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RESEARCH ARTICLE

ANTIBIOTIC SUSCEPTIBILITY PATTERNS AMONG TYPE II DIABETIC PATIENTS WITH UTI IN THIKA LEVEL 5 HOSPITAL, KIAMBU COUNTY, KENYA

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ABSTRACT

Background: Diabetic patients are more prone to severe UTIs, thereby posing challenges in their management. Locally there is paucity of data on the patterns of uropathogens implicated in UTIs. Antibiotics are frequently prescribed empirically which results in excessive prescription of antibiotics with precedent complications including but not limited to resistant microbial agents in the population. This study investigated the antibiotic susceptibility patterns of bacterial pathogens causing UTI in diabetic patients in Thika level 5 hospital, Kiambu County, Kenya. **Methods:** A cross-sectional descriptive study was carried out with one hundred and seventy-eight type IIdiabetic patients attending the diabetic clinic with a positive urinalysis being enrolled into the study. The urine was cultured on cysteine lactose-electrolyte deficient (CLED) agar and blood agar media as per standard urine culture. Antibiotic sensitivity was done on Mueller-Hinton agar using Kirby-Bauer disk diffusion methods according to ClSI guidelines. Appropriate biochemical tests were done to identify the isolated bacteria. Consecutive sampling was used until the sample size was attained. Chi square test of significance was used to determine relationship between the categorical outcome variables with level of significance set at $P < 0.05$. Multivariate Logistics regression models was used to identify relationships between independent and dependent variables. **Results:** A total of 229 participants were included in this study of which 63.8% were females. The mean age of the participants was 52.52 and the most frequently observed symptom suggestive of UTI was frequent urination (67.2%).Among the culture-positive bacterial isolates, prevalence of gram negative bacteria was 88.89% while prevalence of gram positive bacteria was 11.11%. The major microorganisms isolated were *Escherichia coli* (56.7%), *Klebsiella pneumoniae* (16.7%), *Candida albicans* (10%), and *Staphylococcus aureus* (6.7%).E. coli showed higher sensitivity to Imipenem/meropenem (78.6%), gentamicin (73.3%), piperacillin/tazobactam (75.0%), nitrofurantoin (100%), ertapenem (100%), and amikacin (100%) but resistant to amoxiclav (100%), ampicillin (100%), cefuroxime and ciprofloxacin (70.6% each). *S. aureus* was sensitive to gentamicin, ampicillin, and nitrofurantoin (100% each) while resistant to clindamycin and erythromycin (100% each). **Conclusion:** The predominant pathogens causing UTI were gram negative bacilli, the Enterobacteriaceae, particularly E. coli. UTI development had a significant association with the sex of participants, and specific positive urinalysis results (leucocyte esterase, nitrites, pus cells, and appearance of urine). These factors were individually and statistically significant ($p < 0.05$) from the initial binomial regression but with nitrite results as the only factor showing statistical significance following multivariate regression. Based on the antimicrobial susceptibility test results, it may be inferred that amikacin is among the drugs of choice for UTI treatment in this study area. The isolated gram negative micro-organisms also demonstrated high resistance (100%) to commonly used antibiotics; ampicillin, and amoxiclav. Therefore, management should be supported by culture and sensitivity testing and clinicians may need to revise their prescription habits based on the sensitivity findings.

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INTRODUCTION

Urinary Tract Infection (UTI) is an inflammatory response of the urothelium to bacterial invasion that is often associated with bacteriuria and pyuria. Its presentation varies widely from asymptomatic bacteriuria to urosepsis, as does the causative agents. It is among the most common infection encountered in medicine as it affects both men and women of all ages. It is estimated that a woman lifetime incidence for contracting a UTI is roughly 50%. The burden of UTI globally is estimated to be about 150 million annually. Locally there is incomplete data about the UTI incidence rate, because in most cases the diagnosis is made without the benefit of culture due to the high cost of the test, as well as lacking laboratories that can accurately perform tests. Given the magnitude of the burden, UTIs pose in terms of morbidity, mortality, and cost treatment. It is certainly prudent to do more research in this area to better understand the pathogenesis, risk factors and the ever-changing bacterial pattern as well antimicrobial sensitivity. All these will go a long way in prevention strategies as well as optimizing management protocols. The burden of non-communicable diseases like diabetes and its complications on the health care system is increasing. Susceptibility patterns of uropathogens among diabetic patients in Thika level 5 has not been documented. Treatment of UTI without antimicrobial sensitivity guidance may lead to antibiotic resistance of the few available antimicrobials. Because of the ever-changing dynamic nature of antimicrobial sensitivity, institutions must keep abreast by continuous surveillance of the sensitivity patterns within the hospitals. This will reduce antibiotic resistance and play a role in antibiotic stewardship practices. UTI is a common complication among the diabetic patients. Treatment of UTI should be guided by the susceptibility patterns and therefore this study will give information that will be useful in guiding the antibiotic treatment. This study was designed to identify antibiotic susceptibility of bacterial pathogens causing UTI in diabetic patients in Thika level 5 hospital, to identify the uropathogens causing UTI in diabetic patients in Thika level 5 hospital, and to correlate urinalysis and urine culture results among diabetic patients.

MATERIALS AND METHODS

Study setting: The study was carried out in Thika level 5 hospital laboratory located in Kiambu county. Thika level 5 hospital is an inter-county referral hospital. It has a catchment area that covers sub-counties of Thika, Juja, Gatundu North and parts of other counties which include Nairobi, Kitui, Machakos, Kirinyaga, and Murang'a. It has 349 inpatient bed capacity and runs several outpatient clinics including a diabetes out-patient clinic.

Study design: A cross-sectional descriptive study was conducted.

Variables

Independent variables: Age, Sex, and monthly income.

Dependent variables: Uropathogens isolated from urine culture, the sensitivity pattern of the pathogens to antimicrobials and the correlation between urinalysis and urine culture results.

Study population: All type II diabetic patients attending the diabetic clinic at Thika level 5 hospital diagnosed with UTI based on urinalysis.

Inclusion criteria: Type II diabetic patients attending diabetes clinic with UTI diagnosed by urinalysis.

Exclusion criteria: Patients already on antibiotics therapy. Patients with urinary catheters

Sample size calculation

This study will use Fischer et al., 2005 formula: $n = \frac{Z^2P(1-P)}{d^2}$
Where:

n – minimum required sample size
Z – standard normal for a 2-sided test at 95% confidence interval (CI) = 1.96
P – Postulated prevalence (12 %) (7)
d – margin of error of estimation = 5%
n= 162 samples
A minimum of 178 samples will be targeted to include 10% attrition rate.

Sampling techniques: Consecutive sampling of patients was performed for patients attending diabetic clinic which run from Monday to Friday. Patients who met the inclusion criteria were recruited atthe clinic. The study investigators had no direct contact with the patients and were provided with the clean catch mid-stream urine samples containing only identification numbers by the hospital laboratory staff. All samples with a positive urinalysis report were subjected to culture and sensitivity.

Culturing for bacteria: Mid-stream clean catch urine samples collected in sterile containers. Ten millilitres of clean catch midstream urine sample were collected in a wide mouthed sterile container from each study participant. The collected urine samples were labelled and delivered to the microbiology laboratory within 2 hours at ambient temperature. Hands were washed thoroughly with soap to and sterilized with 70% ethanol. All supplies required for procedure were placed on a sterile clean bench and properly labelled to minimize contamination and unnecessary movement. Urine samples were processed using a calibrated loop (0.001 ml) and inoculated cysteine lactose-electrolyte deficient (CLED) agar plates. After overnight incubation at 37 °C for 24–48 h' colonies were counted to check significant growth. Colony counts of bacterial growth $>10^5$/ml of urine were considered significant.

Isolation of bacterial isolates: Standard bacteriology technique employed involved colony morphology, gram smear picture, bench tests such as catalase, oxidase, coagulase, citrate and urea utilization biochemical tests were used for bacterial identification. Antibiotic sensitivity was done on Mueller-Hinton agar using Kirby-Bauer disk diffusion methods according to Clinical & Laboratory Institute Guidelines (ClSI).

Characterization of the isolates: Samples from the pure isolates were analysed physio-chemically to help identify species of bacteria present in the urine. This was done by picking a portion of growth from the surface of the culture and smearing it on a clean glass slide and left to air dry.

Heat was used to fix the smear that was later stained using appropriate stains by following the Gram staining procedure as described by Graham, rinsed and allowed to dry (in order to avoid refraction of light upon addition of oil emersion during microscopy at 100*). Microscopy was done at 4× 10× 40× 100×.so as to facilitate identification of the bacteria. Further characterization was done by carrying out biochemical tests.

Morphological characterization of the isolates: Gram staining technique was used to divide isolates on the basis of reaction and morphology. Air dried smears of the isolates were heat fixed and the smears were flooded with crystal violet for 60 seconds and then rinsed by washing with running water. The smears were then flooded with Gram's iodine for 60 seconds and rinsed with running water. Decolonization of the smears was done using ethanol (95%) for 10 seconds and immediately rinsed with water. The smears were then counterstained with safran in for 60 seconds and gently rinsed with running water before being left to air dry. Microscopy of the stained smears was done at 100 x objectives.

Biochemical and Physiological Characterization

Catalase test: Catalase test was used to investigate whether the bacteria can produce catalase enzyme which breaks down hydrogen peroxide into water and oxygen. The production of catalase was determined by addition of one drop of 3% hydrogen peroxide to 24 hours cultures of each of the pure isolates grown on nutrient agar based on the methods outlined by. Isolates that were found to be positive for catalase test were indicated by the presence of air bubbles while the absence of bubbles indicated a negative catalase test.

Citrate utilization: The ability of the isolates to use Simmons' citrate agar as carbon source for their energy was investigated by inoculation of the isolates using the streak technique on the media containing Simmons' citrate agar. Change in colour from green to deep blue indicated a positive test while retention of the same colour (green) indicated a negative test.

Urease Test: The ability of the isolates to hydrolyse urea was investigated by inoculation of the isolates using the streak technique on media containing urea agar base. Change in colour from orange to pink indicated a positive test and change to yellow colour was indicative of a negative test.

List of Antibiotics: Co-trimoxazole, Ciprofloxacin & Levofloxacin, Cefuroxime, Ceftriaxone & Cefotaxime,Cefepime, Imipenem/ Meropenem, Ampicillin & Piperacillin, Gentamycin, Amikacin, Piperacillin/Tazobactam, Amoxicillin/Clavulanate, Nitrofurantoin, Ertapenem.

Data collection tools: A questionnaire was used to collect the data. The questionnaire contained unique patient identifier with the correct match of specimen information. The information on the bacterial growth and sensitivity findings was input in the questionnaire.

Data analysis: Data was coded, entered and analyzed using statistical software SPSS version 25.0. Descriptive statistics was used to summarize data in order to give meaningful information. Chi square test of significance was used to determine relationship between the categorical outcome variables with level of significance set at $P < 0.05$. Multivariate Logistics regression models was used to identify relationships between independent and dependent variables.

Ethical considerations: Ethical approval was sought from JKUAT ethical review committee and National Commission for Science, Technology & Innovation (NACOSTI). Clearance was sought from Thika level 5 hospital management. Confidentiality was maintained and no patient identifier was used. The participants were informed of the details of this study and informed consent was sought from each participant. All the data was password protected, and questionnaires were locked away after the study.

RESULTS

Socio-demographic Characteristics of Participants: Among 229 participants included in this study, 146 (63.8%) were female and 83 (36.2%) were male. The mean age of all participants was 52.52. Majority of the participants (50.2%, n=115) had a monthly income 0-10000, while 47.6% (n=109) had an income of 10001-50000 (Table 4.1).

Table 4.1. Socio-demographic characteristics of Participants

Variables		n (n%)
Sex	Female	146 (63.8)
	Male	83 (36.2)
Age	14-35	33 (14.4)
	36-58	106 (46.3)
	59-80	90 (39.3)
Monthly Income	0-10000	115 (50.2)
	10001-50000	109 (47.6)
	50000-100000	5 (2.2)

Clinical features of UTI: Symptoms suggestive of UTI were observed in 225 (98.3%) of the participants. The most frequently observed symptoms were frequent urination, which was observed among 154 (67.2%), nocturia 54 (23.6%), persistent urge to urinate 34 (14.8%), and burning sensation while urinating 34 (14.8%). Pelvic pain, fever, cloudy urine, nausea & vomiting, foul smelling urine, red, bright pink or cola colored urine, flank pain and urethral discharge were also observed among 25 (10.9%), 20 (8.7%), 14 (6.1%), 11 (4.8%), 8 (3.5%), 7 (3.1%), 6 (2.6%), and 4 (1.7%) participants, respectively (Table 4.2).

Table 4.2. Frequency of symptoms suggestive of UTI among Type 2 DM patients with UTI

Symptoms of UTI	Frequency	Percentage
Frequent urination	154	67.2%
Persistent urge to urinate	34	14.8%
Cloudy urine	14	6.1%
Nocturia	54	23.6%
Burning sensation while urinating	34	14.8%
Red, bright pink or cola colored urine	7	3.1%
Foul smelling urine	8	3.5%
Pelvic pain	25	10.9%
Urethral discharge	4	1.7%
Fever	20	8.7%
Nausea and vomiting	11	4.8%
Flank pain	6	2.6%

Micro-organisms Isolated: In this study, out of the 229 collected samples, 13.1% were culture positive while 86.9% had no microorganism isolated.

Table 4.3. Antimicrobial susceptibility patterns of gram-negative bacteria

Antimicrobial agent	Micro-organism Isolated											
	E. coli (n =17)			K. pneumonia (n = 5)			P. aeruginosa (n = 1)			P. mirabilis/vulgaris (n = 1)		
	S	I	R	S	I	R	S	I	R	S	I	R
Cotrimoxazole	4 (33.3)	0 (0)	12 (66.7)	3 (60)	0 (0)	2 (40)	ND	ND	ND	1 (100)	0 (0)	0 (0)
Cefuroxime	3 (17.6)	2 (11.8)	12 (70.6)	1 (13)	2 (40)	2 (40)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)
Cefotaxime	7 (43.7)	1 (6.3)	8 (50.0)	2 (40)	1 (13)	2 (40)	ND	ND	ND	0 (0)	0 (0)	1 (100)
Ciprofloxacin/Levofloxacin	5 (29.4)	0 (0)	12 (70.6)	5 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)
Imipenem/Meropemen	11 (78.6)	0 (0)	3 (21.4)	5 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)
Gentamycin	11 (73.3)	0 (0)	4 (26.7)	4 (80)	1 (13)	0 (0)	1 (100)	0 (0)	0 (0)	0 (0)	0 (0)	1 (100)
Ampicillin	0 (0)	0 (0)	14 (100)	0 (0)	0 (0)	4 (100)	ND	ND	ND	0 (0)	0 (0)	1 (100)
Piperacillin/Tazobactam	9 (75.0)	1 (8.3)	2 (16.7)	4 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)
Nitrofurantoin	15 (100)	0 (0)	0 (0)	4 (80)	0 (0)	1 (13)	ND	ND	ND	0 (0)	0 (0)	1 (100)
Amoxiclav	0 (0)	0 (0)	3 (100)	0 (0)	0 (0)	2 (100)	ND	ND	ND	0 (0)	0 (0)	1 (100)
Cefepime	4 (40)	0 (0)	6 (60)	4 (80)	0 (0)	1 (13)	ND	ND	ND	ND	ND	ND
Ertapenem	7 (100)	0 (0)	0 (0)	4 (100)	0 (0)	0 (0)	ND	ND	ND	ND	ND	ND
Amikacin	8 (100)	0 (0)	0 (0)	3 (100)	0 (0)	0 (0)	ND	ND	ND	ND	ND	ND
Aztreonam	ND	ND	ND	ND	ND	ND	0 (0)	0 (0)	1 (100)	ND	ND	ND

ND = NOT DONE

Table 4.4: Antimicrobial susceptibility patterns of gram-positive bacteria

Antimicrobial agent	Micro-organism Isolated					
	S. aureus (n = 2)			E. faecalis (n = 1)		
	S	I	R	S	I	R
Cotrimoxazole	1 (50)	0 (0)	1 (50)	ND	ND	ND
Cefuroxime	ND	ND	ND	ND	ND	ND
Cefotaxime	ND	ND	ND	ND	ND	ND
Ciprofloxacin/Levofloxacin	1 (50)	0 (0)	1 (50)	0 (0)	0 (0)	1 (100)
Imipenem/Meropemen	ND	ND	ND	ND	ND	ND
Gentamycin	2 (100)	0 (0)	0 (0)	ND	ND	ND
Ampicillin	1 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)
Nitrofurantoin	2 (100)	0 (0)	0 (0)	1 (100)	0 (0)	0 (0)
Clindamycin	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	1 (100)
Erythromycin	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	1 (100)
Amikacin	1 (100)	0 (0)	0 (0)	ND	ND	ND
Vancomycin	ND	ND	ND	1 (100)	0 (0)	0 (0)

ND = NOT DONE.

Table 4.5. Isolation rate of microorganisms in Diabetes mellitus patients Investigated for UTI in relation to Associated factors

Variables		Culture Results		COR (95% CI)	AOR (95% CI)	p-value
		Positive n (n%)	Negative n (n%)			
Sex	Male	5 (6.1)	77 (93.9)	1	1	
	Female	25 (17)	122 (83)	3.223 (1.184-8.774)	1.529 (0.481 - 4.861)	0.022
Age	14-35	4 (12.2)	29 (87.8)	0.806 (0.230-2.817)	1.052 (0.207 - 5.348)	0.735
	36-58	17 (16.0)	89 (84)	0.582 (0.246-1.378)	0.522 (0.177 - 1.535)	0.218
	59-80	9 (10)	81 (90)	1	1	
RBS level	<7.0 mmol/l	9 (15)	51 (85)	1.244 (0.535-2.890)	0.661 (0.214 - 2.049)	0.612
	>7.1 mmol/l	21 (12.4)	148 (87.6)	1	1	
Urinalysis Results						
Specific gravity	< 1.021	23 (12)	169 (88)	0.583 (0.230 -1.480)	0.481 (0.079 - 2.915)	0.256
	> 1.021	7 (19)	30 (81)	1	1	
Leucocyte esterase	Negative	15 (7.8)	178 (92.2)	1	1	
	Positive	15 (41.7)	21 (58.3)	8.476 (3.635 - 19.764)	2.644 (0.833 - 8.393)	<0.001
Nitrites	Negative	21 (9.7)	195 (90.3)	1	1	
	Positive	9 (69.2)	4 (30.8)	20.893 (5.921 - 73.721)	9.684 (1.368 - 68.547)	<0.001
Glucose	Negative	11 (9.4)	106 (90.6)	1	1	
	Positive	19 (17)	93 (83)	0.508 (0.230-1.123)	0.885 (0.308 - 2.543)	0.094
Pus cells	Negative	19(9.1)	190 (90.9)	1	1	
	Positive	11 (55)	9 (45)	0.082 (0.030 - 0.222)	0.418 (0.088 - 1.981)	<0.001
Appearance	Pale yellow	10 (8.2)	112 (91.8)	1	1	
	Straw/amber	8 (9.4)	77 (90.6)	13.440 (4.658 - 38.777)	2.892 (0.618 - 13.534)	<0.001
	Cloudy	12 (54.5)	10 (45.5)	11.550 (3.803 - 35.082)	3.296 (0.664 - 16.365)	<0.001

COR: crude odds ratio; AOR: adjusted odds ratio; CI: confidence interval.

Among all the culture-positive bacterial isolates, prevalence of gram negative bacteria was 88.89% (24 out of 27) while prevalence of gram positive bacteria was 11.11% (3 out of 27). The major microorganisms isolated were *Escherichia coli* (56.7%), *Klebsiella pneumoniae* (16.7%), *Candida albicans* (10%), and *Staphylococcus aureus* (6.7%). *Pseudomonas aeruginosa, Proteus mirabilis/vulgaris*, and *Enterococcus faecalis* were also isolated, each with a prevalence of 3.3% (Figure 4.1).

Antimicrobial susceptibility patterns: The antimicrobial susceptibility test was performed on all culture-positive urine samples on Mueller-Hinton agar using the Kirby-Bauer disk

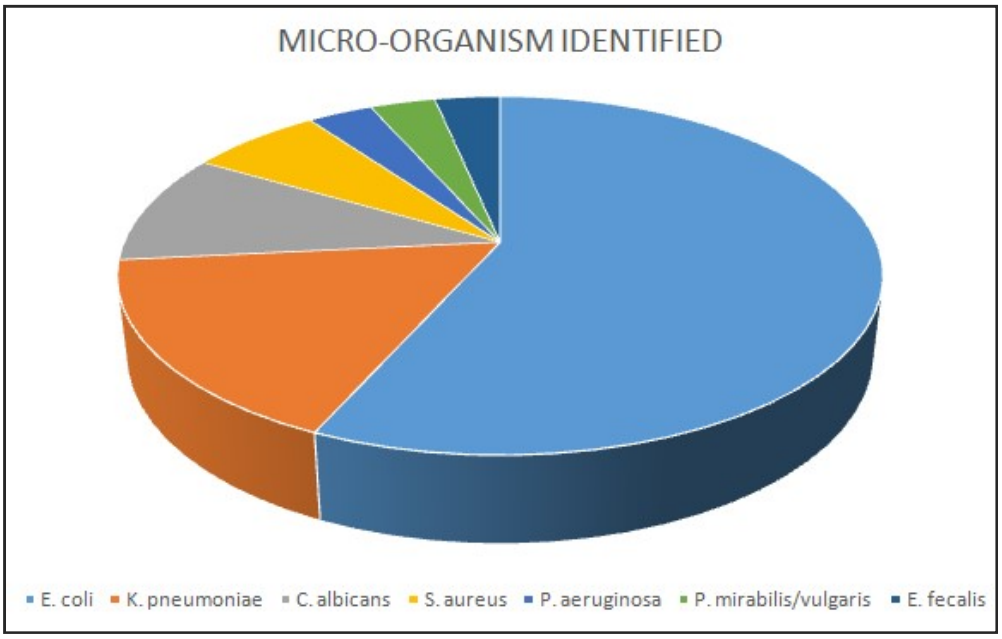

Figure 4.1. Percentages of Microorganisms Isolated

diffusion method. Gram-negative bacterial isolates (n=24) were tested against 14 antibiotics while Gram-positive isolates (n=3) were tested against 9 antibiotics (Table 4.3 and 4.4 respectively). Sensitivity to Gram-negative isolates was highest for ertapenem and amikacin, with a rate of 100% for both E. coli and K. pneumoniae, whereas the highest level of resistance was observed for ampicillin and amoxiclav, with a rate of 100% for E. coli, K. pneumonia, and P. mirabilis/vulgaris. *E. coli*, the most frequently isolated bacteria, was highly resistant to ampicillin (100%) and amoxiclav (100%) (Table 4.3). Overall, Gram-positive bacterial isolates (n = 3) showed 100% sensitivity to five of the tested antibiotics, whereas a high level of resistance was observed to clindamycin and erythromycin (100%) (Table 4.4).

Microorganisms isolated in DM patients in relation to Associated factors: A logistic regression model was conducted to obtain the crude odds ratio (COR) and adjusted odds ratio (AOR) for all the included factors (sex, age, random blood sugar level, and urinalysis results (specific gravity, leucocyte esterase, nitrites, glucose, WBCs, pus cells and appearance)). The dependent variable is the urine culture results of the participants. The COR and the statistical significance for each independent variable was separately determined using binomial logistic regression. The initial results show that sex of participants and specific urinalysis results (leucocyte esterase, nitrites, pus cells, and appearance of urine) are individually and statistically significant factors ($p < 0.05$). The results of this study indicate that the chance of getting a culture positive urinary tract infection among female Diabetes mellitus patients was more than three times greater (COR; 3.223 [95% CI = 1.184–8.774]) than among the male patients. The CORs for leucocyte esterase, nitrites, pus cells, and straw amber and cloudy appearance of urine are 8.476 (95% CI = 3.635–19.764), 20.893(95% CI = 5.921–73.721), 0.082 (95% CI = 0.030–0.222), 13.440 (95% CI = 4.658 – 38.777), and 11.550 (95% CI = 3.803 – 35.082) respectively (Table 4.5).

However, other factors such as age, random blood sugar level, specific gravity, and glucose levels of urine were not statistically associated with culture positive results. A multivariate logistic regression model was then used to calculate the AORs where all independent variables were included. The results of this regression indicated that the nitrite results from the urinalysis is the only factor that shows statistical significance with an AOR of 9.684 (95% CI = 1.368–68.547).

DISCUSSION

Urinary tract infection can be caused by both gram negative and gram positive bacteria. The most commonly encountered bacteria are the gram negative with E. coli making up the largest proportion of bacterial uropathogens (1). The most frequently isolated bacteria in this study was*E. coli* (56.7%). These findings were comparable with similar studies done in Uganda (50%) (2), and Eastern Ethiopia (47.5%) (3). However, another study in Nekemte, Ethiopia (4)found *S. aureus* and Coagulase Negative Staphylococcus (24.2% each) as the most commonly isolated organisms in diabetic patients with UTI followed by E. coli (12.1%). These variations could be attributed to geographical variations or variations over time within a particular population (5). The second most frequently isolated bacteria in this study was*K. pneumoniae* (16.7%), similar to studies in Northwest Ethiopia (6), Addis Ababa, Ethiopia (7), and Sudan (8). In this study, *Staphylococcus aureus*accounted for 6.7% of the organisms isolated while *Pseudomonas aeruginosa, Proteus mirabilis/vulgaris*, and *Enterococcus faecalis* all had a prevalence of 3.3%. A study by Nath et al. (2021)(9)also found *Pseudomonas aeruginosa and Proteus mirabilis/vulgaris* in less numbers among the isolated bacteria from diabetic patients with UTI.This study and prior research indicate a significant amount of Enterobacteriaceae isolated in the urine of diabetic patients with UTI, suggesting potential fecal contamination and poor hygiene practices.

Additionally, *E. coli* has virulence factors that enhance their colonization of the urinary tract epithelial lining and prevent urine flow from expelling the bacteria (10). Generally, all the gram-negative microorganisms isolated in this study exhibited high susceptibility to piperacillin-tazobactam with *K. pneumonia, P. aeruginosa,* and *P, mirabilis* being 100% susceptible. Similarly, Nath et al. (2021) (9)found that these 3 gram-negative organisms were highly susceptible to Piperacillin-tazobactam (100%). In the current study, three of the gram-negative organisms isolated (*E. coli, K. pneumoniae*, and *P. aeruginosa*) were also highly susceptible to Gentamicin (73.3%, 80%, and 100% respectively). These findings were comparable to those of a study in Southwest Ethiopia (10)where *E. coli* and *K. pneumoniae* showed 70% and 87.5% susceptibility to Gentamicin respectively. In the current study, both *E. coli*(100%) and *K. pneumoniae*(80%) were highly susceptible to Nitrofurantoin. Similarly, a study in Addis Ababa, Ethiopia (7)also found that *E. coli* and *K. pneumoniae* were both 100% susceptible to Nitrofurantoin. In this study, *E. coli* and *K. pneumoniae* were 100% susceptible to Ertapenem and Amikacin. On the contrary, Patra et al. (2019)(11) found that *Klebsiella* was 71.5% resistant to Amikacin. Generally, the gram-negative microorganisms in this study were highly resistant to ampicillin, amoxiclav, cefuroxime, and cefotaxime. More specifically, this study found that *E. coli, K. pneumoniae*, and *P. mirabilis/vulgaris* were 100% resistant to ampicillin and amoxiclav. A study in Ethiopia (7) also found high resistance patterns exhibited by gram negative bacteria against ampicillin and amoxiclav, with *E. coli* and *K. pneumoniae* being 100% resistant to these two antimicrobials. In our study, while *E. coli* was highly resistant to ciprofloxacin (70.6%), *K. pneumoniae, P. aeruginosa*, and *P. mirabilis/vulgaris* were highly susceptible (100%). A study in Southwest Ethiopia (10) however, found that *E. coli* and *K. pneumoniae* were highly sensitive to ciprofloxacin, while *P. aeruginosa* and *P. mirabilis* were highly resistant. The current study also found that both *P. aeruginosa*, and *P. mirabilis/vulgaris* were 100% resistant to Cefuroxime and Meropenem/Imipenemwhile *E. coli* and *K. pneumonia* were highly susceptible to Imipenem/Meropenem (78.6% and 100%) respectively.

Notably, all gram-negative isolates in this study showed high resistance to more than one antimicrobial. A study in Kisii, Kenya (12)also found that bacterial pathogens causing UTI among Type 2 Diabetes Mellitus patients exhibited high multi-drug resistance rates. The significantly increased occurrence of resistance to frequently used antibiotics such as ampicillin and amoxiclav could be attributed to various reasons such as the increased accessibility of these medications outside medical facilities, which results in careless usage without prescription (7). Furthermore, factors such as the high prevalence of counterfeit and low-grade versions of these antimicrobials and the frequent use of empiric antibiotics for preventive purposes may contribute to the rising resistance rates (7). The absence of reliable and accurate data regarding antibiotic susceptibility and resistance in most developing countries worsens the antibiotic resistance crisis. Such data is typically useful in implementing interventions that help to combat antibiotic resistance (12). In this study, 2 gram positive isolates were obtained; *Staphylococcus aureus* and *Enterococcus faecalis* each with a rate of 6.7% and 3.3% respectively. *S. aureus* was the leading gram positive isolate in this study, similar to a study done in South Ethiopia (13).

However, both *Enterococcus spp.* and *Coagulase Negative Staphylococcus* in Addis Ababa, Ethiopia(7), and only *Enterococcus spp.* in Sudan (8), were the leading gram-positive isolates, showing some variation in prevalence of gram positive bacterial isolates in different geographic areas. The overall percentage of antimicrobial sensitivity of gram positive isolates in this study was generally high. For instance, *S. aureus* isolates were 100% sensitive to amikacin, nitrofurantoin, gentamycin, and ampicillin. Previous studies from South Ethiopia also reported a high sensitivity rate (100%) for the former 2 antibiotics (13). Similarly*, E. faecalis* isolates were 100% sensitive to ampicillin, nitrofurantoin and vancomycin, a finding that was also observed in previous studies in Ethiopia, where 100% sensitivity was reported to ampicillin, nitrofurantoin and vancomycin (7). The 2 gram positive bacterial isolates demonstrated the highest level of resistance (100%) to clindamycin and erythromycin. Previous studies from South Ethiopia also reported a high level of resistance (100%) against erythromycin (13). However, mixed results were observed in regard to ciprofloxacin/levofloxacin where *S. aureus* was 50% resistant, as was the case in other studies elsewhere (14) while *E. faecalis* was 100% resistant to this drug.

In this study, the sex of participants was shown to be a statistically significant factor ($p = 0.022$) for UTI development. This is evidenced by the proportion of culture positive results being observed more among the females (17%) than among the males (6.1%). The present study indicated that females were 3.2 times more susceptible to culture positive UTI than males (3.223 [1.184 – 8.774]). This was in accordance with previous studies conducted in South Ethiopia (13), Southwest Ethiopia (10) and Northwest Ethiopia (15). The higher risk in females can be attributed to the female anatomy and reproductive physiology characterized with a short urethra and its proximity to the perineum irrespective of diabetic status (4). However, the results of this present study contrast with results obtained in a study conducted in Kisii, Kenya where more male than female participants tested positive for UTI, but without statistical significance(12). The variations in age of participants in each individual study could contribute to the differences observed concerning sex as a variable. In this study, specific positive urinalysis results were statistically significant factors for culture positive results; leucocyte esterase levels (OR 8.476), nitrite levels (OR 20.893), and presence of pus cells (OR 0.082) showed significant associations with positive urine culture results ($p<0.001$ for each). This is in line with a similar study which found that the presence of leucocyte esterase, bacterial cells, white blood cells, and nitrites were independent risk factors for positive urine culture results (16). This study also found that the cloudy (OR 11.550) and straw amber (OR 13.440) appearance of urine are significant factors for positive culture results ($p < 0.001$ each). A similar study reported cloudy or malodorous urine as an indication for obtaining urine culture results in patients (17). However, of all the variables described above that were found in bivariate analysis to have had significant associations with culture positive results, only the nitrite levels in the urinalysis results was found by multivariate analysis to be persistently associated with positive culture results. However, this finding contradicted reports from Harar (3) and South Ethiopia (13) whereby sex had a significant association with UTI in multivariate analysis. On one hand, other variables such as age in South Ethiopia (13),

and blood sugar levels in Ethiopia (18) were not significantly associated with UTI, similar to the findings of this present study. On the other hand, age of participants was found to be statistically significant in a study in Kisii, Kenya (12) whileblood sugar level was found to have a strong association with bacteriuria and UTI development in diabetic patients in studies done inGondar, Ethiopia (19), and in Arba Minch, South Ethiopia (13).

CONCLUSION

The predominant pathogens causing UTI were gram negative bacilli, the Enterobacteriaceae, particularly *E. coli* which accounted for 57.6% of the isolated pathogens in this study. Other pathogens such as *K. pneumonia, C. albicans* and *S. aureus* were the second, third, and fourth dominant isolated bacteria respectively. UTI development had a significant association with the sex of participants, and specific positive urinalysis results (leucocyte esterase, nitrites, pus cells, and appearance of urine). These factors were individually and statistically significant ($p < 0.05$) from the initial binomial regression but with nitrite results as the only factor showing statistical significance following multivariate regression. Based on the antimicrobial susceptibility test results it may be inferred that amikacin is among the drugs of choice for UTI treatment in this study area since both the gram negative and gram positive uropathogens tested in this study were susceptible to amikacin. The isolated gram negative micro-organisms demonstrated high resistance levels(100%) to commonly used antibiotics; ampicillin, and amoxiclav. Therefore, clinicians need to revise their prescription habits based on the sensitivity findings and management should be supported by culture and sensitivity testing.

Conflict of interest: The authors have no conflicts of interest to declare.

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