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Multidrug Resistant Profile of Uropathogenic *Escherichia coli* (UPEC) Isolated from Diabetic Patients in Some Hospitals of Bauchi Metropolis, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background: Urinary Tract Infection (UTI) is a common pathogenic inflammatory, distressing and occasionally life-threatening condition that affects people of all ages and genders, with difficulty in treatment due to the high rate of antibiotic resistance. *Escherichia coli* is the primary cause of UTIs in humans both in diabetic and non-diabetic patients. Diabetic patients are more prone to urinary tract infection due to their immunocompromised system and hyperglycemia level compared to non-diabetic patients. Antibiotics are becoming less and less effective, therefore there is an urgent need to curtail this problem in order to have good administration of antibiotics to patients for effective treatment.

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Aim: To determine the multidrug resistance profile of uropathogenic *Escherichia coli* (UPEC) isolated from diabetic patients in some hospitals of Bauchi metropolis, Nigeria

Methods: A total of 288 study participants were enrolled in the study, (194 diabetic and 94 non-diabetic patients). Clean catch mid-stream urine samples were collected from all the participants in sterile containers. Each urine sample was streaked onto CLED (cysteine lactose electrolyte deficient) agar, incubated at 37^0C for 24hours and the isolates were identified using standard methods. Data obtained were analyzed statistically.

Results: A total of 64 UPEC were isolated from diabetic patients and 35 UPEC was isolated from non-diabetic patients. The age group of 31-40 had high frequency of occurrence in both the study participants, 18(28.1) in DM and 9(25.7) in NDM patients. While age group of 10-20 had 5(7.8) in DM and 2(5.7) in NDM patients and ≥ 71 years 2(3.1) in DM and 1(2.9) in NDM patients had the least. There was no significant difference between age group and the number of isolates as p> 0.05. Highest frequency of UPEC was found within the female 36(56.3) in DM and 20(57.1) in NDM patients than their male counterparts 28(43.8) in DM and 1(2.9). Type2 patients have high frequency of isolates compared to the Type 1 patients in Both the study participants. In the present study, 52 UPEC isolates from diabetic patients and 27 UPEC isolates from non-diabetic patients were resistant to 1 drug in 3 or more antimicrobial agents classes (multidrug resistance). The highest resistance was observed against ampicillin and piperacillin-tazobactams, while the least resistance was in imipenem.

Conclusion: The study established that UPEC infection was more prevalent in diabetic than non-diabetic patients, and also more prevalent in the middle age group, female gender and Type2 diabetic patients. A high rate of multidrug resistance was observed in both the study participants, and this signals a tremendous problem in prescription of antibiotics to patients. The emergence of multi resistant strains of UPEC has added to the need for urgent development of more control measures and policies on the use of antibiotics.

Keywords: UPEC (uropathogenic E. coli), diabetic patients; non-diabetic patients; multidrug resistance.

1. INTRODUCTION

"Urinary Tract Infection (UTI) which is defined as the presence and active multiplication of microorganisms within the urinary tract is one of the commonest bacterial infections seeking treatment in clinical practice" [1]. "250 million people globally experience urinary tract infections (UTIs), it is one of the most common diseases in humans with a variety of etiological factors" [2]. "As stated by Vasudevan, the infection is named after the affected urinary organ or part and is known as cystitis (bladder infection) and pyelonephritis (kidney infection). The symptoms of bladder and kidney infections differ, with cystitis causing painful and frequent urination and pyelonephritis causing high fever and flank pain" [3].

"Diabetes mellitus (DM) is an ever-growing heterogenic disorder altering the metabolic abilities of the body, primarily characterized by persistently high glucose levels (hyperglycemia) resulting from defects in insulin secretion attenuating every bodily function" [4, 5]. It is among the most common non-communicable diseases in emerging and developed nations [6], it has a number of effects on the genitourinary system [7]. According to Ahmad et al,.[8], Diabetes Mellitus (DM) has become a significant public health issue worldwide and has emerged as a significant socio-economic burden for developing nations.

"UTIs are classified based on the type of infection (upper or lower UTI), the presence or absence of symptoms (symptomatic or asymptomatic), the tendency to recur (single episode or recurrent UTI), and the presence or absence of complicating factors (uncomplicated or complicated UTI)" [9,10,11,12,3,2]. Similarly, the risk of UTI increases with age, poor metabolic control, various impairments in the immune system and incomplete bladder emptying due to autonomic neuropathy [13].

"The common symptoms of UTI include burning micturition, urgency, dysuria, cramping in the lower abdomen, mental irritability, back or flank pain, chill, nausea, fever, vomiting, fatigue, and weakness" [14]. According to Kumar et al.,[15], "it is very important to screen diabetic patients for UTIs for timely diagnosis, complete treatment, and prevention of progression to renal complications and ultimately severe renal failure".

"Urinary tract infection (UTI) is among the most common medical condition seen in all age groups with DM" [13]. "Diabetic patients are highly susceptible to UTI compared to non-diabetics [8]. Evidence from various epidemiological studies showed that UTI is more common in females with diabetes than in non-diabetic females" [16], it is more common in diabetes because of a combination of host and local risk factors. Modification of the chemical composition of urine in diabetes mellitus can alter the ability of urine and support the growth of microorganisms [7,17].

"Recent epidemiological studies and analytical experimentation of patients with preexisting diabetes mellitus have authenticated their plausibility of developing UTIs that are potentially perilous with fatal manifestations" [4]. "Various impairments in the immune system, including humoral, cellular, and innate immunity may contribute to the pathogenesis of UTI in diabetic patients" [5].

According to Vasudevan et al., [3], bacteria are the primary cause of UTIs in humans and the most contributed bacterial pathogen of UTIs is *Escherichia coli* in diabetic and non-diabetic patients and others are *Klebsiella pneumonia*, *Staphylococcus saprophyticus*, *Proteus mirabilis*, *Enterococcus faecalis*, Group-B *Streptococcus*, *Pseudomonas aeruginosa*, *Candida* spp, and *Staphylococcus aureus* [14,15,18].

However, "among the bacterial species involved in UTIs, uropathogenic *Escherichia coli* strains (UPEC) are the most common. UPEC account for about 80% of uncomplicated UTIs, 95% of community-acquired infections, and 50% of hospital-acquired infections" [19]. UPEC also remains the most frequent pathogen in complicated UTIs [20]. According to Kot et al.,[2], UPEC is a heterogeneous group of extraintestinal pathogenic *E. coli* (ExPEC) that seem to originate from the gut.

Antimicrobial resistance is naturally occurring as a reaction of microbial organisms to environment [21]. "The emergence of multi-drug resistant (MDR) strains is escalating, causing urinary tract infections increasing both in community and hospital settings" [1,15,22]. Increasing cases of diabetes mellitus which consequently lead to more UTI cases and irrational use of antibiotics has led to emergence of multi-drug resistant strains [23]. "More so, studies in Africa have shown the need to have systematic screening of UTI in diabetic patients due to the increasing prevalence" [23].

"There is widespread concern about the high rates of resistance to antimicrobials used in the treatment of urinary tract infections, particularly in developing countries. Antibiotics, including broad-spectrum antibiotics, are frequently prescribed, which may lead to the development of antibiotic-resistant urinary pathogens. Patients with diabetes mellitus are more likely to have resistant pathogens, necessitating longer and more potent antimicrobial treatment. Improved glycemic control in diabetics may thus aid in the control of UTIs. Accurate screening for UTIs in diabetic patients is also critical to enable appropriate treatment and avoiding related complications" [24].

Diabetes mellitus (DM) has now become a global health issue to health care professionals [8]. **"**Frequent prescription of antibiotics, including the ones with broad-spectrum, has result in development of antibiotic-resistant urinary pathogens. Since patients with DM are more prone to have resistant pathogens, they inevitably require longer and more potent antimicrobial treatment" [24]. Therefore, improved control of glycaemia, timely diagnosis, complete treatment and screening for UTIs in diabetic patients is critical to prevent progression to renal complications and ultimately severe renal failure and other related complications.

2. MATERIALS AND METHODS

2.1 Study Area

The study area was conducted in Bauchi State, Nigeria. The study areas used for the collection of samples include; Abubakar Tafawa Balewa University Teaching Hospital (ATBUTH), Bauchi State, and Bauchi State Specialist Hospital.

2.2 Sample Collection

Each patient was informed to collect approximately 20 ml of midstream urine into a crew cap sterile calibrated urine container. Proper instructions and illustration were given to the patients in order to avoid contamination. At the point of collection, samples were labeled with name, sex and age of the patients. The samples were placed in an ice box and transported to Abubakar Tafawa Balewa University medical laboratory for further analysis, but in cases of delay, the urine samples were refrigerated at 4^{o}C to avoid the multiplication of bacteria [25].

2.3 Data Collection

A structured questionnaire and patient clinical sheet were used to seek for demographic data and clinical details (clinical symptoms, previous antibiotic usage, risk factors/behaviours). Verbal/informed consent was obtained from each patient to be enrolled in this study.

2.4 Inclusion/ Exclusion Criteria

The study will include diabetic and non-diabetic patients regardless of the presence of UTI symptoms. All other patients without these criteria were excluded.

2.5 Sample Size Determination

The number of samples that was collected were determined using the formula of [26]. Prevalence of p= 0.25(25%) based on previous study [27].

Using the formula

$$n = \frac{(Z)2\ p(1-p)}{d2}$$

Where;
n = Desired sample size
Z = 1.96 (The standard normal deviate, corresponds to the 95% confidence level).
p = Prevalence of previous study or related (0.25)
d = Degree of accuracy (5%)

$$\text{Therefore } n = \frac{(1.96)2\times 0.25(1-0.25)}{(0.05)2}$$

$$n = \frac{(1.96)2 \text{ x } 0.25 \text{ x } (0.75)}{(0.05)2}$$

$$n = \frac{3.8416x0.1875}{0\ .0025}$$

$$n = \frac{0.7203}{0.0025}$$

n=288.1
Approximately n= 288

2.6 Blood Glucose Test

Plasma glucose (after an overnight fasting of eight or more hours) was determined using the glucose meter Accu-Chek Active system (Roche Diabetes Care, Basel, Switzerland), using the manufacturer's instruction, this was carried out within fractions for each participant. DM was diagnosed according to World Health Organization [28] criteria with symptoms of diabetes plus a fasting blood glucose level equal to or more than 126 mg/dl.

2.7 Sample Processing

2.7.1 Inoculation and isolation of bacteria from urine samples

Urine samples were observed macroscopically for colour, blood tinge and turbidity. All the urine samples were aseptically inoculated using a sterile wire loop, a loopful of well-mixed uncentrifuged urine was aseptically inoculated unto Cysteine Lactose Electrolyte Deficient (CLED) agar by streak-plate method as described by [29,30,31]. The plates were incubated at 37^{o}C for 18-24 hours.

2.7.2 Identification and characterization of isolates

The colonies were further identified based on colonial morphology and biochemical tests (Indole test, Methyl Red test, Vogues Proskauer test, Citrate Utilization test, Coagulase and Catalase tests) as described by Cheesbrough et al. [29]. Colonies were observed for morphological features such as size, shape, edge consistency, margin, colour, opacity and lactose fermentation. In addition to these morphological features of the colonies, motility, Gram staining reaction, and biochemical tests were then analysed. The isolates were maintained on Nutrient agar slants, until required for further use [30].

2.7.3 Antimicrobial susceptibility testing of the UPEC isolates

The susceptibility pattern of the isolates to commonly used antimicrobial agents was determined using the Kirby-Bauer disc diffusion techniques as described by Vineetha et al., [32]. A loopful of growth of each isolate on agar medium was suspended in a sterile saline and then was diluted in steps of 1:10 to give turbidity equivalent to the 0.5 McFarland standards (a density of 1x10^{8} cells/mL) before inoculation. Muller-Hinton agar medium was prepared according to the manufacturer's instructions and was poured (about 25 ml of the media) into each of the sterile petri-plates, the plates were allowed to solidify. After the adjusting the turbidity of the inoculum, a sterile cotton swab stick was dipped into the suspension, and pressed firmly against the inside wall of the tube; the swab was streaked over the surface of the solidified Muller-Hinton agar plates 3 times rotating the plate after each application to ensure an even distribution and allowed to stand at room temperature for 10 minutes [33].

Antibiotic discs of known concentration ;Amoxicillin-clavulanate (30µg), Ceftriaxone (30 µg), Cefuroxime (30 µg), Ceftazidime (30 µg), Kanamycin (30 µg), Amikacin (30 µg), Gentamicin (10 µg), Streptomycin (10 µg), Ciprofloxacin (5 µg), Levofloxacin (5 µg), Nalidixic acid (30 µg), Ofloxacin (5 µg), Piperacillin tazobactam(100 µg), Imipenem (10 µg), Oxoid Ltd, UK were aseptically placed using sterile forceps and then gently pressed down on the Muller-Hinton agar plates to ensure a firm contact. The plates were then inverted and incubated at 37^{o}C for 24 hours. The diameter of the zone of inhibition produced by each antibiotic disk was measured and interpreted according to Clinical and Laboratory Standard Institute [34] guidelines.

2.8 Data Analysis

The data obtained was recorded in Microsoft Excel and analyzed by using Chi-square statistical analysis to show the association of each variable with the dependent variable.

3. RESULTS AND DISCUSSION

3.1 Characteristics of Participants Based on Blood Sugar Level (FBS)

In this study, patients who had ≥ 126 mg/dl of fasting blood sugar were considered as positive for diabetes mellitus, while those with fasting blood sugar (FBS) < 126 mg/dl were considered nondiabetics. According to World Health Organization [28]. (Table 1).

The amount of glucose in the bloodstream is referred to as blood glucose or blood sugar. Fasting blood glucose test is a simple test, accurate and inexpensive test that can screen for diabetes [28]. Diabetics have an impaired immune system, making them more susceptible to many illnesses, among these is urinary tract infection. Based on several researches, diabetic patients are more likely to develop UTIs than non-diabetic patients. There are numerous reasons that could explain the increased occurrence of UTI in diabetic individuals. Studies indicated that high glucose levels in urine promote the formation of uropathogens [35]. Higher glucose levels in renal parenchyma create a favorable environment for bacterial colonization, resulting in complications including emphysematous pyelonephritis [36]. Increased glucose levels may impair humoral, innate, and cellular immunity. Autonomic neuropathy can cause bladder dysfunction, resulting in urine retention and stasis.

Poor metabolic regulation causes hyperglycemia, which can lead to a decreased renal threshold for glucose reabsorption and glycosuria. Glycosuria provides a rich medium for bacterial species to thrive in the presence of decreased immunity. According to Taher et al., [37], elevated plasma glucose levels cause glucosuria, which promotes bacterial proliferation through an increase in cell count, implying neutrophil dysfunction.

3.2 Sociodemographic Variables of UPEC Infection Among Study Participants

In this study, the age range of 31-40 had the highest rate of *E. coli* infection in both the study participants, 28.1% in diabetic and 25.7% in non-diabetic patients. In this study, the female gender in both the study population has a highest rate of occurrence compared with their male counterparts. In this study, married participants have higher rate of infection in both diabetic and non-diabetic patients. While the literates have a higher rate of infection in NDM patients than NDM patients. And also, Urban dwellers have high rate of occurrence of UTI in both DM and NDM patients than rural dwellers. As shown in Table 2.

UTIs are more common and severe in patients with DM. they are also frequently caused by resistant pathogens [38]. Urinary tract infection is the most common bacterial infection with a high rate of morbidity and financial cost. The Uropathogenic *E. coli* (UPEC) being the most common etiological agent of UTI in diabetic and non-diabetic patients. UPEC associated UTIs among diabetic and non-diabetic patients have been reported in previous studies [39,36,37]. The most frequently isolated microorganism from urine sample of this study is *E. coli*. The risk of developing urinary tract infection in diabetes is higher due to abnormalities in the host defence and high glucose in urine, the occurrence and infection with UPEC have been increased in diabetic patients because hyperglycemia suppresses the level of the immune system among this category of people [40].

Table 1. Distribution of Study Participants Based on Blood Sugar Level (FBS)

Blood glucose level (mg/dL)	No (%) of patients tested (n=288)	Percentage (%)
High (Diabetic)	194	67.4
Normal (Non-diabetic)	94	32.6

Table 2. Distribution of UPEC Isolates in Diabetic and Non-Diabetic Patients According to Demographic Variables

Patients details	No of samples collected N=288	No (%) of UPEC in DM Patients (n=64)	No (%) of UPEC in NDM Patients (n=35)	χ2
Age (years)				
10-20	10	5(7.8)	2(5.7)	0.99
21-30	**30**	11(17.2)	7(20)	
31-40	**38**	18(28.1)	9(25.7)	
41-50	76	14(21.9)	8(22.9)	
51-60	68	9(12.5)	6(17.1)	
61-70	55	5(7.8)	3(8.6)	
≥71	11	2(3.1)	1(2.9)	
Gender				
Female	168	36(56.3)	20(57.1)	0.93
Male	120	28(43.8)	15(42.9)	
Marital status				
Single	14	10(15.6)	5(14.3)	0.62
Married	216	42(65.6)	20(57.1)	
Divorce	28	8(12.5)	8(22.9)	
Widow	30	4(6.3)	2(5,7)	
Education				
Literate	189	40(62.5)	19(54.3)	0.42
Illiterate	99	24(37.5)	16(45.7)	
Residence				
Rural	70	21(32.8)	11(31.4)	0.88
Urban	218	43(67.2)	24(68.6)	

Key: UPEC= uropathogenic E. coli, DM= Diabetic Mellitus, NDM= Non-Diabetic Mellitus

In this study, the age range of 31-40 had the highest rate of *E. coli* infection in both the study participants, 28.1% in diabetic and 25.7% in non-diabetic patients. This is in agreement with previous researches done by Jameel et al, [41,42] who all reported the high rate of urinary tract infection in this range: reported high-rate UTI in that age range. While this study is not in agreement with the reports of [43], who conducted his research in Sudan reported high rate in the age range 44 and above, [44] reported age range of 40-49 have the highest range of infection and also [45] from Kebbi Nigeria who reported high rate of frequency in the age range of 61-65. High rate of occurrence of UTI infection in this age range (31-40) may be attributed to the fact that people are more sexually active at this age range, and also difference might be due to the competent immune system and high treatment-seeking behavior at a young age [46].

The gender distribution showed that among female patients, 56.3% of diabetic patients and 57.1% of non-diabetic patients were infected with UPEC. For male patients, 43.8% of diabetics and 42.9% of non-diabetics had UPEC isolates.

In this study, the female gender in both the study population has a high rate of occurrence compared with male counterparts. This could be attributed to the fact that the female gender anatomical structure, short urethra, close proximity of the urethra to the anus, decreases of normal vagina flora, in general lifestyle habits of women are some of the predisposing factors that can increase the occurrence of UTI in females than males regardless of diabetic status [47,40].The result is in disagreement with the reports of [45,44] who reported a higher rate of infection in males than their female counterparts.

The marital status of patients was categorized as single, married, divorced, or widowed. Among single patients, UPEC was found in 15.6% of diabetic patients and 14.3% of non-diabetic patients. In married patients, the prevalence was 65.6% in diabetics and 57.1% in non-diabetics. For divorce divorced patients, 12.5% of diabetics and 22.9% of non-diabetics had UPEC isolates. Among widowed patients, UPEC was present in 6.3% of diabetic patients and 5.7% of non-diabetic patients

In this study, married participants have higher rate of infection in both diabetic and non-diabetic patients. This may be attributed to the fact that they are sexually active at this status, while the widows have the lowest rate of infection in both the study population. This is in accordance with the report of [16].

This among literate patients, 62.5% of diabetic patients and 54.3% of non-diabetic patients were infected with UPEC. For illiterate patients, the prevalence was 37.5% in diabetics and 45.7% in non-diabetics.

Literate have high rate of infection in DM compared to NDM patients. While illiterate have high rate of infection in NDM patients than NDM patients.

The residence of patients was classified as rural or urban. Among rural residents, UPEC was found in 32.8% of diabetic patients and 31.4% of non-diabetic patients. For urban residents, the prevalence was 67.2% in diabetics and 68.6% in non-diabetics. Urban dwellers have high rate of occurrence of UTI in both DM and NDM patients than rural dwellers. This may be attributed to the fact that the study was conducted in the city and most of the study participants live in urban areas.

3.3 Clinical Profile of UPEC Infection Among Participants Investigated in the Study

In this study, the rate of occurrence of UPEC infection based on the history of UTI is higher in first-time encounters of UTI in both diabetic and non-diabetic patients. In this study, history of antibiotic usage shows a higher rate in DM than NDM patients in those who that did not use antibiotics, while slightly higher in those who use antibiotics in NDM than DM patients. (Table 3).

Among patients with a history of UTI, 15.6% of diabetic patients and 25.7% of non-diabetic patients were infected with UPEC. Probably those with previous history of UTI will be more prone or have the second chance of acquiring the infection. For those without a history of UTI, the prevalence was 84.4% in diabetics and 74.3% in non-diabetics. The chi-square test for this variable resulted in $p = 0.22$, indicating no significant association between UTI history and UPEC prevalence.

In this study, DM patients with no previous history of UTI had higher rate of contracting UTI compared with those who had a previous history of the UTI.

Table 3. Distribution of UPEC Infection According to Clinical Variables of Patients

Clinical Variables	No of Samples Collected (n=288)	No (%) of UPEC in DM (n=64)	No (%) of UPEC in NDM (n=35)	χ2
History of UTI				
Yes	84	10 (15.6)	9 (25.7)	0.22
No	204	54 (84.4)	26 (74.3)	
History of Antibiotic Treatment				
Yes	23	5 (7.8)	3 (8.6)	0.89
No	265	59 (92.2)	32 (91.4)	
Types of Diabetes				
Type 1	92	16 (25)	N.A	
Type 2	196	48 (75)	N.A	-
Duration of Diabetes				
< 5 years	113	35 (54.7)	N.A	
≥ 5 years	175	39 (60.9)	N.A	-

Key: N.A = non-applicable, DM = Diabetic Mellitus

In this study, the frequency of UTI was higher among duration of DM greater than 5 years compared to those patients of DM duration less than 5 years. This is in agreement with the studies conducted by [22,43] from Sudan found high rate of infection present in ≥5 years of DM duration. It is very well known that patients with a longer duration of DM have an increased prevalence of chronic diabetic complications, which may lead to an increased presence of UTI [38]. In many of these patients, autonomic neuropathy results in dysfunctional voiding and urinary retention. [48].

The history of antibiotic treatment was also analyzed. Among patients with a history of antibiotic treatment, 7.8% of diabetic patients and 8.6% of non-diabetic patients had UPEC isolates. For those without such history, the prevalence was 92.2% in diabetics and 91.4% in non-diabetics. The chi-square test for this variable resulted in 0.89, indicating no significant association between antibiotic treatment history and UPEC prevalence.

Various studies have demonstrated that different outbreak of urinary tract infection in type 2 diabetic patients. Factors such as immune system disorders, weakening of white blood cells, poor blood supply, bladder dysfunction due to nephropathy and glucosuria can cause urinary tract infections in type 2 diabetic patients [5]. Dysuria is a complication of urinary tract infection in diabetic patients due to organ damage and even death due to the complexity of pyelonephritis. Also, these patients experience urinary retention, urgency, and incontinence during the night due to increased urination to excrete excess glucose. In this study, Type 2 DM patients have high rate of infection compared to Type1 DM patients, Type 2 has a prevalence of 25% while Type 1 has a prevalence of 25% in this study. This is similar to a study conducted by [49] where high rate of infection was observed in type 2 DM patients

3.4 Prevalence of UPEC Isolates According to Antibiotic Resistant Pattern in Diabetic and Non-diabetic Patients

Ampicillin and piperacillin-tazobactam have the highest rate of resistance in DM and NDM patients, while least resistance was observed in imipenem, ceftriaxone and ceftazidime. While the other antibiotics have moderate rate of resistance to the isolates.

The presence of multidrug resistance in this study could be attributed to the dissemination of antibiotic resistance among UPEC isolates. UPEC can be seen as one of the most common pathogens causing UTI in immunocompromised patients such as diabetics. In this study, a high rate of MDR was encountered in UPEC isolate of both DM and NDM patients. Ampicillin has resistance rate of 92.3% and 81.5% in diabetic and non-diabetic patients respectively. This is in agreement with studies of [50,40]. UPEC isolates were resistant also to piperacillin-tazobactam, nalidixic acid.

In this study, resistance rate was higher in older quinolones such as nalidixic acid in both the study participants than the newer quinolones such as ciprofloxacin, levofloxacin and ofloxacin. Findings by Maharjan et al, [51] reported similar observation in their study. Resistance of UPEC isolates to fluoroquinolones in both the study participants could be attributed to the common and overuse of quinolones and fluoroquinolones worldwide in the treatment of UTI worldwide [2]. Secondly, they are the most prescribed antibiotics in the treatment of UTI in this country [52].

On the other hand, imipenem, ceftriaxone, and ceftazidime were found to show the least resistance among the drugs used. This is in agreement with the reports of [52,36,40]. This could be attributed to the fact that they are not among the highly prescribed antibiotics for UTI treatment in the study area, and secondly because they are not easily available and highly expensive for purchasing them.

Among the aminoglycosides, kanamycin and gentamicin showed high rate of resistance than amikacin and streptomycin.

3.5 Multidrug Resistance Profile of UPEC Isolates According to Patients Status

The study showed 52 MDR UPEC isolates among diabetic patients and 27 UPEC isolates among non-diabetic patients. This indicates danger with respect to the global fight against antibiotic resistance among organisms especially in immunocompromised patients. The isolates resistant to three or more classes of antibiotics were termed MDR. Diabetes can be a factor associated with MDR *E. coli.* in this study, high rates of MDR *E. coli* in both diabetic and non-diabetic patients was observed as with the reports of [40,51]

Table 4. Distribution of UPEC isolates according to Antibiotic Resistant Pattern in Diabetic and Non-diabetic patients

Antibiotics(µg)	No (%) of UPEC isolates and MDR pattern n=64-for DM, n=35 for NDM	
	No (%) Resistant isolates in Diabetic	No (%) Resistant isolates in non diabetic
Ampicillin (10)	48(92.3)	22(81.5)
Amoxicillin-clavulanate (30)	39(75)	11(40.7)
Ceftriaxone (30)	16(30.8)	08(29.6)
Cefuroxime (30)	31(60.0)	16(59.3)
Ceftazidime (30)	17(32.7)	08(29.6)
Kanamycin (30)	42(80.8)	21(77.8)
Amikacin (30)	39(75)	20(74.1)
Gentamicin (10)	42(80.8)	19(70.4)
Streptomycin (10)	38(73.1)	18(66.7)
Ciprofloxacin (5)	27(51.9)	13(48.1)
Levofloxacin (5)	26(50)	11(40.7)
Nalidixic acid (30)	47(90.4)	21(77.8)
Ofloxacin (5)	28(53.8)	10(37.0)
Piperacillin tazobactam (100)	48(92.3)	22(81.5)
Imipenem (10)	10(19.2)	03(11.1)

Key DM- Diabetic mellitus, NDM- non diabetic mellitus, UPEC-Uropathogenic E.coli, MDR-multidrug resistance

Table 5. Distribution of Isolates According to Multidrug Resistance Pattern

Patient status	No of UPEC isolates	No of MDR isolates
Diabetic patients	64	52
Non- diabetic patients	35	27

The rapid development of resistance could be attributed to the irrational use of antibiotics and practices of self-medication among the general population thereby causing a problem in antibiotic therapy especially in developing countries due to lack of awareness and lack of effective implementation of the policy that regulates the use of antibiotics [53].

4. CONCLUSION

UPEC isolates were high in diabetic than non-diabetic patients. It could be observed that most of the UPEC isolates from both the groups exhibited a remarkable rate of antibiotic resistance to commonly prescribed antibiotics for UTI irrespective of diabetic status. The study revealed that a high rate of multidrug resistance from both the study participants, this reaffirms for the need for proper diagnosis and drug administration in the treatment of urinary tract infection especially in diabetic patients due to their immunological status.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

ETHICAL APPROVAL AND CONSENT

Ethical approval was granted by; Abubakar Tafawa Balewa University Teaching Hospital, reference number (ATBUTH/ADM/42/VOL.1). Ministry of Health Bauchi State Government Ethical Steering Committee, with reference number (BSMOH/REC/14/2023). More so, written informed consent was obtained from all patients prior to specimen collection. to Abubakar Tafawa Balewa University medical

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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