HSI Health Sciences Investigations Journal

share

Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

ISSN Online 2704-4890 | ISSN Print 2720-7609

Online first publication

Original Research Article

HSI Journal (2025) Volume 7 (Issue 1):1167-1177. https://doi.org/10.46829/hsijournal.2022.6.7.1.1167-1177

Open Access

High antibiotic resistance and elevated plasma IFNγ from type 2 diabetes mellitus (T2DM) patients with uropathogens visiting Cape Coast Teaching Hospital

Richard KYEREMEH [1], Benjamin AMOANI [2], Samuel A SAKYI [3], Daniel BOISON [4], Cynthia A ADINORTEY [5], Justice K TURZIN [2], Sulemana MOHAMMED [2], Emmanuel K ADOM [2], Prince A BARNIE [6]*

[1] Department of Microbiology and Immunology, School of Medical Sciences, College of Health and Allied Sciences, University of Cape Coast, Cape Coast, Ghana; [2] Department of Biomedical Sciences, College of Health and Allied Sciences, School of Allied Health Sciences, University of Cape Coast, Cape Coast, Ghana; [3] Department of Molecular Medicine, School of Medicine and Dentistry, Kwame Nkrumah University of Science and Technology, Kumasi, Ghana; [4]Department of Biochemistry, School of Biological Sciences, College of Agriculture and Natural Sciences, University of Cape Coast, Cape Coast, Ghana; [5] Department of Molecular Biology and Biotechnology, School of Biological Sciences, College of Agriculture and Natural Sciences, University of Cape Coast, Cape Coast, Ghana; [6] Department of Forensic Science, School of Biological Sciences, College of Agriculture and Natural Sciences, University of Cape Coast, Cape Coast, Ghana.

Received December, 2024 ; Revised May, 2025; Accepted May, 2025

Abstract

Background: Diabetes mellitus (DM) is a polygenic metabolic disorder characterised by persistent elevated plasma glucose levels, which can lead to a range of complications, including an increased susceptibility to infections such as urinary tract infections (UTIs). Studies have shown that DM significantly increases the incidence of UTIs, and this is primarily due to a weakened immune system and the presence of glucosuria.

Objective: The study aimed to determine cytokine profiles in the peripheral blood, identify common uropathogens and analyse their antibiotic susceptibility patterns in DM patients reporting for treatment at Cape Coast Teaching Hospital (CCTH).

Methods: In a prospective study design, midstream urine and peripheral blood samples were collected from 202 known Type 2 diabetic patients recruited for the study. Using standard bacteriological methods, uropathogens were isolated and identified, and antibiogram testing was performed using the Kirby–Bauer disk diffusion method. Plasma concentrations of IL1β, IL6, IL10, IL17, IFNγ, and TNF-α cytokines were measured using an ELISA kit.

Results: This study recorded a 43.1% prevalence of UTIs among diabetic patients, with the main uropathogens identified as Escherichia coli (18.8%), Citrobacter *spp.* (11.4%), and Enterobacter *spp.* (5.4%). The study also observed a high level of antibiotic resistance among the uropathogens, particularly to widely used broad-spectrum antibiotics such as Nalidixic Acid, Cefuroxime, Aztreonam, Cefotaxime, Ceftriaxone, Ceftazidime, Cefixime, and Cefdinir. There were significantly higher levels of IFNγ among the diabetic patients with UTI, but there were no significant changes in the levels of IL1β, IL6, IL10, IL17 and TNF-α cytokines among the diabetes patients with or without uropathogens.

Conclusion: Our findings suggest that patients with diabetes have frequent UTIs, and the isolated uropathogens were highly resistant to antibiotics. Again, there were higher levels of pro-inflammatory cytokine IFNγ in diabetic patients with UTI. Our findings suggest that patients with diabetes experience frequent UTIs, and the isolated uropathogens show high levels of resistance to antibiotics. Additionally, we observed higher levels of the pro-inflammatory cytokine IFN-γ in diabetic patients with UTI. This elevated cytokine level could play a role in the immune response to infections and may serve as a potential biomarker for identifying UTIs in type 2 diabetic patients. The combination of frequent UTIs and antibiotic resistance highlights the need for improved management strategies and targeted therapies in this population.

Keywords: Antibiotics, cytokines, diabetes, uropathogens, prevalence

Cite the publication as Kyeremeh R, Amoani B, Sakyi SA, Boison D et al. High antibiotic resistance and elevated plasma IFNγ from type 2 diabetes mellitus (T2DM) patients with uropathogens visiting Cape Coast Teaching Hospital. HSI Journal 7 (1):1167-1177. https://doi.org/10.46829/hsijournal.2025.6.7.1.1167-1177

INTRODUCTION

Diabetes mellitus (DM) is a condition characterised by persistent hyperglycemia, resulting from either insulin deficiency or poor cellular response to insulin [1,2]. According to the International Diabetes Federation (IDF), an estimated 537 million adults aged 20 – 79 years worldwide, representing 10.5% of all adults in this age group, are living with DM. By 2030, this number is projected to rise to 643 million [3]. The increase in DM cases is expected to be predominantly in low and middle-

* *Corresponding author*
Email: pamoah-barnie@ucc.edu.gh

income countries, with 94% of the growth occurrin by 2045 [3]. Uncontrolled DM can lead to life-threatening complications such as stroke, nephropathy, neuropathy, and retinopathy [4,5]. Moreover, uncontrolled DM can be accompanied by common uropathogens and other UTIs [6,7,8], which, if not properly managed, may often lead to complications such as disability and, in severe cases, premature death. DM has been found to be associated with reduced immunity and bladder dysfunction, which makes a diabetic individual more vulnerable to UTI [9].

Studies have shown that immunological deficiencies in diabetic patients, including impaired neutrophil migration, intracellular killing, phagocytosis, and abnormal levels of cytokines like interleukin (IL)-1β, IL-2, IL-6, IL-12, tumour necrosis factor (TNF)-α, and interferon-gamma (IFN)-γ [10,11], can contribute to bacterial colonisation and infection [12,13]. Also, pro-inflammatory cytokines, such as IL-1β, IL-6, and TNF-α, have been shown to significantly influence the pathophysiology of diabetic peripheral neuropathy (DPN) [14], which is a debilitating complication of diabetes mellitus.

Researchers have argued that the irrational use of antibiotics in diabetic patients has contributed to the increase in antibiotic-resistant uropathogens [15,16]. This improper or overuse of antibiotics can promote the development of resistance, making infections harder to treat and further complicating the management of UTIs in diabetic individuals. The etiologic agents responsible for UTIs and the varying resistance and susceptibility rates to commonly prescribed antibiotics can lead to longer hospital stays and increased treatment costs [17]. Moreover, antibiotic resistance to newer and more potent antimicrobials is reducing treatment options for UTIs, particularly affecting DM patients who are already more vulnerable to infections [18]. Unfortunately, there has been limited research in Ghana focused on identifying common uropathogens in DM patients, their antibiotic susceptibility profiles, and the levels of pro-inflammatory cytokines in the peripheral blood of these patients. This gap in research hinders a deeper understanding of UTIs in DM individuals and the effectiveness of treatment options. The purpose of the current study is to evaluate the peripheral blood immune environment (cytokine profiles of Th1, Th2, and Th17), identify common uropathogens, and assess their antibiotic resistance and susceptibility patterns in diabetic patients visiting Cape Coast Teaching Hospital. This research aims to provide valuable insights into the immunological and microbiological aspects of UTIs in diabetic individuals, ultimately contributing to more effective management and treatment strategies for these patients.

MATERIALS AND METHODS

Study design and sites

The study was a cross-sectional design conducted from October 2020 to December 2020 at the diabetic unit of the CCTH, a tertiary hospital with about 400-bed capacity within the Cape Coast Metropolitan District in the Central Region of Ghana. The patients were selected from those receiving treatment and glucose level monitoring at the diabetic unit, using a convenient sampling method. Medical records of participants were reviewed to obtain additional relevant information on demographic and clinical data.

Recruitment of study participants

From a study population of approximately 412 type 2 diabetic patients who visited the CCTH daily for check-ups, a total of 202 patients aged between 18 and 83 years were recruited for the study using a convenience sampling technique.

The formula $n = \frac{\frac{Z^2 \, x \, P(1-P)}{E^2}}{1+\left(\frac{Z^2 \, x \, P(1-P)}{E^2 N}\right)}$

Where E = 0.05, N = 412, Z = 1.96 and P = 0.5 was used to evaluate and determine the required minimum sample size [19].

N = Population size
Z = z-score
E = margin of error
P = standard of deviation

$$n = \frac{\frac{1.96^2 \, x \, 0.5(1-0.5)}{0.05^2}}{1+\left(\frac{1.96^2 \, x \, 0.5(1-0.5)}{0.05^2 X 412}\right)} = \frac{\frac{3.8416x \, 0.25}{0.0025}}{1+\left(\frac{3.8416 \, x \, 0.25}{1.03}\right)} = \frac{\frac{0.9604}{0.0025}}{1+\left(\frac{0.9604}{1.03}\right)} = \frac{384.16}{1.932} = 199$$

Inclusion criteria

Study participants were known type 2 diabetics for at least 3 years prior to the study and were actively receiving treatment in the diabetes clinic of CCTH. They had individually consented before being included in this research.

Exclusion criteria

Patients were excluded from the study if they were known type 1 diabetics, were on antibiotic therapy or had a malaria infection within 14 days prior to recruitment. Individuals who were known as HIV-positive, pregnant, with gynaecological/urological disorders, undergone a kidney transplant, or using a catheter were all excluded from this study. Additionally, exclusion criteria included recent type 2 diabetics who had any of the following conditions: genitourinary surgery, urinary incontinence, urinary retention, psychiatric disorders or age above 83 years were excluded from this study. Furthermore, urine cultures that showed Candida growth were not included in the analysis of uropathogens.

Sample collection and processing

Sociodemographic data and clinical history

Information on age, gender, duration of diabetes, complications, previous infections, medications, and laboratory findings upon admission were extracted from the patient's folder and electronic medical records. This was

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

done through an open-loop interview and a structured questionnaire.

Fasting Plasma Glucose (FPG) measurement.
Fasting Plasma Glucose (FPG) levels of the study participants, including both known type 2 diabetics and non-diabetics, were measured using a glucometer (Morepen Gluco One Blood Glucose Monitor, Model BG 03) prior to the collection of their urine samples.

Specimen collection
All participants were carefully instructed to collect midstream urine samples using a sterile, graduated, wide-open plastic container. Female participants were also provided with sterile gauze to perform a front-to-back cleaning before urination. The urine samples were stored in the refrigerator after collection. Further microbiological investigations were conducted at the Microbiology Laboratory Department of the CCTH.

Microbiological analysis
Bacterial isolation and identification: Urine specimens were directly inoculated onto cysteine lactose electrolyte deficient (CLED) agar using a standard graduated wire loop. After 24 hours of aerobic incubation at 37◦C, the plates were examined macroscopically for morphological appearance as presumptive identification. The growth of bacterial colonies on the media was defined as a positive urine culture which was greater than 105 CFU/ml. Examination of the morphological appearance of the colonies was investigated. Gram staining was used for the identification of the bacteria. Citrate tests, indole tests, urease tests, and triple sugar iron (TSI) agar were the biochemical tests that were used to confirm the presence and isolation of the bacteria.

Antimicrobial susceptibility testing
The antimicrobial susceptibility test (AST) was done for each of the Uropathogens isolated, using the modified Kirby-Bauer disc diffusion method to identify resistant and sensitive isolates. A uniform lawn over the entire surface of Mueller-Hinton agar, using a sterile cotton swab, was dipped into the peptone water. Norfloxacin (NOR/10 µg), Aztreonam (AT/30 µg), Cefotaxime (CTX/30 µg), Nalidixic acid (NA/30 µg), Nitrofurantoin (NI/300 µg), Cefuroxime (XM/30 µg), Gentamycin (GM/10 µg), Amikacin (AK/30 µg), Ciprofloxacin (CI/5 µg), Ofloxacin (OF/5 µg), Cefixime (FIX/5 µg), Cefdinir (CD/5 µg), Ceftazidime (CAZ/30 µg), Levofloxacin (LEV), Ceftriaxone (CTR), Cotrimoxazole (COT), Chloramphenicol (CHL), Tetracycline (TET), Ampicillin (AMP), a total of 12 antibiotics were used on the bacteria isolates.

Quality control
The sterility and performance of the culture media were tested prior to using the culture media. Standard reference strains of E. coli (ATCC 25922) and S. aureus (ATCC 25923) were used as controls for culture and sensitivity testing.

Cytokine measurement
About 5 mL of venous blood was collected from each participant and placed into the EDTA tubes to obtain plasma. The plasma was then collected and stored in cryovials at −80 °C until ready to be used for the cytokine assays. Plasma concentrations of interleukin-6, interleukin-1β, interleukin-17, interleukin-10, interferon-gamma, and tumour necrotic factor-alpha were assessed using sandwich ELISA kits from CUSABIO Bihmmnn;otech (Wuhan, China). Strict manufacturer's protocols were followed. Cytokines in stored plasma were analysed using the Mindray MR-96A ELISA plate reader (Shenzhen, China).

Statistical analysis
All statistical analyses were performed using the GraphPad Prism version 8.0.1 (244) software. The results were expressed as means and standard deviations (SDs). For comparisons within groups, Analysis of Variance (ANOVA) was used. Continuous and categorical variables were summarised as counts and percentages. Univariable and multivariate logistic regression models were performed. Correlation analysis was performed by using the Pearson Correlation Coefficient. $P < 0.05$ was considered statistically significant in all analyses.

RESULTS

As shown in Table 1, 87 out of 202 diabetic patients were found to have UTI, resulting in a prevalence of 43.1%. The percentage of female participants with positive urine cultures (50%) was significantly higher than that of their male counterparts ($p = 0.0001$). Moreover, there was a significant difference in UTI prevalence among the age groups ($p < 0.0001$). The 60 - 79 years age group had the highest prevalence of UTI at 49.6%, followed by the 20 - 39 years age group with 41.7%, and the 80 - 83 years age group had the lowest prevalence at 25%.

Married participants had the highest UTI prevalence at 47%, compared to divorced participants ($p = 0.009$) and widowed participants ($p = 0.025$), though the difference was not significant when compared to single participants ($P = 0.114$). There was no significant difference between single and divorced participants, single and widowed participants, or divorced and widowed participants. Most participants with high Fasting Plasma Glucose (FPG). (FBS ≥ 7.00) had a higher UTI prevalence (46.5%) compared to those with FBS < 5.6 ($p = 0.0007$). The prevalence of uropathogens was significantly higher in patients with diabetes for at least 5 years compared to those with diabetes for less than 5 years ($p = \leq 0.0005$). However, there was no significant difference between patients with diabetes for 5-20 years and those with diabetes for more than 20 years ($P = 0.6842$). Participants with tertiary and secondary education levels had the lowest prevalence of uropathogens, at 33.3% and 38.5%, respectively ($p > 0.05$), compared to those with no or primary level education, who had the highest prevalence of uropathogens at 50%. The findings on the common uropathogens isolated from the

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

Table 1. Demographic and clinical characteristic of study participants

Variable	Frequency (%) N=202	Frequency Positive for UTI (%) N=87	P value
Gender			
Male	46 (22.8%)	9 (19.6%)	0.0001
Female	156 (77.2%)	78 (50%)	
Age			
20-39	46 (22.8%)	5 (41.7%)	< 0.0001
40-59	156 (77.2%)	25 (34.3%)	
60-79	12 (5.9%)	56 (49.6%)	
80-83	73 (36.1%)	1 (25%)	
Marital status			
Single	15 (7.4%)	6 (40%)	0.0063
Married	115 (56.9%)	54 (47%)	
Divorced	22 (10.9%)	8 (36.4%)	
Widowed	50 (24.8%)	19 (38%)	
FPG mmol/L			0.0007
<5.6	45 (22.3%)	14 (31.1%)	
≥7	157 (77.7%)	73 (46.5%)	
Duration of diabetes			
<5 years	43 (21.3%)	14 (32.6%)	0.0002
5-20 years	110 (54.4%)	50 (45.5%)	
≥20 years	49 (24.3%)	23 (46.9%)	
Level of education			
None	44 (21.8%)	22 (50%)	0.0009
Primary	50 (24.7%)	25 (50%)	
Secondary	78 (38.6%)	30 (38.5%)	
Tertiary	30 (14.8%)	10 (33.3%)	

FPG: Fasting Plasma Glucose.

Table 2. Prevalence of common uropathogens and other UTI infections amongst Diabetic Patients

Isolates	Frequency	Prevalence (%)
Escherichia coli	38	18.8
Citrobacter *spp*	23	11.4
Enterobacter *spp*	11	5.4
Candida albicans	5	2.5
Salmonella typhi	5	2.5
Shigella *spp*	3	1.5
Proteus vulgaris	1	0.5
Pseudomonas *spp*	1	0.5

diabetic patients with UTI (Table 3) show that Escherichia coli was dominant with frequency of 38 cases (18.8%). This was followed by Citrobacter *spp* with 23 cases (11.4%) and Enterobacter spp with 11 cases (5.4%). Other pathogens identified included Candida and Salmonella typhi, each with 5 cases (2.5%), Shigella *spp* with 3 cases (1.5%) and Proteus *spp* and pseudomonas *spp*, each with 1 case (0.5%). The findings on the susceptibility patterns of uropathogen isolates from diabetic patients to antibiotics (Figure 1) reveal that Amikacin demonstrated the highest activity, with 89.2% of bacterial strains being susceptible. It was followed by Gentamycin, with 70.7% susceptibility (Figure 1A). All six bacterial strains were sensitive to both Amikacin and Ofloxacin.

Amikacin was particularly effective against nearly all gram-negative bacterial strains (Figures 1B, 1C, 1D, 1E, 1F, and 1G). With the exception of Pseudomonas, all five other isolates were sensitive to Nitrofurantoin, Ciprofloxacin, and Gentamycin. All isolates, except Pseudomonas and Shigella, were also sensitive to Norfloxacin. Three of the six isolates were sensitive to Nalidixic acid. Resistance patterns revealed that four isolates were resistant to Cefotaxime, while five isolates were resistant to Aztreonam, Ceftriaxone, Ceftazidime, and Cefixime. All isolates were resistant to Cefuroxime and Cefdinir. Shigella was found to be the most sensitive isolate, as it was susceptible to 11 out of the 14 antibiotics tested (Figure 1F). On the other hand, Pseudomonas was the most resistant isolate, being resistant to all antibiotics except Amikacin and Ofloxacin (Figure 1E).

There was a significantly higher level of pro-inflammatory cytokine IFNγ in diabetes patients with uropathogens

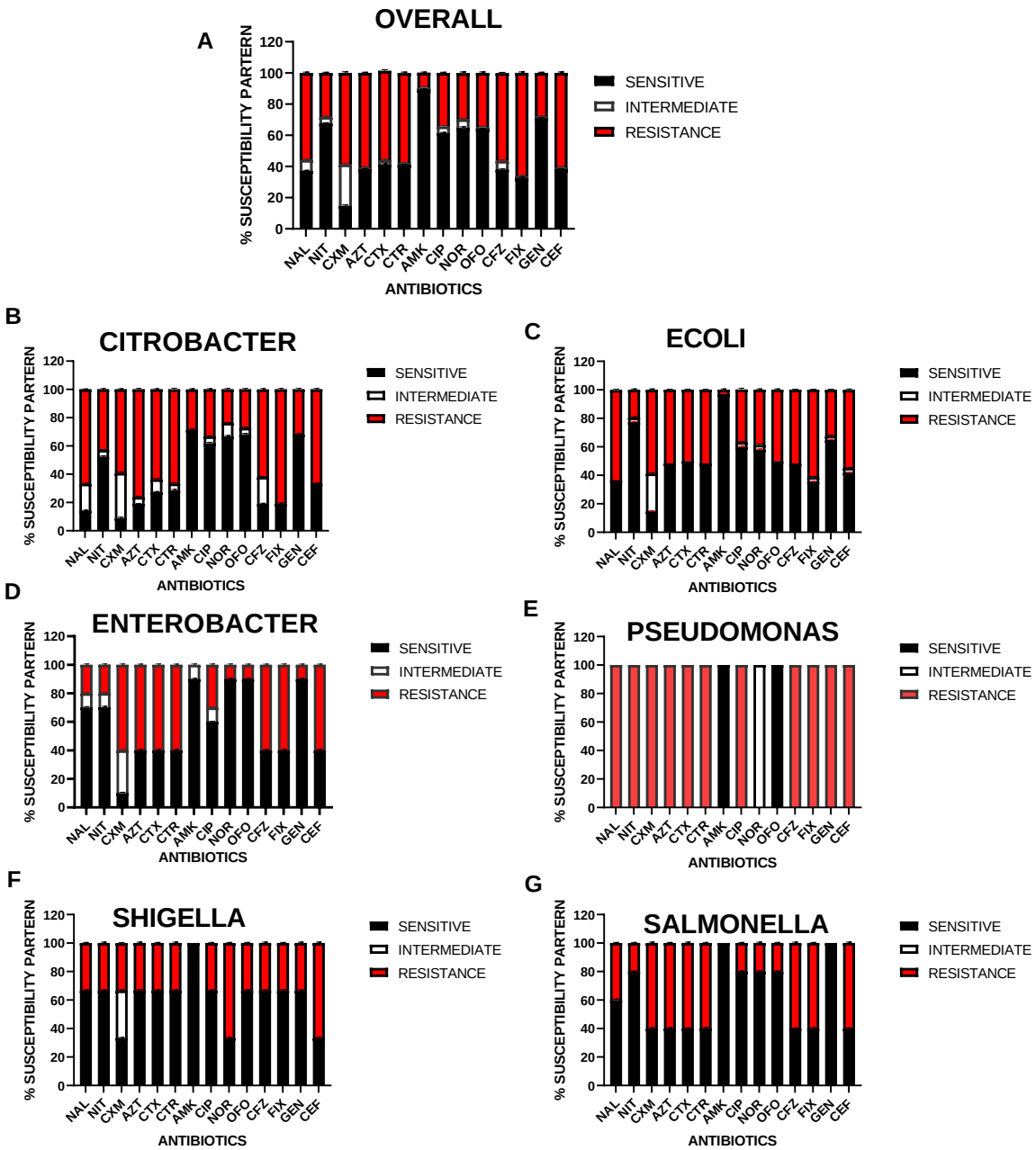

Figure 1. Antibiotic susceptibility pattern of gram-negative bacteria isolated from urine culture of diabetic patients

A. % susceptibility pattern of overall bacterial strains. B. % susceptibility pattern of Citrobacter C. % susceptibility pattern of E Coli. D. % susceptibility pattern of Enterobacter. E. % susceptibility pattern of Pseudomonas. F. % susceptibility pattern of Shigella. G. % susceptibility pattern of Salmonella

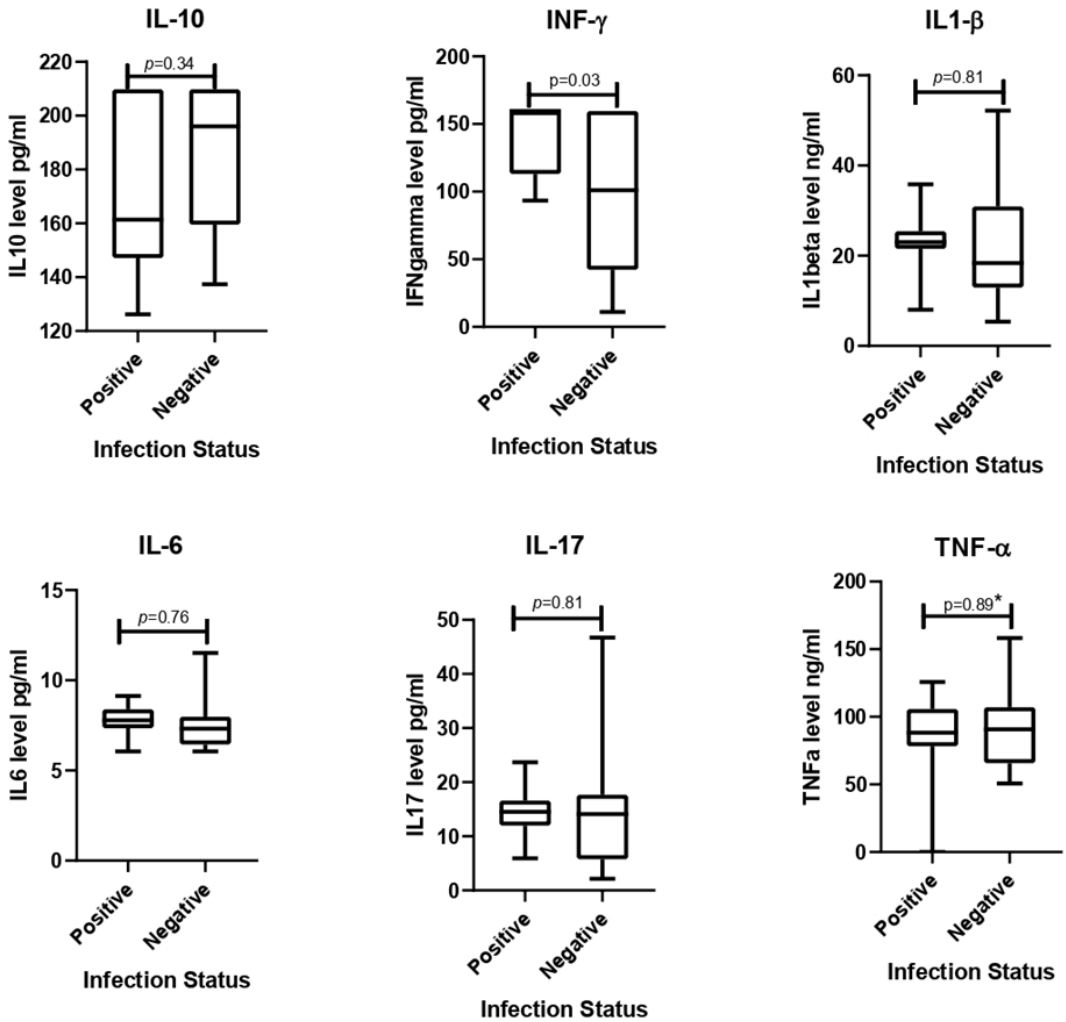

Figure 2. Mean plasma cytokine levels among diabetes patients with or without uropathogens. Number of diabetes patients with uropathogens (positive; n = 20) and without uropathogens (negative; n = 20). A significant difference between the two groups was assessed using an independent t-test. P values < 0.05 were considered statistically significant. The error bar represents the standard error of the mean. TNFα; tumor necrosis factor alpha, IFNγ; interferon gamma.

compared to diabetic patients without uropathogens (p = 0.03) (Figure 2). However, there were no significant changes in the levels of IL-1β, IL-6, IL-10, IL-17 and TNF-α cytokines among the diabetes patients with or without uropathogens (Figure 2).

DISCUSSION

This study focused exclusively on type 2 diabetic patients to explore the immunological and microbiological aspects of UTIs and assess factors associated with UTI within this group, building on existing studies that compare diabetics and non-diabetics [20]. Our present study revealed that diabetes was associated with the incidence of UTI (Table 3.1). The total prevalence of UTI among the diabetic patients in this study was 43.1%, which was relatively high compared to other studies: 39.3% in Saudi Arabia [21], 31.1% in Uganda [22], 22.6% and 11.6% in Ethiopia [18,23], 19.5% in Sudan [24] and 8.08% in Pakistan [25]. The relatively high prevalence in this study could be attributed to factors such as poor diabetes management, duration of diabetes, sociodemographic variables, poor personal hygiene and lifestyle factors that may make diabetic individuals more susceptible to developing UTIs [26,27].

In this study, female diabetic patients were found to be more prone to developing UTIs, with a prevalence of 78 out

share
Send us an email: hsijournal@ug.edu.gh
Visit us: https://www.hsijournal.ug.edu.gh

of 156 (50%), compared to male diabetic patients, with a prevalence of 9 out of 46 (19.6%). This finding is supported by several studies [18,28-31] and could be due to the anatomical proximity of the female urethra to the anus, which increases the risk of bacterial movement into the bladder, especially if proper hygiene is not maintained. However, this finding contradicts some studies conducted in Ghana [32] and Sudan [24], where the prevalence of UTI did not show an association with sex. The differences in findings may be attributed to other factors, such as prostatic hypertrophy in males, biological or immunological changes, or potentially higher levels of personal hygiene among females in those studies.

The study found that the incidence of UTIs increased with age, particularly among the 60 - 79 years age group, where the prevalence was 49.6%. This aligns with previous studies [28,33-35], suggesting that age-related immune system decline [36], especially in uncontrolled diabetes, could contribute to the higher UTI incidence in this age group. However, other studies have shown varying UTI incidences across age groups [37], which may be due to differences in study methodologies, expertise of investigators, geographical factors, and screening practices [38]. Additionally, the study indicated that patients with diabetes for more than five years had a higher frequency of bacterial isolates compared to those with diabetes for less than five years. This may be due to prolonged diabetes impairing the immune system and complicating bladder emptying, which increases the risk of UTIs, particularly when blood sugar levels are not well controlled [9]. The study found that a higher bacterial count (46.5%) was associated with diabetic patients who had an FPG level of 7 mmol/l or higher. In contrast, only 31% of diabetic patients with FPG levels below 5.6 mmol/l had a high bacterial count. This suggests that controlling blood glucose levels could help reduce the risk of UTIs in diabetic patients, as glucose in the urinary tract provides a nutrient source for bacteria, potentially leading to infections.

The study found that married couples had the highest incidence of UTIs, likely due to the transmission of uropathogens during sexual intercourse [34]. As a result, it is recommended that patients with UTIs avoid sexual contact until the infection is fully treated to prevent the introduction of additional bacteria, which could worsen the infection and slow healing. Additionally, the study highlighted an association between education level and UTI prevalence in diabetic patients. Those with tertiary or secondary education had a lower prevalence of UTIs compared to those with only primary education or no education. This suggests that individuals with higher education may be better at managing their diabetes, which could reduce the risk of developing UTIs [39,40]. The study revealed, based on medical records, that 72% of the participants were on metformin (500 mg or 1000 mg taken twice daily), while the remaining 28% were on glibenclamide (15 mg daily). Studies have shown that type 2 diabetic patients who use metformin have a lower risk of UTI compared with those who do not use metformin [41,42]. Metformin stimulation has been shown to enhance the innate immune response of uroepithelial cells, resulting in increased extracellular and intracellular bacterial killing [43]. This suggests a beneficial role of metformin in supporting host defence mechanisms against urinary tract infections. On the other hand, glibenclamide is known to cause severe hypoglycaemia [44], and therefore, its use in diabetic patients requires careful monitoring during infections, as the combined effects can significantly increase the risk and severity of hypoglycaemic episodes, potentially complicating disease management and patient outcomes [45].

This study identified the prevalence of common uropathogens and other infections in diabetic patients (Table 3.2). The least isolated uropathogens were Proteus vulgaris and Pseudomonas *spp*., both with a prevalence of 0.5%, followed by Shigella *spp*. (1.5%), Candida (2.5%), and Salmonella typhi (2.5%). E. coli was the most common uropathogen, with a prevalence of 18.8%, followed by Citrobacter *spp*. (11.4%) and Enterobacter *spp*. (5.4%), consistent with findings from previous studies [23,38,46-50]. E. coli was noted as the most virulent uropathogen, likely due to its various virulence factors (toxins, adhesins, fimbriae, lipopolysaccharide capsules, and invasions), which help it to invade and attach to its host. Given the rise in antibiotic resistance, especially the multidrug resistance of E. coli, effective management of UTIs is crucial [51].

Interestingly, no gram-positive organisms, such as Staphylococcus *spp*., were isolated, which contrasts with other studies where these organisms were found [22,33,46]. This could be due to differences in diagnostic methods, geographic variations, expertise, sample sizes, and diabetic blood glucose control. Additionally, Candida *spp*., Pseudomonas, and Proteus were isolated only from female diabetic patients, aligning with findings from other studies [18,52]. The study examined the antibiotic susceptibility patterns of bacterial isolates (Figure 1) and found that all six bacterial isolates were sensitive to Amikacin and Ofloxacin. These two antibiotics were the only ones effective against Pseudomonas. Additionally, five isolates (except Pseudomonas) were sensitive to Nitrofurantoin, Ciprofloxacin, and Gentamycin, while four isolates (except Pseudomonas and Shigella) were sensitive to Norfloxacin. The higher susceptibility rates for these antibiotics could be due to their limited availability and higher cost compared to more commonly used antibiotics. As a result, Amikacin, Ofloxacin, Nitrofurantoin, Ciprofloxacin, Gentamycin, and Norfloxacin may be considered therapeutic alternatives for treating and managing UTIs in diabetic patients.

The study observed a high level of resistance to several antibiotics, including Nalidixic Acid, Cefuroxime, Aztreonam, Cefotaxime, Ceftriaxone, Ceftazidime, Cefixime, and Cefdinir, with Cefuroxime and Cefdinir being inactive against all the bacterial isolates. This resistance could be attributed to factors such as the low cost,

widespread availability, and the frequent broad-spectrum use of these antibiotics without proper medical prescriptions [18, 38]. Additionally, while individual antibiotics showed sensitivity to certain specific organisms, they were resistant to others, highlighting the need for careful selection of antibiotics based on the specific pathogens involved.

In this study, Amikacin emerged as the most active antibiotic, as was shown in other studies [53], with 89.2% of bacterial strains showing susceptibility, followed by Gentamycin, which was effective against 70.7% of strains. This result aligns with studies showing Gentamycin's effectiveness against S. aureus and MRSA, particularly among HIV-infected individuals in Cape Coast [54]. Both Amikacin and Gentamycin are aminoglycosides, which work by binding irreversibly to the 30S and 50S units of the bacterial ribosome, disrupting protein synthesis. Aminoglycoside-inactivating enzymes are known to be the primary cause of resistance to these antibiotics [55]. However, Amikacin has an advantage over Gentamycin because it is less susceptible to these inactivating enzymes due to structural differences between the two antibiotics.
The study also found that Nitrofurantoin, the only nitrofuran antibiotic included, exhibited a susceptibility rate of 67.6%, which was comparable to the fluoroquinolones. Ciprofloxacin (61.4%), Norfloxacin (64.8%), and Ofloxacin (64.0%) all had similar susceptibility rates, while Nalidixic Acid was found to be inactive against the bacterial strains.

On the other hand, all the cephalosporins tested (Cefuroxime, Cefotaxime, Ceftriaxone, Ceftazidime, Cefixime, and Cefdinir) were inactive against the bacterial strains. Aztreonam, the sole beta-lactam antibiotic tested, was also found to be inactive. These findings suggest that while Amikacin and Gentamycin remain highly effective, many commonly used antibiotics, including cephalosporins and beta-lactams, showed little to no activity against the bacterial strains, highlighting the importance of proper antibiotic selection in the treatment of UTIs in diabetic patients. In this study, Amikacin showed the highest activity against most of the gram-negative bacteria, with the predominant isolate E. coli exhibiting a high sensitivity rate of 97.1% to Amikacin. This was compared to other antibiotics, such as Nitrofurantoin (77.4%), Gentamycin (64.7%), Ciprofloxacin (60.0%), Norfloxacin (58.1%), Ofloxacin (50.0%), and Cefotaxime (50.0%). In terms of specific uropathogens, Citrobacter *spp*. showed high sensitivity to Amikacin (71.4%), Gentamycin (68.2%), Ofloxacin (68.2%), Norfloxacin (66.7%), Ciprofloxacin (61.9%), and Nitrofurantoin (52.4%). Enterobacter *spp*. showed high sensitivity to Amikacin (90%), Gentamycin (90%), Norfloxacin (90%), Ofloxacin (90%), Nalidixic Acid (70%), Nitrofurantoin (70%), and Ciprofloxacin (60%), while showing resistance to Aztreonam, Cefotaxime, Ceftriaxone, Ceftazidime, Cefixime, Cefdinir, and Cefuroxime. Pseudomonas *spp*. showed complete sensitivity (100%) to Amikacin and Ofloxacin, with no activity from the other antibiotics. Shigella *spp*. was highly sensitive to Amikacin, with the other antibiotics showing moderate sensitivity, except for Norfloxacin and Cefdinir, which were resistant. Salmonella typhi was highly sensitive to Amikacin, Gentamycin, Ciprofloxacin, Norfloxacin, Nitrofurantoin, Ofloxacin, and Nalidixic Acid.

These results highlight that Amikacin is the most effective antibiotic against a wide range of uropathogens, particularly for E. coli and other gram-negative bacteria, while other antibiotics showed varying levels of efficacy depending on the specific bacterial isolate. It is highly concerning that broad-spectrum antibiotics such as Nalidixic Acid, Cefuroxime, Cefdinir, Cefixime, Aztreonam, Ceftazidime, Ceftriaxone, and Cefotaxime showed a high rate of resistance among uropathogens in diabetic patients in this study. This contradicts other studies where Nalidixic Acid demonstrated high susceptibility to uropathogens [32]. In addition, studies from Nepal and Ethiopia also reported conflicting resistance patterns [23,37], which further underscores the variability in resistance across regions. The high resistance to these antibiotics could be attributed to their overuse and inappropriate application, particularly in treating complicated UTIs, which may lead to the development of resistance. The widespread and irrational use of these antibiotics is a known contributing factor to resistance in uropathogens, as highlighted by other studies [18].

In contrast, the antibiotics Amikacin, Gentamycin, Nitrofurantoin, Ofloxacin, Norfloxacin, and Ciprofloxacin have proven to be the most effective against almost all UTI infections in this study. Similar findings were reported by Addo et al., who also observed that Amikacin and Gentamycin were highly effective against uropathogens [32]. These results emphasise the importance of using targeted therapy rather than relying on a single antibiotic for all UTI infections. Thus, the study underlines the need for diagnostic testing to identify and isolate specific uropathogens before administering antibiotics. This approach ensures that the most appropriate and potent antibiotic is used, minimising the risk of resistance and improving treatment outcomes for diabetic patients suffering from UTIs. Asymptomatic UTI is common among diabetic patients [36], making its diagnosis challenging. Identifying specific biomarkers or profiles that can indicate the presence of UTI in diabetic patients would be valuable for early detection and effective management. In this study, cytokine levels were assessed to explore their potential as indicators of UTI in diabetic patients, and comparisons were made between those with uropathogens and those without, as shown in Figure 2.

A significant finding from this study was the higher level of the pro-inflammatory cytokine IFN-γ in diabetic patients with uropathogens compared to those without (p=0.03). IFN-γ plays a crucial role in mediating cellular immunity, particularly in the defence against infections. Several studies have highlighted the importance of IFN-γ in

enhancing antibacterial immune responses. For example, IFN-γ has been shown to protect epithelial monolayers from pathogen-mediated damage during Staphylococcus aureus infections [56]. It also contributes significantly to protection against Chlamydia and mycobacterial infections by activating effector cells and generating antibody-mediated responses [57]. Furthermore, IFN-γ is known for its role in combating viral and intracellular infections by activating macrophages' cellular immune responses. However, it's worth noting that excessive IFN-γ can also contribute to the pathogenesis of diabetes by promoting the expression of MHC class I and II molecules, as well as adhesion molecules on cells, including pancreatic β-islets. This leads to macrophage polarisation from an anti-inflammatory M2 to a pro-inflammatory M1 phenotype [58,59]. These findings may explain the elevated IFN-γ levels observed in diabetic patients with uropathogens in this study.

No significant differences were observed in the levels of other cytokines, including IL-1β, IL-6, IL-10, IL-17, and TNF-α, between diabetic patients with and without uropathogens. However, there was a slight increase in IL-1β and IL-6 among those with uropathogens, while IL-17 and TNF-α showed a slight increase in diabetic patients without uropathogens. In summary, this study suggests that cytokine profiling could serve as a potential surrogate tool for diagnosing UTIs in asymptomatic diabetes patients. Elevated IFN-γ levels may act as important markers to differentiate between diabetic patients with and without uropathogens. Further studies and larger sample sizes are needed to fully understand the role of cytokines in UTI pathogenesis in diabetes and to refine this marker for clinical use.

Conclusion

This study reported higher incidences of UTIs among diabetic patients, with a significant presence of antibiotic-resistant uropathogens. The findings highlighted that common uropathogens in diabetic patients showed resistance to frequently prescribed antibiotics. Based on the high susceptibility rates observed, this study recommends Amikacin, Gentamycin, Nitrofurantoin, Ofloxacin, Norfloxacin, and Ciprofloxacin as potent antibiotics for managing UTIs in diabetic patients. Furthermore, a strong association between elevated levels of IFN-γ and the presence of UTIs in diabetic patients was observed. This suggests that IFN-γ may play a crucial role in the immune response to UTIs in this population.

The findings support the potential for using cytokine profiling, specifically IFN-γ levels, as a proxy for diagnosing UTIs in asymptomatic diabetic patients and guiding more effective treatment strategies. In conclusion, the study emphasises the importance of targeted antibiotic therapy and the potential role of immune markers like IFN-γ in improving the diagnosis and management of UTIs in diabetic patients.

DECLARATIONS

Ethical consideration

The research protocol was approved by the Cape Coast Teaching Hospital Ethical Review Committee (Ref: CCTHERC/EC/2020/086). Consent was obtained from the participants before their inclusion in the study.

Consent to publish

All authors agreed on the content of the final manuscript.

Funding

None

Competing Interest

The authors declare no conflict of interest

Author contribution

PAB conceived the idea of the study. PAB, RK and BA designed the study. PAB, RK, BA, DB, SAK, CAA, JKT, SM and EKA collected data. PAB, RK, BA, DB, SAK, CAA, JKT, SM and EKA did data analysis and interpretation. PAB and DB prepared the first draft of the manuscript with input from all co-authors. All co-authors edited the manuscript and endorsed the final version before submission.

Acknowledgement

The authors wish to thank the research department of Family Health Medical School, Accra.

Availability of data

Data is available upon request to the corresponding author

REFERENCES

1. Adinortey CA, Kwarko GB, Koranteng R, Boison D, Obuaba I, Wilson MD, Kwofie SK. (2022) Molecular structure-based screening of the constituents of Calotropis procera identifies potential inhibitors of diabetes mellitus target alpha glucosidase. Current Issues in Molecular Biology 44:963–87.
2. Razaq RA, Mahdi JA, Jawad RA. (2020) Information about Diabetes Mellitus. Journal of University of Babylon for Pure and Applied Sciences :243–52.
3. Sun H, Saeedi P, Karuranga S, Pinkepank M, Ogurtsova K, Duncan BB, Stein C, Basit A, Chan JC, Mbanya JC, Pavkov ME. (2022) IDF Diabetes Atlas: Global, regional and country-level diabetes prevalence estimates for 2021 and projections for 2045. Diabetes Research and Clinical Practice 183:109119.
4. Chen L, Magliano DJ, Zimmet PZ. (2012) The worldwide epidemiology of type 2 diabetes mellitus—present and future perspectives. Nature Reviews Endocrinology 8:228–36.
5. Steinmetz JD, Bourne RR, Briant PS, Flaxman SR, Taylor HR, Jonas JB, Abdoli AA, Abrha WA, Abualhasan A, Abu-Gharbieh EG, Adal TG. (2021) Causes of blindness and

vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study. The Lancet Global Health 9:e144–60.

6. Sewify M, Nair S, Warsame S, Murad M, Alhubail A, Behbehani K, Al-Refaei F, Tiss A. (2016) Prevalence of urinary tract infection and antimicrobial susceptibility among diabetic patients with controlled and uncontrolled glycemia in Kuwait. Journal of Diabetes Research 2016:6573215.

7. FICMS AH. (2014) Bacteriological finding of urinary tract infection in diabetic patients. International Journal 2:274–9.

8. Anwar S, Benyamin J, Rauf MK. (2025) Frequency of uropathogens in patients admitted with urinary tract infection and diabetes mellitus. J Pak Soc Intern Med 6:71–77.

9. Shah MA, Kassab YW, Anwar MF, Al Dahoul HK, Menon S, Kaur HJ, Ifzaal M, Muthanna FM, Searan WM. (2019) Prevalence and associated factors of urinary tract infections among diabetic patients. Health Science Journal 13:1–5.

10. Devaraj S, Glaser N, Griffen S, Wang-Polagruto J, Miguelino E, Jialal I. (2006) Increased monocytic activity and biomarkers of inflammation in patients with type 1 diabetes. Diabetes 55:774–9.

11. Alnek K, Kisand K, Heilman K, Peet A, Varik K, Uibo R. (2015) Increased blood levels of growth factors, pro-inflammatory cytokines, and Th17 cytokines in patients with newly diagnosed type 1 diabetes. PLoS One 10:e0142976.

12. Valerius NH, Eff C, Hansen NE, Karle H, Nerup J, Søeberg B, Sørensen SF. (1982) Neutrophil and lymphocyte function in patients with diabetes mellitus. Acta Medica Scandinavica 211:463–7.

13. Hasan MK, Nazimuddin K, Ahmed AS, Sarker RS, Haque M, Musa AK. (2007) Differences in bacteriological and antibiotic sensitivity patterns in UTI among hospitalised diabetic and non-diabetic patients. Journal of Medicine 8:10.

14. Nashtahosseini Z, Eslami M, Paraandavaji E, Haraj A, Dowlat BF, Hosseinzadeh E, Oksenych V, Naderian R. (2025) Cytokine signaling in diabetic neuropathy: A key player in peripheral nerve damage. Biomedicines 13:589.

15. Alanis AJ. (2005) Resistance to antibiotics: are we in the post-antibiotic era?. Archives of Medical Research 36:697–705.

16. Hossain MJ, Jabin N, Ahmmed F, Sultana A, Abdur Rahman SM, Islam MR. (2023) Irrational use of antibiotics and factors associated with antibiotic resistance: findings from a cross-sectional study in Bangladesh. Health Science Reports 6:e1465.

17. Casqueiro J, Casqueiro J, Alves C. (2012) Infections in patients with diabetes mellitus: A review of pathogenesis. Indian Journal of Endocrinology and Metabolism 16:S27–36.

18. Woldemariam HK, Geleta DA, Tulu KD, Aber NA, Legese MH, Fenta GM, Ali I. (2019) Common uropathogens and their antibiotic susceptibility pattern among diabetic patients. BMC Infectious Diseases 19:1–0.

19. How To Calculate Sample Size Using a Sample Size Formula.

20. Owusu E, Adjei H, Afutu E. (2022) Similarities in bacterial uropathogens and their antimicrobial susceptibility profile in diabetics and their non-diabetic caregivers at a National Diabetes Management and Research Centre, Accra-Ghana. Diseases 10:124.

21. Ahmed AE, Abdelkarim S, Zenida M, Baiti MA, Alhazmi AA, Alfaifi BA, Majrabi RQ, Khormi NQ, Hakami AA, Alqaari RA, Alhasani RA. (2023) Prevalence and associated risk factors of urinary tract infection among diabetic patients: A cross-sectional study. Healthcare 11:861.

22. Odoki M, Bazira J, Moazam ML, Agwu E. (2015) Health-point survey of bacteria urinary tract infections among suspected diabetic patients attending clinics in Bushenyi district of Uganda. Spec Bact Pathog J 1:01.

23. Alemu M, Belete MA, Gebreselassie S, Belay A, Gebretsadik D. (2020) Bacterial profiles and their associated factors of urinary tract infection and detection of extended spectrum beta-lactamase producing gram-negative uropathogens among patients with diabetes mellitus at Dessie Referral Hospital, Northeastern Ethiopia. Diabetes, Metabolic Syndrome and Obesity 2935–48.

24. Hamdan HZ, Kubbara E, Adam AM, Hassan OS, Suliman SO, Adam I. (2015) Urinary tract infections and antimicrobial sensitivity among diabetic patients at Khartoum, Sudan. Annals of Clinical Microbiology and Antimicrobials 14:1–6.

25. Aamir AH, Raja UY, Asghar A, Mahar SA, Ghaffar T, Ahmed I, Qureshi FM, Zafar J, Hasan MI, Riaz A, Raza SA. (2021) Asymptomatic urinary tract infections and associated risk factors in Pakistani Muslim type 2 diabetic patients. BMC Infectious Diseases 21:1–6.

26. Confederat LG, Condurache MI, Alexa RE, Dragostin OM. (2023) Particularities of urinary tract infections in diabetic patients: A concise review. Medicina 59(10):1747.

27. Vicar EK, Acquah SE, Wallana W, Kuugbee ED, Osbutey EK, Aidoo A, Acheampong E, Mensah GI. (2023) Urinary tract infection and associated factors among pregnant women receiving antenatal care at a primary health care facility in the northern region of Ghana. International Journal of Microbiology 2023:3727265.

28. He Y, Zhao J, Wang L, Han C, Yan R, Zhu P, Qian T, Yu S, Zhu X, He W. (2025) Epidemiological trends and predictions of urinary tract infections in the global burden of disease study 2021. Scientific Reports 15:4702.

29. Anwar S, Benyamin J, Rauf MK. (2025) Frequency of uropathogens in patients admitted with urinary tract infection and diabetes mellitus.

30. Abdul-Sahib KY. (2008) Study of ciprofloxacin resistant Escherichia coli (CREC) in type 2 diabetic patients with symptomatic urinary tract infections. Iraqi J Comm Med 21:58–63.

31. Fu AZ, Iglay K, Qiu Y, Engel S, Shankar R, Brodovicz K. (2014) Risk characterisation for urinary tract infections in subjects with newly diagnosed type 2 diabetes. Journal of Diabetes and its Complications 28:805–10.

32. Addo MG, Adu-Poku M. (n.d.) Antimicrobial susceptibility profile of urinary tract pathogenic infections

in diabetic patients attending a health facility in Kumasi, Ghana.

33. Nabaigwa BI, Mwambi B, Okiria J, Oyet C. (2018) Common uropathogens among diabetic patients with urinary tract infection at Jinja Regional Referral Hospital, Uganda. African Journal of Laboratory Medicine 7:1–3.

34. Raoofi A, Ghavami M, Shahhamzeh M, Ghasemi M, Hedartabar R, Salehi L. (2016) The impact of demographic factors and blood sugar control on the incidence of urinary tract infections in Khorramabad in 2013. Iranian Red Crescent Medical Journal 18:.

35. Zubair KU, Shah AH, Fawwad A, Sabir R, Butt A. (2019) Frequency of urinary tract infection and antibiotic sensitivity of uropathogens in patients with diabetes. Pakistan Journal of Medical Sciences 35:1664.

36. Maggini S, Pierre A, Calder PC. (2018) Immune function and micronutrient requirements change over the life course. Nutrients 10:1531.

37. Kumar Jha P, Baral R, Khanal B. (2014) Prevalence of uropathogens in diabetic patients and their susceptibility pattern at a tertiary care center in Nepal-a retrospective study. Int J Bio Lab Sci 3:29–34.

38. Bashir H, Saeed K, Jawad M. (2017) Causative agents of urinary tract infection in diabetic patients and their pattern of antibiotic susceptibility. Khyber Medical University Journal 9.

39. Nuryati E. (2024) The relationship between level of education and the incidence of diabetic ulcers in diabetes mellitus patients at Griya Luka Pringsewu in 2024. In Proceeding of International Conference Social Technology Education and Health Science 2.

40. Lamb KE, Crawford D, Thornton LE, Shariful Islam SM, Maddison R, Ball K. (2021) Educational differences in diabetes and diabetes self-management behaviours in WHO SAGE countries. BMC Public Health 21:1–2.

41. Yen FS, Wei JC, Shih YH, Pan WL, Hsu CC, Hwu CM. (2022) Role of metformin in morbidity and mortality associated with urinary tract infections in patients with type 2 diabetes. Journal of Personalized Medicine 12:702.

42. Tseng CH. (2023) Effect of metformin on lower urinary tract symptoms in male patients with Type 2 diabetes mellitus: a retrospective cohort study in Taiwan. The World Journal of Men's Health 41:680.

43. Majhi RK, Mohanty S, Kamolvit W, White JK, Scheffschick A, Brauner H, Brauner A. (2021) Metformin strengthens uroepithelial immunity against E. coli infection. Scientific Reports 11:19263.

44. Clemens KK, McArthur E, Dixon SN, Fleet JL, Hramiak I, Garg AX. (2015) The hypoglycemic risk of glyburide (glibenclamide) compared with modified-release gliclazide. Canadian Journal of Diabetes 39:308–16.

45. Irawan J, Melissa I. (2024) Severe and recurrent hypoglycemia in an elderly patient with type 2 diabetes: the role of glibenclamide and urinary tract infection. Surabaya Medical Journal 2:66–72.

46. Al-Zaidi OS, Abdulhady Zwain L, Mahmoud EA. (2025) Statistical study of bacterial urinary tract infections for the period 2019 to 2023. Journal of University of Babylon for Pure and Applied Sciences :91–101.

47. Magliano E, Grazioli V, Deflorio L, Leuci AI, Mattina R, Romano P, Cocuzza CE. (2012) Gender and age-dependent etiology of community-acquired urinary tract infections. Scientific World Journal 2012:349597

48. Sharma V, Gupta V, Mittal M. (2012) Prevalence of uropathogens in diabetic patients and their antimicrobial susceptibility pattern. National Journal of Laboratory Medicine 1:26–8.

49. Yusuf A, Begum A, Ahsan CR, Bauer K. (2015) Antibiotic sensitivity pattern of gram-negative uropathogenic bacilli at a private hospital in Dhaka city. Al Ameen Journal of Medical Sciences 8:189–94.

50. Al-Naqshbandi AA, Chawsheen MA, Abdulqader HH. (2019) Prevalence and antimicrobial susceptibility of bacterial pathogens isolated from urine specimens received in Rizgary Hospital—Erbil. Journal of Infection and Public Health 12:330–6.

51. Kudinha T. (2017) The pathogenesis of Escherichia coli urinary tract infection. In: Escherichia coli—Recent Advances on Physiology, Pathogenesis and Biotechnological Applications. InTech .:45–61.

52. Bonadio M, Costarelli S, Morelli G, Tartaglia T. (2006) The influence of diabetes mellitus on the spectrum of uropathogens and the antimicrobial resistance in elderly adult patients with urinary tract infection. BMC Infectious Diseases 6:1–7

53. Shaikh SM, Tiwari S, Purandare VB, Bhalekar P, Bhake R, Patil NB, More HP, Unnikrishnan AG. (2025) Clinico-microbiological profile of urinary tract infections in patients with type 2 diabetes: A study based in a hospital dedicated to diabetes care. Chronicle of Diabetes Research and Practice 4:26–30.

54. Boison D, Akwetey SA, Osei SA, Kelechi S, Barnie PA. (2022) Nasal colonisation of methicillin-resistant Staphylococcus aureus in HIV-infected patients at the Cape Coast Teaching Hospital, Ghana. Frontiers in Tropical Diseases 3:976567.

55. Thacharodi A, Lamont IL. (2022) Aminoglycoside-modifying enzymes are sufficient to make Pseudomonas aeruginosa clinically resistant to key antibiotics. Antibiotics 11:884.

56. Kak G, Raza M, Tiwari BK. (2018) Interferon-gamma (IFN-γ): Exploring its implications in infectious diseases. Biomolecular Concepts 9:64–79

57. Memon AA, Sundquist J, Wang X, Palmér K, Sundquist K, Bennet L. (2013) The association between cytokines and insulin sensitivity in Iraqi immigrants and native Swedes. BMJ Open 3:e003473

58. Santetti D, de Albuquerque Wilasco MI, Dornelles CT, Werlang IC, Fontella FU, Kieling CO, Dos Santos JL, Vieira SM, Goldani HA. (2015) Serum pro-inflammatory cytokines and nutritional status in pediatric chronic liver disease. World Journal of Gastroenterology 21:8927.

59. Turner MD, Nedjai B, Hurst T, Pennington DJ. (2014) Cytokines and chemokines: At the crossroads of cell signalling and inflammatory disease. Biochimica et Biophysica Acta (BBA) - Molecular Cell Research 1843:2563–82.