Prevalence Of Bacterial Urinary Tract Infection And Antimicrobial Susceptibility Patterns Among Diabetes Mellitus Patients Attending Zewditu Memorial Hospital, Addis Ababa, Ethiopia

Gebremedhin Yenehun Worku
Emergency Care Research Institute: ECRI Institute

Yerega alamneh belete (yereb2000@gmail.com)
Saint Paul's Hospital Millennium Medical College

Woldaregay Erku Abegaz
Addis Ababa University Faculty of Medicine: Addis Ababa University School of Medicine

---

Research

Keywords: Urinary tract infections, Antibiotic susceptibility, diabetes mellitus, significant bacteriuria

Posted Date: November 2nd, 2020

DOI: https://doi.org/10.21203/rs.3.rs-97783/v1

Abstract

Background: Urinary tract infection (UTI) is caused by colonization and growth of microorganisms within the urinary system. Diabetic patients are more prone to bacterial urinary tract infections due to impaired host defense and high glucose concentration in urine. Surveillance of urinary tract pathogens and their antibiogram is a key to patient management. The aim of this study was to determine the prevalence of bacterial UTI and antimicrobial susceptibility patterns (AST) among diabetes patients.

Methods: Hospital-based cross-sectional study was conducted from May to July, 2018. Two hundred twenty-five mid-stream urine samples were collected for culture and identification based on the standard protocol. Antimicrobial susceptibility test was done for all positive urine cultures by Kirby Bauer's disk diffusion method based on CLSI guidelines. Data were entered into Epi-data version 3.2.1 and exported to the Statistical Package for the Social Science (SPSS) version 20 statistical software. Binary and multiple logistic regression test results were used.

Results: The study result revealed 9.8% overall UTI prevalence. Five species of bacterial uropathogens were isolated. Among these, *E. coli* (63.6%) was the leading followed by *K. pneumoniae* (13.6%). In this study, significant bacteriuria was strongly associated with duration of diabetics, previous UTI and symptomatic UTI. Gram-negative bacterial isolates showed high level of sensitivity (100%) to nitrofurantoin and meropenem. On the contrary, high level of resistance (100 %) for ampicillin, doxycycline, cefuroxime, and (94.4 %) amoxacillin-clavulanate were observed. No resistance was observed among gram positive bacterial isolates except penicillin (100 % resistance). Over all prevalence of MDR was 100 % For Gram-negative bacteria.

Conclusion: Presence of previous urinary tract infection and duration of diabetes were found as important factors that increase the prevalence of UTI among diabetes patients. This study also showed high prevalence of drug resistance to doxycycline, amoxacillin-clavulanate, cefuroxime and penicillin for both Gram- negative and Gram- positive bacteria. Therefore, since therapeutic selection for empirical treatment and management should be based on the knowledge of the local bacterial profile and antimicrobial response, we suggest physicians take this high resistance profile in to consideration when prescribing antimicrobials against the pathogens in question.

Background

Urinary tract infection (UTI) is caused by colonization and growth of microorganisms such as bacteria, fungi and viruses within the urinary tract (UT) [1, 2]. Urinary tract infection results in inflammation of both upper and lower parts of the urinary tract and ranges from asymptomatic to acute or chronic infections [3].

Under normal circumstance, urinary tract (UT) is resistant to long term colonization and growth of microorganisms [4]. This resistance emanates from various physiological processes, one of which being emptying out urine that flushes out harmful microbes that temporarily colonize urine in the bladder [5, 4,

7–9]. Additionally, innate immunity such as cytokines, chemokines [5, 8], secretory immunoglobulin A [4, 5], mucous production, prostatic secretion, barrier formation [8] and high concentration of urea [8, 9] prevent persistent microbial colonization and infection of UT. Nevertheless, structural and functional abnormality that blocks urine flow [6] and other risk factors that break host immunity may lead to UTI [10]. When such breaks occur, UT can be struck by uropathogens like *Escherichia coli, Klebsiella pneumoniae*, and *Proteus mirabilis*, which possess virulence factors that enable them to colonize urinary epithelial cells [9].

Due to anatomic and physiologic nature, UTI is more common in women than men [1, 11]. Nearly half of all women have been affected by this infection at least once in their life time [12]. Some of the factors that enhance UTI in female include short urethra [1, 11], short distance between the anus and urethral meatus, moist environment around the urethra and lack of prostatic fluid; whereas in healthy men risk factors may be sexual activity with infected women, homosexuality and lack of circumcision [11]. Other important risk factors that enhance UTI include: diabetes mellitus (DM), hypertension, allergies, catheterization, use of diaphragms, birth control pills and spermicidal agents, age, delays in micturition, abuse of antibiotics and other immune suppressive conditions [10].

Chronic diseases are emerging as one of the leading causes of worldwide morbidity and mortality [13, 14]. Among these, diabetes mellitus is one of the dominant non-communicable, chronic and endocrine diseases [13]. Diabetes mellitus is a group of metabolic disorder characterized by hyperglycemic phenomena. The disease is mainly divided into two broad groups; type 1 and type 2 DM. Type 1 diabetes mellitus is characterized by complete or nearly total insulin deficiency, whereas type 2 is characterized by inadequate insulin production or insulin resistance [8, 15]. According to estimate from 2017 International Diabetics Federation, globally 451 million (8.4%) people within the age ranges of 18–99 years were living with diabetes mellitus and 5 million people in the age range of 20–79 years died due to this disease. However, this disease is projected to rise to 693 million (9.9%) by 2045. From the African region in 2017, Ethiopia has highest number (2.6 million) of people with diabetes with 5.2% national prevalence [16]. Similarly, higher prevalence of DM was also found in a retrospective study between January 2010 and December 2013 in Addis Ababa [13].

DM causes secondary patho-physiologic changes on multiple organs of patients such as cardiovascular disease, neuropathy, nephropathy and eye disease [8, 16] and abnormal host immune system [17]. Host immune system abnormalities such as impaired migration, chemotaxis, phagocytosis and intracellular killing potential of polymorphonuclear cells; local complications related to neuropathy like impaired bladder emptying and higher glucose concentration of urine in diabetic patients enhance UTI [17, 18]. Different documents in the world show that UTI is more common [19–21], sever, and produce serious outcomes on patients with DM patients [22–24].

The increased risk of UTI among diabetic patients, coupled with the increase in the incidence of diabetes mellitus worldwide in recent years may impose a substantial burden on medical costs [23]. In addition, the high rates of antibiotic prescription, including broad-spectrum antibiotics, for UTI in this group of

patients may further induce the development of antibiotic-resistant urinary pathogens [25]. Even though it is known that more patients with DM than without suffer from frequent and severe UTIs, current treatment guidelines do not distinguish treatment recommendation practices between the two patient groups [26]. Moreover, the inappropriate use of antibiotics often results in the increased resistance of UT pathogens to most commonly used antimicrobial drugs [27].

Studies regarding UTI in DM patients are limited in Ethiopia, particularly in the study area. Therefore, this study was designed to determine bacterial profile and antimicrobial susceptibility patterns among DM patients attending Zewditu Memorial Hospital (ZMH) in Addis Ababa, Ethiopia, with the aim of generating reliable information about bacterial profile and antibiotic susceptibility pattern of urinary bacterial pathogens for desirable empirical therapy of diabetic patients with UTI within Addis Ababa.

Methods And Materials

Study setting and period

The study was conducted from May to July, 2018 at Zewuditu Memorial Hospital, Addis Ababa, Ethiopia. Addis Ababa is the capital city of Ethiopia. According to the 2007 census report [28], Addis Ababa city had a total population of 2,738,248 with growth rate of 2.1%. Based on this figure central statically agency of Ethiopia estimates that the population of Addis Ababa is projected to reach around 3.95 million in 2018. The city has 13 governmental and 36 private hospitals. The city also has 96 health centers and over 700 different levels private clinics. Zewditu Memorial Hospital (ZMH) is one of the biggest hospitals in Ethiopia, which is located in central Addis Ababa. It was built, owned and operated by the Seventh–Day Adventist Church, but was later nationalized during the Derg regime in 1976. Currently, this hospital is operated under Addis Ababa Health Bureau. It provides all round health care services. It is also the leading hospital in the treatment of ART patients and other chronic diseases including DM.

Study design and Participants

Hospital-based cross- sectional study was conducted to determine the prevalence of urinary tract bacterial infection and antimicrobial resistance patterns of bacterial uropathogens among diabetes mellitus patients at Zewditu Memorial Hospital, Addis Ababa, Ethiopia.

Source population

The source population is all diabetic patients visiting ZMH

Study population

Diabetic patients who satisfied the inclusion criteria and visiting ZMH during the study period

Inclusion

All DM patients above 18 years were included in the study.

Exclusion criteria

DM patients who have been taking antibacterial drugs for the last two weeks, DM women with pregnancy and DM patients previously exposed to catheterization were excluded from the study.

Operational definition

Asymptomatic bacteriuria: the presence of significant bacteriuria ($\geq 10^5$cfu/ml) in urine culture without signs and symptoms of urinary tract infection

Multi- drug resistance: non- susceptibility at least one agent in three or more antimicrobial categories. .

Symptomatic bacteriuria: the presence significant bacteria in urine culture ($\geq 10^5$cfu/ml) accompanied with at least two complaints of UTI symptoms such as dysuria, urgency for urination, frequent urination, suprapubic pain, flank pain, fever and chills.

Sample size and Sampling technique

Sample size was calculated by applying the single population proportion formula, $n=(Z\alpha/2)^2 \times p(1-p)/d^2$),where, n = sample size, z = statistic for a level of confidence, d = margin of error, and p = expected prevalence or proportional, 95% level of confidence with a margin of error of 5% and 17.8% prevalence from a previous study [29] done at Gondar University Hospital. The calculation resulted in 225 samples size. Therefore, 225 study participants were selected using systematic random sampling technique via lottery method from DM patients' follow up records. It was learned from the Hospital DM follow up record that the total DM patients attending ZMH for treatment follow up during the sample collection period was 750.

Data collection and Laboratory Methods

Clinical Examination

After obtaining an informed consent from the patients, socio-demographic data and clinical data were collected from patient using pre-structured questioners by nurses.

Specimen collection

A freshly voided midstream urine sample (10–20 mL) was collected in a wide mouthed sterile, dry and leak-proof container after instructing the enrolled DM patients to clean their genitals with soap and water.

Culturing and Identification procedure

Urine specimens obtained from DM patients were inoculated onto MacConkey agar (HKM, China) and Blood agar (Biomark, India) [30] by using a calibrated loop (0.001mL). Cultures were incubated in aerobic atmosphere at 37°C for 24 hours. A positive urine culture was defined as colony count $\geq 10^5$CFU/mL for midstream urine [31]. A Stuart scientific colony counter was used for counting. All positive cultures were further identified by their colony characteristics, and Gram staining. Further identification was done using different biochemical tests including catalase, manitol salt agar and PYR test for Gram-positive bacteria and manitol utilization, hydrogen sulphide production (H_2S), indole production, citrate utilization, lysine iron agar test, gas production, hydrolysis of urea, and motility tests and carbohydrate metabolism for Gram-negative bacteria [32].

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was done on all isolates by the standard Kirby-Bauer disk diffusion method, using commercial disks (Oxoid) based on CLSI 2016 guideline [33]. When pure culture was obtained, a loopful of bacteria was taken from a colony and transferred to a tube containing 5mL normal saline and mixed gently until it formed a homogenous suspension. Then, the turbidity of the suspension was adjusted to the density of a McFarland 0.5 (Mary-l'Etoil, France) in order to standardize the inoculum size. A sterile cotton swab was dipped into the suspension, and excess suspension was removed by gentle rotation of the swab against the surface of the tube. The swab was then used to distribute the bacteria evenly over the entire surface of Mueller Hinton agar (Oxoid). The inoculated plates were left at room temperature to dry for 3–5 minutes. With the aid of disc dispenser, the following concentration of antibiotic discs were put on the surface of Mueller-Hinton agar (Oxoid): nitrofurantoin (30 µg), ciprofloxacin (15 µg), doxycycline (30µg), ampicillin (10µg), vancomycin (30µg), co-trimoxazole (25µg), gentamycin (10µg), cefoxitin (30µg), penicillin (10 units), meropenem (10µg), ceftazidime (30µg), cefuroxime (5µg), cefepime (30µg), and amoxacillin-clavulanate (30µg). These antimicrobial agents were selected based on recommended drugs for treatment of UTI from CLSI 2016 guideline [33] and Ethiopian hospital treatment guideline, 2014. The plates were incubated at 35°C-37°C for 16-18 hours [30,32]. The result was interpreted as sensitive and resistant based on CLSI guidelines [30]. Multidrug resistance is defined as non-susceptibility of tested bacteria at least one antimicrobial agent in three or more antimicrobial categories [34]. Positive results from urine culture and antimicrobial sensitivity test results were reported to the attending physicians for subsequent treatment and follow up.

Quality assurance

Completeness of the questionnaires was properly checked by applying pre-test before the actual data collection. Collection and examination of the specimen were done following the standard operating

procedure (SOP) for urinalysis, culture and antimicrobial susceptibility patterns. Proper specimens labeling and matching with respective identification numbers were checked. Sterility and performance of culture media was tested prior to the actual work. Sterility of media was checked by incubating overnight at 37°c. In addition, *Escherichia coli* (ATCC 25922)*, Klebsiella pneumoniae* (ATCC 700603)*, Proteus mirabilis* (ATCC 35699) and *Staphylococcus aureus* (ATCC 25923) were used as reference strains. Training was given for data collectors who were all nurses.

Data analysis and interpretation

Quantitative data were cleaned, edited and entered onto Epi-data version 3.2.1 and exported to the Statistical Package for the Social Sciences (SPSS) version 20 statistical software for further analysis. Different variables were described and characterized by frequency distribution. Binary and multivariate logistic regressions were used and P value of less than or equal 0.05 was considered as statistically significant.

Results

Socio- demographic characteristics

A total of 225 diabetic patients with and without symptoms of UTI were investigated during the study period. Of them, 75(33.3%) were males and 150 (66.7%) were females. The age of the patients ranges between 20 and 80 years with mean age of 45.52 years and majority of the study participants 158 (70.2%) were married. All study participants were from urban and majority of them (206 (91.6%)) had type II diabetic mellitus. Nearly half of the study participants' monthly income was 1651 – 5250 Ethiopian Birr. About 80% of the study participants were literate (Table 1).

Table 1
Socio demographic characteristics of diabetes mellitus patients investigated for urinary tract infection at Zewditu Memorial Hospital, Addis Ababa, Ethiopia May to July, 2018

Variables		Frequency	Percentage
Gender	Male	75	33.3
	Female	150	66.7
Marital status	Single	28	12.4
	Married	158	70.2
	Separated/divorced	39	17.3
Residence	Urban	225	100
	Rural	0	0
Educational status	No modern schooling	47	20.9
	Primary schooling	71	31.6
	Secondary schooling	71	31.6
	Above secondary schooling	36	16.0
Average monthly income in Birr	≤ 1650	86	38.2
	1651–5250	111	49.3
	> 5250	28	12.4

Clinical features of urinary tract infection

Symptoms suggestive of UTI were observed in 97 (43.11%) of the study subjects. The most frequently observed complaints were flank/loin pain which was observed among 90 (40%), frequent urination 80 (35.56%) and urgent urination 66 (29.3%). Fever, dysuria, suprapubic pain, nausea and vomiting were also observed among 52 (23.2%), 42 (18.7%), 38 (16.9%), 26 (11.6%) and 5 (2.2%) of the study participants, respectively (Table 2).

Table 2
Frequency of symptoms suggestive of UTI in diabetes mellitus patients in Zewditu Memorial Hospital, Addis Ababa, Ethiopia May to July, 2018

Symptoms of UTI	Frequency	Percentage
Flank/loin pain	90	40.00
Frequent urination	80	35.56
Urgent urination	66	29.33
Fever	52	23.11
Dysuria	42	18.67
Suprapubic pain	38	11.56
Nausea	26	16.89
Vomiting	5	2.22

Culture results

Significant bacteriuria was observed in 22 of 225 (9.8 %) urine samples cultured. Of these, 15 (68.2%) were from symptomatic and 7 (37.8%) were from asymptomatic UTI DM patients. Out of total 22 positives, 3 (13.6 %) were from males and 19 (86.4 %) from females. Bivariate logistic regression analysis determined significant bacteriuria to be strongly associated with duration of diabetics, previous UTI and current symptoms of UTI (P<0.05). The results of the study indicate that the chance of getting UTI among DM patients who have long duration of diabetics (for more than 10 years) was more than 4 fold (COR; 4.364 [95 % CI**,** 1.637- 11.629] than DM patients who had 10 or less years of diabetics. Similarly, DM patients with previous UTI had 4.709 times more chance of developing UTI (COR; 4.709 [95% CI**;** 1.873-11.842]) than those patients without previous UTI; and those patients with symptomatic UTI were 3 times at risk of having significant bacteriuria than those asymptomatic patients (COR; 3.162 [95% CI, 1.235-8.094]).

However, other factors like gender, educational status, DM types, marital status, and frequency of previous UTI and fasting blood glucose levels were not statistically associated with significant bacteriuria. The odds of getting significant bacteriuria were not statistically significant between age groups (P> 0.05), as significant bacterial isolates were distributed in all age groups of the study participants. However, the highest (20.0%) and the lowest (4.7%) prevalent significant bacteriuria were observed among the age groups ≥64 years and 50-64 years, respectively. Regarding marital status, the highest (14.3%) significant bacteriuria was isolated from single DM patients but this association was not statically significant (P> 0.050). Similarly, 19/22 (86.4%) of the bacteria were isolated from female diabetics. Even though, the risk of getting UTI in female patients was higher (3.481 times) than male, no statistically significant association was observed between gender and significant bacteriuria, albeit the failure was marginal (P= 0.051).

In multivariate logistic regression analysis, duration of diabetics and previous UTI were statistically significant associated with significant bacteriuria with adjusted odd ratio (AOR) (95%CI) 3.477 [1.266-9.554] and 3.645 [1.403-9.473], respectively, whereas symptomatic condition was not shown to have significant association with AOR (95%CI) 2.354 [0.881, 6.294] (Table 3).

Table 3: The isolation rate of UTI in of diabetes mellitus patients investigated for urinary tract infection in relation with the associated factors at Zewditu Memorial Hospital, Addis Ababa, Ethiopia May to July, 2018

Category	Significant Bacteriuria		Crude		Adjusted	
	Yes N (%)	No N (%)	P value	Odd ratio (95% CI)	P value	Odd ratio (95% CI)
Gender						
Male	3 (4.0)	72 (96.0)		1		
Female	19 (12.7)	131 (87.3)	0.051	3.481 [0.974-1.036]		
Total	22 (100 %)	203(100%)				
Age in years						
20-34	5 (9.4)	48 (90.6)		1		
35-49	9 (10.8)	74 (89.2)	0.792	1.168 [0.369-3.695]		
50-64	3 (4.7)	61 (95.3)	0.320	0.472 [0.107-2.075]		
>64	5 (20.0)	20 (80.0)	0.202	2.40 [0.625-9.210]		
Marital status						
Single	4 (14.3)	24 (85.7)		1		
Married	14 (8.9)	144 (90.1)	0.376	0.583 [0.177-1.922]		
divorced	4 (10.3)	35 (89.7)	0.617	0.686 [0.156-3.012]		
Educational status						
No schooling	7 (14.9)	40 (85.1)	0.098	6.125 [0.718-52.259]		
Primary	9 (12.7)	62 (87.3)	0.131	5.081 [0.618-41.786]		
Secondary	5 (7.0)	66 (93.0)	0.382	2.652 [0.298-23.592]		
Above secondary	1 (2.8)	35 (97.2)		1		
Average monthly income in birr						
≤1650	14 (16.3)	72 (83.7)	0.118	5.250[0.658-41.873]		
1651-5250	7 (6.3)	104 (93.7)	0.584	1.817[0.214-		

				15.409]		
>5250	1 (3.6)	27 (96.4)		1		
Types of DM						
Type 1 DM	3 (15.8)	16 (84.2)		1		
Type 2 DM	19 (9.2)	187 (90.8)	0.363	0.542 [0.145-2.029]		
Durations of DM						
≤10 years	6 (4.5)	126 (95.5)		1		1
>10 years	16 (17.2)	77 (82.8)	**0.003**	4.364 [1.637-11.629]	**0.016**	3.477 [1.266-9.554]
Fasting blood glucose						
<126 mg/dl	3 (5.4)	53 (94.6)		1		
≥126 mg/dl	19 (11.2)	150 (88.8)	0.209	2.238 [(0.636-7.868]		
Previous UTI						
No	8 (5.1)	148 (94.9)		1		
Yes	14 (20.3)	55 (79.7)	**0.001**	4.709 [1.873-11.842]	**0.008**	3.645 [1.403-9.473]
Frequency of previous UTI						
Once	6 (15.8)	32 (84.2)		1		
Twice	2 (12.5)	14 (87.5)	0.757	0.762 [0.137-4.251]		
Three and above	6 (40.0)	9 (60.0)	0.066	3.556 [0.920-13.740]		
Present symptoms of UTI						
Asymptomatic	7 (5.5)	121(94.5)		1		1
Symptomatic	15 (15.5)	82 (84.5)	**0.016**	3.162 [1.235-8.094]	0.088	2.354 [0.881-6.294]

Bacterial Etiologies

A total of 22 bacterial uropathogens were isolated. Out of this, 4(18.2 %) were Gram-positive bacteria and 18 (81.8 %) were Gram-negative bacteria. *E. coli* was the most frequently isolated uropathogen [14(63.6

%)] followed by *K. pneumoniae* [3 (13.7 %)] and *P. rettgeri* [1 (4.5 %)]. Among Gram-positive bacteria, only *Enterococcus* species [2 (9.1 %)] and CoNs [2(9.1 %)] were isolated (Figure 1).

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility test was performed for all culture-positive urine samples using disk diffusion method. Gram-negative bacterial isolates (n=18) were tested against 12 antibiotics while Gram-positive isolates were tested against 9 antibiotics (Tables 4 and 5, respectively). The percentage of sensitivity for Gram-negative isolates were highest for meropenem with rate of 18/18 (100 %), nitrofurantoin 18/18 (100 %) and gentamicin 16/18 (88.9 %), whereas the highest level of resistance was observed for doxycycline with rate of 18/18 (100 %), ampicillin 18/18 (100 %), Cefuroxime 18/18 (100 %) and amoxacillin-clavulanate 17 (94.4%). *E. coli*, the most frequently isolated bacteria, was highly resistant to doxycycline (100 %), ampicillin (100 %) and amoxacillin-clavulanate (92.9 %) (Table 4). Overall, Gram-positive bacterial isolates (n=4) showed (100 %) sensitivity for six of the tested antibiotics, whereas high level resistance was observed to penicillin (100 %) (Table 5).

Table 4: Antimicrobial susceptibility patterns of Gram-negative bacteria isolated from diabetic mellitus patients investigated for UTI at Zewditu Memorial Hospital, Addis Ababa, Ethiopia May to July, 2018.

Antimicrobial agents	Bacterial isolates							
	E. coli (n=14)		*K. pneumoniae* (n= 3)		*P. rettgeri* (n=1)		Total (n=18)	
	S N (%)	R N (%)	S N (%)	R N (%)	S N (%)	R N (%)	S N (%)	R N (%)
Meropenem	14 (100)	0(0)	3 (100)	0(0)	1 (100)	0(0)	18 (100)	0(0)
Nitrofurantoin	14 (100)	0(0)	3 (100)	0(0)	1 (100)	0(0)	18 (100)	0(0)
Co-trimoxazole	4 (28.6)	10 (71.4)	1 (33.3)	2 (66.7)	0(0)	1(100)	5 (27.8)	13 (72.2)
Gentamicin	12 (85.7)	2 (14.3)	3 (100)	0(0)	1(100)	0(0)	16 (88.9)	2 (11.1)
Ciprofloxacin	6 (42.9)	8 (57.1)	0(0)	3 (100)	1(100)	0(0)	7 (38.9)	11 (61.1)
Doxycycline	0(0)	14 (100)	0(0)	3 (100)	0(0)	1(100)	0(0)	18 (100)
Amoxacillin-clavulanate	1 (7.1)	13 (92.9)	0(0)	3 (100)	0(0)	1(100)	1(5.6)	17 (94.4)
Ampicillin	0(0)	14 (100)	0(0)	3 (100)	0(0)	1(100)	0(0)	18 (100)
Cefuroxime	0(0)	14 (100)	0(0)	3 (100)	0(0)	1(100)	0(0)	18 (100)
Cefotaxime	8 (57.1)	6 (42.9)	1 (33.3)	2 (66.7)	1(100)	0(0)	10 (55.6)	8 (44.4)
Ceftazidime	10 (71.4)	4 (28.6)	0(0)	3 (100)	1(100)	0(0)	11(61.1)	7 (38.9)
Cefepime	11 (78.6)	3 (21.4)	2 (66.7)	1(33.3)	1(100)	0(0)	14 (77.8)	4 (22.2)

Abbreviations: N- number, R=resistance, S=Sensitive

Table 5: Antimicrobial susceptibility patterns of Gram-positive bacteria isolated from diabetic mellitus patients investigated for UTI at Zewditu Memorial Hospital, Addis Ababa, Ethiopia, May to July, 2018.

Antimicrobial agents	Bacterial Isolates					
	Enterococcus species(n=2)		Coagulase Negative *Staphylococcus* (n=2)		Total (n=4)	
	S N (%)	R N (%)	S N (%)	R N (%)	S N (%)	R N (%)
Nitrofurantoin	2 (100)	0(0)	2 (100)	0(0)	4 (100)	0(0)
Ciprofloxacin	1 (50)	1 (50)	2 (100)	0(0)	3 (75)	1 (25)
Doxycycline	0(0)	2 (100)	2 (100)	0(0)	2 (50)	2 (50)
Ampicillin	2 (100)	0(0)	ND	ND	2 (100)	0(0)
Vancomycin	2 (100)	0(0)	ND	ND	2 (100)	0(0)
Co-trimoxazole	ND	ND	2 (100)	0(0)	2 (100)	0(0)
Gentamicin	ND	ND	2 (100)	0(0)	2 (100)	0(0)
Cefoxitin	ND	ND	2 (100)	0(0)	2 (100)	0(0)
Penicillin	ND	ND	0 (0%)	2 (100)	0(0)	2 (100)

Abbreviations: ND- not done, N- number, R=resistance, S=Sensitive

Multiple drug resistance patterns

The frequency of multi-drug resistance (MDR) was found in all Gram-negative bacteria (100%), whereas none of the Gram-positive bacteria showed MDR.

Table 6: Multi-drug resistance patterns of Gram-negative bacterial isolates from mid-stream urine samples among diabetes mellitus patients at Zewditu Memorial Hospital, Addis Ababa, Ethiopia May to July, 2018.

Number of antimicrobial agents	Bacterial isolates		
	E.coli (n=14)	*K. pneumoniae* (n=3)	*P. rettgeri* (n=1)
Cotr, Cip, Dox, Amp, AMC, Cetz, Cef, Cft	-	1 (33.33%)	-
Cotr, Cip, Dox, Amp, AMC, Cetz, Cef, Cft, Cep	-	1 (33.33%)	-
Cip, Dox, Amp, AMC, Cetz, Cef	-	1 (33.33%)	-
Cotr, Dox, Amp, AMC, Cef	-		1 (100%)
Cotr, Dox, Amp, AMC, Cef, Cft	1 (7.14%)		
Dox, Amp, Cef	1(7.14%)		
Cotr, Cip, Dox, Amp, AMC, Cef,	1(7.14%)		
Dox, Amp, AMC, Cef,	3 (21.42%)		
Cotr , Gen, Cip, Dox, Amp, AMC, Cef	1(7.14%)		
Cotr, Cip, Dox, Amp, AMC, Cetz, Cef, Cft, Cep	2 (14.29%)		
Cotr, Dox, Amp, AMC, Cef	1(7.14%)		
Cotr, Cip, Dox, Amp, AMC, Cef, Cft	2 (14.29%)		
Cotr , Gen, Cip, Dox, Amp, AMC, Cetz, Cef, Cft, Cep	1(7.14%)		
Cotr, Cip, Dox, Amp, AMC, Cetz, Cef,	1(7.14%)		
Total	14 (100%)	3 (100%)	1 (100%)

Abbreviation; Cotr: Co-trimoxazole, Gen: Gentamicin, Cip: Ciprofloxacin, Dox: Doxycycline, Amp: Ampicillin, AMC: Amoxacillin-clavulanate, Cetz: Ceftazidime, Cef: Cefuroxime, Cft: Cefotaxime, Cep:Cefepime

Discussions

In the present study, the overall prevalence of UTI from both symptomatic and asymptomatic UTI diabetes patients was 9.8%. This rate is comparable to the rates reported from other studies in Ethiopia (Debre Tabor (10.9%) [20], Hawassa 13.8% [35], Addis Ababa 10.9% [36]), India 12.2% [18] and Romania (10.7%) [37]. However, much higher prevalence rates were reported from Bahir Dar (30.5%) [38], and Arbaminch (33.8%) [39] in Ethiopia, Sudan (19.5%) [40], India (22%) [21], Pakistan (52.76%) (41)], Egypt (52.2%) [19], and Nepal (54.25%) [42]. Inclusion of asymptomatic DM patients and exclusion of catheterized DM patients, which is a known determinant factor that may increase the prevalence of UTI [19, 42], could be reasons for detecting lower prevalence of UTI in our study compared to the latter reports.

In the present study, 22 bacterial uropathogens belonging to five species were isolated. Gram-negative bacteria were more prevalent (81.8%) than Gram-positive bacteria (18.2%), as has been the case in most studies conducted elsewhere in the world. Our finding of high Gram–negative bacterial isolates in DM patients is in concordance with reports from Mekelle (83%) [43],India (92%) [44] and Sudan (87.2%) [40]. However, relatively lower prevalence were reported from other similar studies in Ethiopia such as in Debre Tabor (41.9%) [20] and Bahir Dar (61.9%) [45].

Generally, in the present study (63.6%) and in most other studies conducted elsewhere (Pakistan (60.0%) [24], India 67.6% [46], Dessie, 63% (47)], Sudan 54.6% [40] and Romania (68.9%) [37], *E. coli* was the most frequently isolated uropathogen. This dominance of *E. coli* among UTI patients may not be surprising since it is the commonest flora of the gastrointestinal tract and bowel from which it ascends to urinary tract where it uses its well characterized virulence factors to colonize the urinary tracts. The second leading bacterial isolate in our study was *K. pneumoniae* (13.7%), as was true for reports from Bahir Dar [38], Dessie [47], Sudan [40] and Nigeria [22]. On the contrary, *Proteus* species, *Pseudomonas* species and CoNs were reported to be the second abundant bacterial isolates from UTI from studies in Addis Ababa [48], Bahir Dar [49] and Pakistan [24], respectively.

In the present study, small proportion of *Enterococcus* species and CoNs were isolated each with the rate of 9.1% among the overall bacterial isolates. The 9.1% prevalence rate for *Enterococcus* species was also reported from Sudan [40]. However, *S. aureus* and *S. saprophyticus* in Debre Tabor [20], *S. saprophyticus* in Bahir Dar [49], *S. aureus* in Arbaminch [39] and CoNs in Dessie [47] were the leading Gram-positive isolates, showing variations in the dominance of UTI bacterial isolates among the different geographic locations in Ethiopia.

In the present study, duration of DM was shown to be an important risk factor for UTI development ($p = 0.003$), as evidenced by proportion of significant bacteriuria being observed more (17.2%) from those with diabetic history of > 10 years than those (4.5%) who were diabetic for only < 10 years. This is likely to be because of the progressive nature of diabetics that may damage genitourinary system (neuropathy) leading to dysfunctional bladder thereby creating micturition abnormality, a condition important for the developments of UTI [19, 50]. In fact, previous other studies from Egypt [19] and India [51] also reported the same conclusion in that the longer duration of DM the higher the rate of UTI observed. However, some studies from Iran [52] and Addis Ababa [27] reported no statistically significant association between duration of diabetics and UTI.

Another identified risk factor associated with significant bacteriuria in this study was previous history of UTI. Sixty-nine of the study participants in the present study had history of previous UTI. However, 14 of the 22 (63.63%) participants with significant bacteriuria were among those who had previous history of UTI. In fact, the likelihood of developing significant bacteriuria was 4.709 times greater among participants with history of UTI than without ($P < 0.05$). Other in-country studies have reported the same trend of higher rate of significant bacteriuria among those with previous history of UTI [27, 29, 53]. However, two studies from Hawassa [35] and Arbaminch [39] reported a contradictory finding, where they

found statistically significant association of significant bacteriuria among DM patients with no history of UTI. Probably the latter studies might have introduced real biases during recruitment of participants.

Only 97/225 (43.1%) of the participants in our study had symptoms of UTI. However, the majority (15/22; 68%) of participants with significant bacteriuria were among the symptomatic ones ($p < 0.05$). This is not unexpected, as was the case from reports of other studies [27, 36], because long duration of DM and delayed medical intervention are likely to result in renal defects that in turn would lead to occurrence of UTI symptoms. On the contrary, our finding disagrees with the studies conducted in Hawassa [35], Sudan [40] and Italy [53] where symptomatic UTI had no significant association with significant bacteriuria. The difference might be due to respondent bias in accurately telling the symptoms characterizing symptomatic UTI.

Of the three variables described above that were found in bivariate analysis to have had significant association to significant bacteriuria in this study, only previous history of UTI and current symptoms of UTI were found by multivariate analysis to be persistently associated with significant bacteriuria. Surprisingly, however, this finding was in contradiction with the reports from the Sudan [40], where duration of diabetics and previous history of UTI had no significant association with significant bacteriuria in multivariate analysis. Moreover, in reports of other studies in Ethiopia, multivariate analysis showed previous history UTI to have had statistically significant association with significant culture positive bacteria in diabetic patients [35, 53]. However, other variables such as gender in Harar [53] and educational status in Hawassa [35] were also as important in this association, which were not even significant by bivariate analysis in our study.

Regarding antimicrobial sensitivity test results, the Gram-negative uropathogens were highly sensitive to meropenem (100%), nitrofurantoin (100%) and gentamicin (88.9%). The latter two antimicrobials were also shown previously to be highly effective against Gram-negative bacteria with sensitivity of 95.5% and 73.3% for nitrofurantoin and gentamicin, respectively from Dessie, Ethiopia [47]. A 100% sensitivity to nitrofurantoin was also recorded from a study in Arbaminch [39] and Gondar [29].

In the contrary, high level resistance was exhibited by the Gram-negative isolates against a number of tested antimicrobials that are commonly used against bacterial UTI: ampicillin (100%), doxycycline (100%), cefuroxime (100%), amoxacillin-clavulanate (94.4%), co-trimoxazole (72.2%), and ciprofloxacin (61.1%). The most disturbing observation in this connection is that all the Gram-negative isolates had shown resistance to more than at least one antimicrobial in three classes tested (100% MDR level). Such high levels of resistance among uropathogens against these same antimicrobials seems widespread both in Ethiopia (E.g. 91.4% against ampicillin and 79.2% against amoxacillin-clavulanate [38], 100% against co-tromoxazole, greater than 75% against amoxacillin-clavulanate [53], and between 60–100% against ampicillin [18, 29, 35, 36]) and elsewhere in the world [18]. Still more studies have confirmed that detection of high MDR among the Gram-negative uropathogens is common both in Ethiopia and elsewhere [20, 35, 47, 49, 53]. The remarkably higher prevalence of resistance, including MDR, against these commonly prescribed antibiotics may be due to: their wider availability and ease of access outside

treatment centers, and so, indiscriminate use of the drugs without prescription [55]; or/and fake drugs, sub-standard or expired drugs may circulate that are likely to be used for self-treatment; frequent use of broad-spectrum antibiotics as prophylactics; and lack of laboratory tests both AST and pathogen identification [32].

E. coli, the leading uropathogen in the present study, was 100% sensitive to meropenem and nitrofurantoin, and 87.5% to gentamicin, although a very high level of resistance was observed to doxycycline (100%), ampicillin (100%), cefuroxime (100%) and amoxacillin-clavulanate (92.9%). Such high sensitivity of *E. coli* to the former two antibiotics was also reported previously from the Sudan [40], where it was 100% and 86.3%sensitive to gentamicin and nitrofurantoin, respectively; and in Ethiopia, where it was observed to be 100% sensitive to nitrofurantoin in Addis Ababa [27] and Hawassa [35]. However, this pathogen has been found to exhibit very high resistance (100%) to Ampicillin, which is also supported by the report from Hawassa (100%) [35] and Bahir Dar [49]. On the contrary, the 92.2% and 100% resistance of *E. coli* to amoxacillin-clavulanate and ampicillin, respectively, in our study disagrees with the report from the Sudan [40] in that amoxacillin-clavulanate (sensitivity rate 90.9%) and ampicillin (sensitivity rate 72.7%) were presented as effective drugs. The deterioration in the effectiveness of amoxacillin-clavulanate and ampicillin against *E. coli* from UTI is a matter of concern, given the facts that the primary etiology of UTI infection for DM patients is this uropathogen, and these antimicrobials are among the most commonly used drugs in Ethiopia.

In the present study, the overall percentage of antimicrobial sensitivity of Gram-positive bacterial isolates to majority of the tested antibiotics was high. For instance, *Enterococcus* species were 100% sensitive to nitrofurantoin, ampicillin and vancomycin. Previous studies from Ethiopia and the Sudan [20, 29, 40] also reported same high sensitivity rate for the former two antibiotics. Similarly, CoNs were highly sensitive (100%) to six of the tested antimicrobials, namely, nitrofurantoin, Ciprofloxacin, co-trimoxazole, Gentamicin, Cefoxitin, and Doxycycline, which was also observed in other previous studies in Ethiopia, where 100% sensitivity were reported against doxycycline [20], gentamicin [35] and ampicillin [40].

Mixed result was observed in regards to resistance among the two Gram-positive bacterial species isolated, *Enterococcus* sp. and CoNs. On the one hand, *Enterococcus* isolates were 100% resistant to doxycycline but CoNs were 100% sensitive to this drug. On the other, resistance to Ciprofloxacin was 50% for *Enterococcus* while it was 0% to CoNs. Moreover, CoNs isolates were 100% resistant to Penicillin, as was the cases in other studies elsewhere [35, 54]. Overall, gram positive isolates presented better options for empiric treatment than the gram negative isolates since they were 100% sensitive to all tested antimicrobial drugs except 100% resistance to penicillin and doxycycline.

Conclusion

Significant bacteriuria was obtained from 9.8% of participants, and *Escherichia coli* (63.6%) was the leading uropathogen. Presence of previous urinary tract infections and duration of diabetes were found to be important factors responsible for increased prevalence of laboratory-confirmed urinary tract infection

among the diabetes patients. Nitrofrantoin and gentamicin were effective aganist both Gram-positive and Gram-negative bacterial uropathogens in the current study, which may be used for empirical therapy when urine culture is unavailable. This study also showed high prevalence of drug resistance against common antimicrobials, particularly to co-trimoxazole, ciprofloxacin, doxycycline, ampicillin, amoxacillin-clavulanate, cefuroxime and penicillin. The prevalence of MDR was also high for Gram-negative bacteria. Therefore, cautious use of antibiotic therapy and immediate treatment of urinary tract infections in DM patients is mandatory. Moreover, therapeutic selection for empirical treatment and management should be based on the knowledge of the local bacterial profile and antimicrobial response, and there should be a continuous monitoring and review of antimicrobial policy in the hospital and the country at large.

Limitation Of This Study

The present study did not include non-diabetic patients as a control group which makes difficult to indicate how much DM may increase the prevalence of UTI compared with non-DM patients. In addition, the present study did not address UTI caused by bacterial pathogens that are difficult to culture in the ordinary culture media and anaerobic bacterial pathogens which might change the prevalence of UTI.

Abbreviations

AAU: Addis Ababa University; ATCC: American type culture collection; ASB: Asymptomatic bacteriuria; CLSI: Clinical laboratory standard institute; CoNs: Coagulase negative staphylococci; COR: Crude odd ratio; DMIP: Department of Microbiology, Immunology and Parasitology; DM: Diabetic Mellitus; MSU: Mid-Stream Urine; NDM: Non-diabetes Mellitus; PYR: Pyrrolidonyl Arylamidase, SPSS: Statistical Package for the Social Science; SB: Symptomatic bacteriuria; UTI: Urinary tract infection; WHO: World Health Organization; ZMH: Zewuditu memorial Hospital

Declarations

Acknowledgements

The authors would like to thank Addis Ababa University, Department of Microbiology, Immunology and Parasitology, faculty of Medicine for sponsoring the research. Our special thanks and appreciation go to the staff members of Zewditu Memorial Hospital medical director, physicians, nurses and laboratory staffs working in diabetic clinic for their support in screening of symptomatic and asymptomatic study participants and organizing the preconditions of sample and data collection. Our deepest thanks also go to Addis Ababa Health Bureau Public Health Research and Emergency Management directorate for their unreserved material and reagent supply that made this study possible. We also extend our profound gratitude to the study participants for their willingness without whom this research work would not have been possible.

Authors’ contributions

GY: Principal investigator of the study, study design, data collection, laboratory work, data analysis, critically reviewed the data and drafted the manuscript; WEA: study design, supervision of data collection, data analysis, critically reviewed the data and drafted the manuscript; YB: critically reviewed the data and drafted the manuscript. All authors gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Funding

This study was sponsored by Addis Ababa University, Addis Ababa, Ethiopia.

Availability of data and materials

Data is available upon request.

Ethics approval and consent to participate

Ethically clearance was obtained from Department Research and Ethical Review Committee and was approved by the Department of Microbiology, Immunology and Parasitology, School of Medicine, Addis Ababa University. Ethical clearance was also secured from Addis Ababa public health research and emergency management directorate. Official permission was also obtained from ZMH. In addition, written consent was obtained from the study participants before the initiation of data collection. The individual results of any investigation remained confidential. The laboratory findings of the study participants were communicated to the responsible health professional assigned to the diabetic clinic for the purpose of managing the cases accordingly.

Consent for publication

Not applicable. This study does not contain any individual or personal data.

Competing interests

The authors declare that they have no competing interests

References

1. Vasudevan R. Urinary tract infection: an overview of the infection and the associated risk factors. J Microbiol Exp. 2014;1(2):00008.
2. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infection and treatment options. Nature Reviews Microbiology. 2015 May;13(5):269–84.
3. Odoki M, Bazira J, Agwu E. Health-point survey of bacteria urinary tract infections among suspected diabetic patients attending clinics in Bushenyi district of Uganda. Special Bacterial Pathogens Journal. 2015;1(1):1–5.

4. Hanson LA, Fasth A, Jodal U, Kaijser B, Svanborg Edén C. Biology and pathology of urinary tract infections. J Clin Pathol. 1981 Jul;34(7):695–700.
5. Moura A, Nicolau A, Hooton T, Azeredo J. Antibiotherapy and pathogenesis of uncomplicated UTI: difficult relationships. Journal of Applied Microbiology. 2009;106(6):1779–91.
6. Hickling DR, Sun T-T, Wu X-R. Anatomy and Physiology of the Urinary Tract: Relation to Host Defense and Microbial Infection. In: Urinary Tract Infections [Internet]. John Wiley & Sons, Ltd; 2016 [cited 2020 Jun 3]. p. 1–25. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1128/9781555817404.ch1
7. Sussman M PhD, Gally DL PhD. The Biology of Cystitis: Host and Bacterial Factors. Annual Review of Medicine. 1999;50(1):149–58.
8. Fauci AS. Harrison's principles of internal medicine. Vol. 2. McGraw-Hill, Medical Publishing Division New York; 2008.
9. M. Sussman P, D. L. Gally P. The Biology of Cystitis: Host and Bacterial Factors [Internet]. https://doi.org/10.1146/annurev.med.50.1.149. Annual Reviews 4139 El Camino Way, P.O. Box 10139, Palo Alto, CA 94303-0139, USA; 2003 [cited 2020 Jun 3]. Available from: https://www.annualreviews.org/doi/abs/10.1146/annurev.med.50.1.149
10. Jatileni NJV, Maposa I, Mavenyengwa RT. A Retrospective Study of the Variability in Etiological Agents of Urinary Tract Infections among Patients in Windhoek-Namibia. Open Journal of Medical Microbiology. 2015;05(04):184.
11. Hooton TM. Pathogenesis of urinary tract infections: an update. J Antimicrob Chemother. 2000 Aug 1;46(suppl_1):1–7.
12. François M, Hanslik T, Dervaux B, Le Strat Y, Souty C, Vaux S, et al. The economic burden of urinary tract infections in women visiting general practices in France: a cross-sectional survey. BMC Health Services Research. 2016 Aug 9;16(1):365.
13. Gizaw M, Harries AD, Ade S, Tayler-Smith K, Ali E, Firdu N, et al. Diabetes mellitus in Addis Ababa, Ethiopia: admissions, complications and outcomes in a large referral hospital. Public Health Action. 2015 Mar 21;5(1):74–8.
14. Bloom DE, Cafiero E, Jané-Llopis E, Abrahams-Gessel S, Bloom LR, Fathima S, et al. The Global Economic Burden of Noncommunicable Diseases [Internet]. PGDA Working Papers. Program on the Global Demography of Aging; 2012 Jan [cited 2020 Jun 3]. (PGDA Working Papers). Report No.: 8712. Available from: https://ideas.repec.org/p/gdm/wpaper/8712.html
15. Kerner W, Brückel J. Definition, Classification and Diagnosis of Diabetes Mellitus. Exp Clin Endocrinol Diabetes. 2014 Jul;122(7):384–6.
16. Zibaeenezhad MJ, Sayadi M, Mohammadi SS, Khorshidi S, Hadiyan E, Mowla A, et al. Clinical outcomes after percutaneous coronary intervention in patients with and without history of diabetes mellitus with different stent size. 2020;
17. Boyko EJ, Fihn SD, Scholes D, Chen C-L, Normand EH, Yarbro P. Diabetes and the Risk of Acute Urinary Tract Infection Among Postmenopausal Women. Diabetes Care. 2002 Oct 1;25(10):1778–83.

18. Senthamarai S, Sivasankari S, Anitha C, Vasumathi A, Venugopal V, Thenmozhivalli PR, et al. A study on clinical presentation, bacterial profile and its antibiotic sensitivity pattern in urinary tract infections among diabetic patients attending tertiary care hospital. Tamilnadu infect. 2016;2:4.
19. El-Nagar MMG-A, Abd El-Salam AE-D, Gabr HM, Abd El EE-DM. Prevalence of urinary tract infection in Damietta diabetic patients. Menoufia Medical Journal. 2015;28(2):559.
20. Worku S, Derbie A, Sinishaw MA, Adem Y, Biadglegne F. Prevalence of Bacteriuria and Antimicrobial Susceptibility Patterns among Diabetic and Nondiabetic Patients Attending at Debre Tabor Hospital, Northwest Ethiopia [Internet]. Vol. 2017, International Journal of Microbiology. Hindawi; 2017 [cited 2020 Jun 3]. p. e5809494. Available from: https://www.hindawi.com/journals/ijmicro/2017/5809494/
21. Sharma E, Thakuriya R. Clinical profile of urinary tract. 2015;
22. Abubakar E-MM. Antimicrobial susceptibility pattern of pathogenic bacteria causing urinary tract infections at the Specialist Hospital, Yola, Adamawa state, Nigeria. JCMR. 2009 Oct 31;1(1):1–8.
23. Yu S, Fu AZ, Qiu Y, Engel SS, Shankar R, Brodovicz KG, et al. Disease burden of urinary tract infections among type 2 diabetes mellitus patients in the U.S. Journal of Diabetes and its Complications. 2014 Sep 1;28(5):621–6.
24. Kumar R, Kumar R, Perswani P, Taimur M, Shah A, Shaukat F. Clinical and Microbiological Profile of Urinary Tract Infections in Diabetic versus Non-Diabetic Individuals. Cureus [Internet]. [cited 2020 Jun 15];11(8). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6802799/
25. Nitzan O, Elias M, Chazan B, Saliba W. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. Diabetes Metab Syndr Obes. 2015 Feb 26;8:129–36.
26. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International Clinical Practice Guidelines for the Treatment of Acute Uncomplicated Cystitis and Pyelonephritis in Women: A 2010 Update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. Clin Infect Dis. 2011 Mar 1;52(5):e103–20.
27. Woldemariam HK, Geleta DA, Tulu KD, Aber NA, Legese MH, Fenta GM, et al. Common uropathogens and their antibiotic susceptibility pattern among diabetic patients. BMC Infectious Diseases. 2019 Jan 10;19(1):43.
28. Schmidt E, Kedir M. Urbanization and Spatial Connectivity in Ethiopia: Urban Growth Analysis Using GIS [Internet]. Africa Portal. International Food Policy Research Institute (IFPRI); 2009 [cited 2020 Jun 3]. Available from: https://www.africaportal.org/publications/urbanization-and-spatial-connectivity-in-ethiopia-urban-growth-analysis-using-gis/
29. Yismaw G, Asrat D, Woldeamanuel Y, Unakal CG. Urinary Tract Infection: Bacterial etiologies, drug resistance profile and associated risk factors in diabetic patients attending Gondar University Hospital, Gondar, Ethiopia. European Journal of Experimental Biology. 2012;2(4):889–898.
30. Vandepitte J, Engbaek K, Rohner P, Piot P, Heuck CC, Organization WH. Basic laboratory procedures in clinical bacteriology/J. Vandepitte...[et al.]. In: Basic laboratory procedures in clinical bacteriology/J

Vandepitte.[et al]. 2003.

31. Graham JC, Galloway A. ACP Best Practice No 167: the laboratory diagnosis of urinary tract infection. Journal of Clinical Pathology. 2001;54(12):911–919.
32. Cheesbrough M. District Laboratory Practice in Tropical Countries, Part 2. Cambridge University Press; 2006. 464 p.
33. Wayne PA. Clinical and laboratory standards institute. Performance standards for antimicrobial susceptibility testing. 2011;
34. Magiorakos A-P, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical Microbiology and Infection. 2012 Mar 1;18(3):268–81.
35. Nigussie D, Amsalu A. Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients. Turk J Urol. 2017 Mar;43(1):85–92.
36. B Y, S G-S, Y F. Asymptomatic bacteriuria and symptomatic urinary tract infections (UTI) in patients with diabetes mellitus in Tikur Anbessa Specialized University Hospital, Addis Ababa, Ethiopia. Ethiop Med J. 2012 Jul 1;50(3):239–49.
37. Chiţă T, Licker M, Sima A, Vlad A, Timar B, Sabo P, et al. Prevalence of Urinary Tract Infections in Diabetic Patients. Romanian Journal of Diabetes Nutrition and Metabolic Diseases. 2013 Jun 1;20(2):99–105.
38. Derbie A, Hailu D, Mekonnen D, Abera B, Yitayew G. Antibiogram profile of uropathogens isolated at Bahir Dar Regional Health Research Laboratory Centre, Northwest Ethiopia. Pan Afr Med J [Internet]. 2017 Mar 10 [cited 2020 Jun 3];26. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5429430/
39. Mama M, Manilal A, Gezmu T, Kidanewold A, Gosa F, Gebresilasie A. Prevalence and associated factors of urinary tract infections among diabetic patients in Arba Minch Hospital, Arba Minch province, South Ethiopia. Turk J Urol. 2019 Jan;45(1):56–62.
40. Hamdan HZ, Kubbara E, Adam AM, Hassan OS, Suliman SO, Adam I. Urinary tract infections and antimicrobial sensitivity among diabetic patients at Khartoum, Sudan. Ann Clin Microbiol Antimicrob [Internet]. 2015 Apr 21 [cited 2020 Jun 15];14. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4406170/
41. Zubair KU, Shah AH, Fawwad A, Sabir R, Butt A. Frequency of urinary tract infection and antibiotic sensitivity of uropathogens in patients with diabetes. Pak J Med Sci. 2019;35(6):1664–8.
42. Kumar Jha P, Baral R, Khanal B. 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. 2014;3:29–34.
43. Tesfahunegn Z, Asrat D, Woldeamanuel Y, Estifanos K. Bacteriology of surgical site and catheter related urinary tract infections among patients admitted in Mekelle Hospital, Mekelle, Tigray, Ethiopia. Ethiopian Medical Journal. 2009;47(2):117–27.

44. Akram M, Shahid M, Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India. Ann Clin Microbiol Antimicrob. 2007 Mar 23;6(1):4.
45. Melaku S, Kibret M, Abera B, Gebre-Sellassie S. Antibiogram of nosocomial urinary tract infections in Felege Hiwot referral hospital, Ethiopia. African Health Sciences. 2012;12(2):134–9.
46. Sharma N, Gupta A, Walia G, Bakhshi R. Pattern of antimicrobial resistance of Escherichia coli isolates from urinary tract infection patients: a three year retrospective study. Journal of Applied Pharmaceutical Science. 2016;6(01):062–065.
47. Kibret M, Abera B. Prevalence and antibiogram of bacterial isolates from urinary tract infections at Dessie Health Research Laboratory, Ethiopia. Asian Pacific Journal of Tropical Biomedicine. 2014 Feb 1;4(2):164–8.
48. Mamuye Y. Antibiotic Resistance Patterns of Common Gram-negative Uropathogens in St. Paul's Hospital Millennium Medical College. Ethiopian Journal of Health Sciences. 2016 Mar 30;26(2):93–100.
49. Belete Y, Asrat D, Woldeamanuel Y, Yihenew G, Gize A. Bacterial Profile And Antibiotic Susceptibility Pattern Of Urinary Tract Infection Among Children Attending Felege Hiwot Referral Hospital, Bahir Dar, Northwest Ethiopia. Infect Drug Resist. 2019 Nov 18;12:3575–83.
50. Fu AZ, Iglay K, Qiu Y, Engel S, Shankar R, Brodovicz K. Risk characterization for urinary tract infections in subjects with newly diagnosed type 2 diabetes. Journal of Diabetes and its Complications. 2014 Nov 1;28(6):805–10.
51. Janifer J, Geethalakshmi S, Satyavani K, Viswanathan V. Prevalence of lower urinary tract infection in South Indian type 2 diabetic subjects. Indian Journal of Nephrology. 2009 Jul;19(3):107.
52. Raoofi A, Ghavami M, Shahhamzeh M, Ghasemi M, Hedartabar R, Salehi L. The Impact of Demographic Factors and Blood Sugar Control on the Incidence of Urinary Tract Infections in Khorramabad in 2013. Iran Red Crescent Med J [Internet]. 2016 Feb 14 [cited 2020 Jun 4];18(5). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4939233/
53. Abate D, Kabew G, Urgessa F, Meaza D. Bacterial Etiologies, Antimicrobial Susceptibility Patterns and Associated Risk Factors of Urinary Tract Infection among Diabetic Patients Attending Diabetic Clinics in Harar, Eastern Ethiopia. East African Journal of Health and Biomedical Sciences. 2017 May 11;1(2):11–20.
54. Bonadio M, Costarelli S, Morelli G, Tartaglia T. 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. 2006 Mar 17;6(1):54.
55. Damtew E. Prevalence of Diabetes mellitus among active pulmonary tuberculosis patients at St. Peter specialized hospital, Addis Ababa Ethiopia [Internet] [Thesis]. Addis Ababa University; 2014 [cited 2020 Jun 3]. Available from: http://etd.aau.edu.et/handle/123456789/4375

Figures

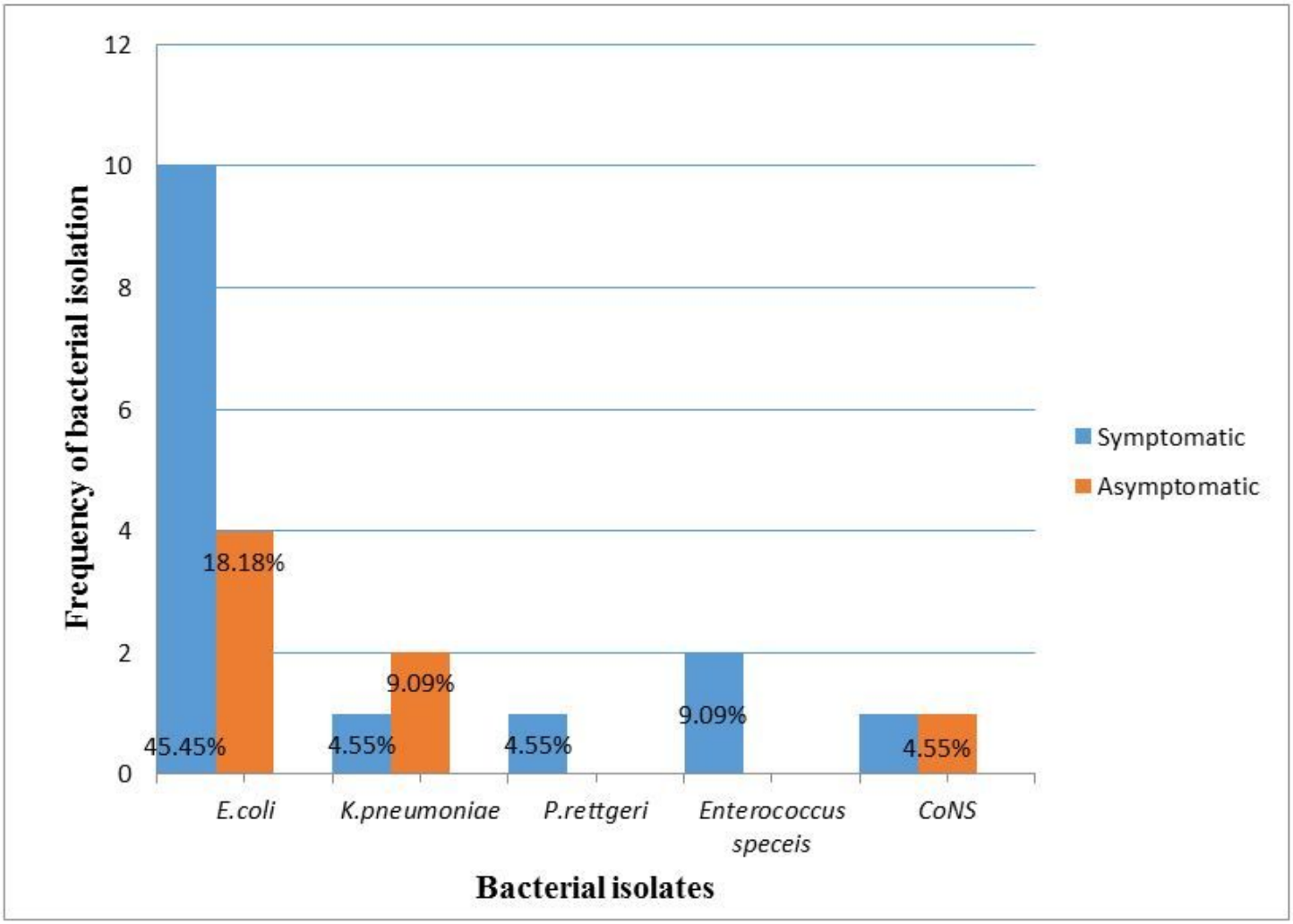

Figure 1

Distribution of bacterial uropathogens isolated from symptomatic and asymptomatic urinary tract infections among Diabetic patients at Zewditu Memorial Hospital, Addis Ababa, Ethiopia, May to July, 2018