. The most sensitive antibiotics across all groups were meropenem, polymyxin B, amikacin and doxycycline. In an investigation of antibiotic sensitivity in UTI cases, Alhamadani and Oudah, 2022, found that *E. coli* was the most common bacterium with extremely high sensitivity to amikacin and meropenem, and our results support their findings.[27] Group B demonstrated significantly lower sensitivity, these findings are consistent with those of Lee et al., 2024, who also observed declining sensitivity patterns among bacterial isolates in UTI patients.[28] However, discrepancies exist with Zúniga-Moya et al., 2016, who reported lower resistance rates for cotrimoxazole in a Costa Rican cohort, likely due to regional differences in prescribing practices.[29]

Regarding antibiotic resistance, our study found significant differences for amoxicillin-clavulanic acid, norfloxacin, cephalexin, cefoperazone/sulbactam and cefoperazone. The controlled diabetic group A, generally showed lower resistance rates with no notable resistance to meropenem, while the non-diabetic group C exhibited intermediate resistance levels. The most resistant antibiotics across all groups were oxacillin, ceftazidime, ciprofloxacin and cefotaxime. Our findings corroborate the work of Alotaibi et al., 2023, who reported that the majority of gram-negative bacteria that cause UTIs are resistant to many drugs.[30]

However, our findings contrasted with the results of Alhamadani & Oudah, 2022, who reported that cefotaxime was highly sensitive in UTI[27] and with AL-Khikani et al., 2023 who found that ciprofloxacin had higher rate of sensitivity (75%) against *E. coli*, possibly because of variances in study design and patient populations.[31] Antifungal sensitivity results revealed no significant differences, though *Candida albicans* was more sensitive to fluconazole in group B. These results are in agreement with those of Tannupriya et al., 2022, who found similar antifungal susceptibility trends.[32] However, antifungal resistance to itraconazole was significantly higher in group B, paralleling findings by Obul Reddy, 2020, who linked fungal resistance with metabolic disturbances in diabetic patients.[33] These findings contrast with those of Ramos et al., 2015, who reported lower resistance rates, possibly due to differences in antifungal treatment protocols.[34]

Regarding serum IL-6 levels, the present study demonstrated significantly elevated serum IL-6 levels in groups A and B contrasted with the control group, reinforcing the findings of Ali & Jaafar, 2022 and Mahyar et al., 2013, who linked serum IL-6 elevations with UTIs.[22,35]

Furthermore, our results align with those of Obeagu et al., 2022, who emphasized the role of IL-6 as an inflammatory marker. And with Ali & Jaafar, 2022, who reported that individuals without diabetes who had a urinary tract infection had a higher level of IL-6 than the control group.[22]

However, our findings differed from those of Sheu et al., 2006, who reported more elevation of serum IL-6 in pediatric populations, highlighting potential age-related variations.[37]

Our study highlighted critical insights into bacterial and antifungal resistance, as the role of serum IL-6 in UTIs with DM. These findings align with a broad range of previous research studies, underscoring the need for continuous surveillance and antibiotic stewardship to mitigate resistance trend. In conclusion, based on our study findings, we recommend regular monitoring of serum IL-6 levels in diabetic patients with UTIs to improve early detection and diagnosis.

Author Contributions

ESAS; Contributed to the study design, patient selection, data collection, laboratory procedures, statistical analysis, and drafting of the manuscript. MMA; Supervised the overall research process and critically revised the manuscript for intellectual content. EMH; Participated in the interpretation of immunological data and contributed to the final revision of the manuscript. EAE; Responsible for patient enrollment, clinical assessment, and ensuring the accuracy and completeness of clinical data.

Declaration of Conflicting Interests

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Ethical approval

The study protocol was reviewed and approved by the Research Ethical committee of the Faculty of Medicine Al–Azhar University, (Cairo) for girls, (approval number 2231, and dated 2/1/2024).

Informed consent

All participants were informed about the purpose of the study and provided written informed consents.

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