Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients

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ABSTRACT

Objective: Diabetes mellitus (DM) and antibiotic resistance is an emerging public health problem in Ethiopia. Urinary tract infections (UTIs) are common and occasionally life- threatening condition among diabetic patients. Despite, all these problems, antibiotics are prescribed empirically which may adversely affect antibiotic resistance so far. Therefore the aim of this study was to identify the etiologic agents of UTI and their antibiotic resistance pattern among diabetic patients attending diabetic clinic of Hawassa University Referral Hospital.

Material and methods: A cross-sectional study was conducted in a total of 240 diabetic patients from June to October, 2014. After obtaining an informed written consent, socio-demographic and clinical data were collected using pre-structured questionnaire. Clean catch mid-stream urine samples were collected and processed for identification of uropathogen through culture using standard microbiologic procedure. Antibiotic susceptibility test was carried out using Kirby-Bauer disc diffusion method.

Results: The overall prevalence of diabetic UTI was 13.8%. Out of the total number of patients, 11.2% and 23.1% had asymptomatic and symptomatic bacteriuria respectively. DM patients with no previous history of UTI [AOR=3.55; 95% CI=1.186-10.611] and illiterate [AOR=2.5; 95% CI=1.052-5.989] had higher odds of UTI compared with their counterparts. *E. coli* was the commonest isolated uropathogen followed by coagulase- negative *Staphylococci*. All the isolated bacteria were resistant to ampicillin but sensitive to nitrofurantoin. Gram- negative isolates demonstrated high level of resistance to trimethoprim-sulphamethoxazole in 9 (81.8%), gentamicin in 8 (72.7%) and ceftriaxone in 7 (63.6%) patients. Gram- positive bacteria showed resistance to penicillin in 14 (87.5%), norfloxacin in 10 (62.5%) and ciprofloxacin in 8 (50.0%) patients. Multidrug resistance was observed in 93.9% of the isolated uropathogens.

Conclusion: Illiterate DM patients with no previous history of UTI were significantly associated with UTI. Nitrofurantoin can be used as a drug of choice for empiric treatment of UTI in the study area. Multidrug resistance to commonly used antibiotics is an alarming phenomenon. Therefore, performing of urine cultures and periodic surveillance of UTI among DM patients is necessary.

Keywords: Antibiotic resistance; bacteriuria; diabetes mellitus; urinary tract infectio

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Submitted:
22.06.2016

Accepted:
06.09.2016

Available Online Date:
27.01.2017

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Available online at
www.turkishjournalofurology.com

Introduction

The prevalence of diabetes mellitus (DM) is alarmingly increasing throughout the world and becoming a serious public health problem, especially in the developing countries.[1] Patients with DM are at increased risk for urinary tract infection (UTI).[2] The exact reason for this relationship remains unclear; however, few studies have reported that diabetic patients have immunologic impairment,[3] inadequate bladder emptying which necessitates subsequent urological manipulation predisposing to UTI.[4] Moreover, in addition to expression of different virulence factors, a higher glucose concentration in the urine may create a culture medium for the growth of pathogenic microorganisms.[4]

Urinary tract infections are generally asymptomatic in DM patients before development of symptomatic UTI.[5] Females are more commonly affected with UTI than males.[6] In addition, the prevalence of asymptomatic bacteri-

Turk J Urol 2017; 43(1): 85-92
DOI:10.5152/tud.2016.86155

uria is higher among women with type II diabetes[7] which leads to serious complications especially if glycemic control is poor.[8]

Several studies have showed that *Escherichia coli, Klebsiella spp, Proteus spps*, Group B *Streptococcus*, coagulase- negative *Staphylococci* (CoNS), *S. aureus*, *Enterococcus spp*, *Enterobacter spp., Citrobacter spp., Serratia spp, pseudomonas aeroginosa* and candidia spp. have been isolated among DM patients with a varying frequency.[9-13]

Antibiotic resistance is a major global public health problem both for hospital and community- acquired infections.[14] The problem is challenging in low-income countries because of high prevalence of infection, irrational uses of antibiotics, over-the-counter availability of antibiotics and poor infection prevention practices. Hence the emerging prevalence of antibiotic resistance[15, 16] and DM in Ethiopia[17] is a cause of concern for health care providers. Therefore, retrieval of updated information on the spectrum of uropathogens and their antibiotic resistance patterns in a specific hospital is mandatory. In few hospital- based studies conducted in the Central and Northwest part of Ethiopia reported incidence of antibiotic-resistance in UTI ranging between 10.4%, and 17.8%[9-11] and higher rate of multidrug resistance varying between 59.8%, and 71.7%.[9,10] among diabetic patients. However, there is no study conducted on antibiotic-resistance patterns in the Southern part of Ethiopia. Therefore this study was undertaken to identify the etiologic agents of UTI and their antibiotic resistance patterns among diabetic patients at Hawassa University Referral Hospital, Southern Ethiopia.

Material and methods

Study design and area

A cross-sectional study was conducted from June to October 2014 at Hawassa University Referral Hospital, Southern Ethiopia. The hospital is a tertiary level teaching Hospital that provides health services to over six million inhabitants in southern Ethiopia and it is located 275 km south from the capital city, Addis Ababa.

Study subject

Two hundred- forty DM patients visiting the hospital for their diabetic checkup during the study period were enrolled in the study. All socio-demographic and clinical data were taken after obtaining an informed written consent from each DM patient with or without symptoms of UTI. Patients treated with antibiotics within the preceding 2 weeks, and known anatomic and neurologic urinary tract abnormalities, also diabetic pregnant women were excluded from the study.

Sample collection

Clean-catch mid- stream urine samples (5-10 mL) were obtained from each patient in a sterile screw-capped wide-mouth container after informing them about proper urine collection methodi. The containers were labeled with a unique sample number, date and time of collection. The urine samples were processed within an hour after collection in the microbiology laboratory of Hawassa University Training and Research Hospital.

Culture and identification of bacterial species

Urine samples were directly inoculated on blood agar, mannitol salt agar and MacConkey agar plate (Oxoid, Ltd., Basingstoke, and Hampshire, England), using calibrated loops each delivering 0.002 mL of urine. Streaked culture plates were incubated under aerobic conditions at 37°c for 24 hours. On the next day, the bacterial growth on the respective media was controlled, and total colony count was calculated. Urine culture was considered significant bacteriuria (SB) when for a single isolated uropathogen colony forming units (CFUs) were $\geq 10^5$/mL of voided urine. However, $\geq 10^3$ CFU/mL was considered SB for group B streptococcus.[18] A single colony was picked and suspended in nutrient broth, and then subcultured onto either blood agar or MacConkey agar plate and finally incubated at 37°c for further identification. Pure isolates of bacterial pathogen were priorly characterized by colony morphology and gram-stain. Further identification was done by their colony characteristic appearance on their respective media and pattern of biochemical reaction using the standard procedure.[19]

Antibiotic susceptibility test

Antibiotic susceptibility testing was performed using Kirby-Bauer disc diffusion method.[20] Bacterial suspension was prepared using nutrient broth by peaking-up 3-5 colonies from pure culture and adjusted to 0.5 Mc-Farland standard equal to 10^8 cells/mL and swab inoculated onto Mueller-Hinton Agar (Oxoid, Ltd., Basingstoke, and Hampshire, England). Antibiotic impregnated discs were placed onto the surface of culture medium using an automated disc dispenser. The isolates were tested for ampicillin (AMP) (10 µg), amoxicillin (20 µg)-clavulanic acid (10 µg) (AMC) (30 µg), ceftriaxone (CRO) (30 µg), ciprofloxacin (CIP) (5 µg), norfloxacin (10 µg), nitrofurantoin (300 µg), gentamicin (CN) (10 µg), and oxacillin (OX) (1 µg), sulfamethoxazole+trimethoprim (SxT) (25 µg) and penicillin (G) (10 IU) (Oxoid, Ltd., Basingstoke, and Hampshire, England). After 18-24 hours of incubation at 37°C, zone of growth inhibition zone was measured to the nearest whole millimeter using a caliper. The zone of inhibition were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guideline as susceptible (S), intermediate (I) or resistant (R).[21] Quality control strains of *E. coli* (ATCC-25922), *S. aureus* (ATCC 25923) and *P. aeruginosa* (ATCC 27853), were used to validate the results of culture and antibiotic susceptibility test.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS Inc; Chicago, IL, USA) software version

16.0. Logistic regression analysis was done to determine the association between independent and dependent variables. All independent variables with a p- value less than or equal to 0.2 in the bivariate analysis were included in the multivariate logistic regression model to identify variables which were associated independently. Odds ratio (OR) within 95% confidence interval (CI) was calculated to measure the strength of association, and p-value <0.05 was considered statistically significant.

Ethical consideration

The study was approved by the institutional review committee, of Hawassa University College of Medicine and Health Sciences. After obtaining an informed written consent socio-demographic and clinical data were obtained from each DM patients. All data obtained in the course of the study were kept confidential and used exclusively for the purpose of the study. The laboratory findings of study participants were communicated with the responsible clinicians assigned at diabetic clinic and treated accordingly.

Results

Socio-demographic characteristics

A total of 240 patients with DM were investigated for UTIs. Of these, 188 (78.3%) patients had no symptoms of UTIs (asymptomatic UTI) and the remaining 52 (21.7%) cases presented with symptoms of UTIs (symptomatic UTI). Sixty seven (27.9%) had type I and 173 (72.1%) type II DM. Majority of the patients were male 146 (60.8%) and the remaining 94 (39.2%) were female with male to female ratio of 1.55:1. The mean age of the patients was 44.2±16.3 years (range, 15 -86) years (Table 1).

Significant bacteriuria and associated risk factors

The overall prevalence of diabetic UTI was 33 (13.8%). In 12 (23.1%) symptomatic and 21 (11.2%) asymptomatic diabetic patients SB was isolated. All patients had not any previous history of catheterization and hospitalization. In bivariate logistic regression analysis, the distribution of UTI was shown to be influenced by sex, level of education, current symptoms of UTI and history of previous UTI. However, blood glucose level had borderline significant association with UTI. Other factors such as age, previous antibiotic usage, type of diabetes and duration of diabetes were not associated with UTI (Table 2).

In multivariate logistic regression analysis, previous history of UTI and level of education were statistically significant. DM patients without any previous history of UTI [AOR=3.55; 95% CI=1.186-10.611 p=0.024] had higher odds of SB compared with those who had previous history of UTI. Similarly, DM patients who are illiterate [AOR=2.5; 95% CI=1.052-5.989; p=0.038] had higher odds of SB compared with those who are literate. While, patients with blood glucose level of ≥126 mg/dL [AOR=0.402; 95% CI=0.161-1.001; p=0.050] were less likely to develop UTI compared with blood glucose level ≤126 mg/dL, with borderline significant association. However, sex and current symptoms of UTI didn't show significant association with SB (Table 2).

Isolated uropathogens

Seven different bacterial species were isolated from 33 diabetic symptomatic (n=21; 63.4%), and asymptomatic (n=12; 36.4%) patients without any significant difference in the isolation frequency of each pathogen between two groups (p=0.199). The overall predominant bacterial isolate was *Escherichia coli* in 11

Table 1. Socio-demographic characteristics of diabetic patients investigated for UTIs

Characteristics	Total (n=240) n (%)	Symptomatic Diabetic patient (n=52) n (%)	Asymptomatic Diabetic patient n (%)
Age (years)			
15-20	26 (10.8)	1 (1.9)	25 (13.3)
21-40	74 (30.8)	16 (30.8)	58 (30.9)
41-60	109 (45.4)	28 (53.8)	81 (43.1)
61-86	31 (13.0)	7 (13.5)	24 (12.8)
Sex			
Male	146 (60.8)	26 (50.0)	120 (63.8)
Female	94 (39.2)	26 (50.0)	68 (36.2)
Education			
Illiterate	52 (21.7)	13 (25.0)	39 (20.7)
Literate	188 (78.3)	39 (75.0)	149 (79.3)
Type of diabetes			
Type I	67 (27.9)	6 (11.5)	61 (32.4)
Type II	173 (72.1)	46 (88.5)	127 (67.6)
History of UTI			
Yes	22 (9.2)	14 (26.9)	8 (4.3)
No	218 (90.8)	38 (73.1)	180 (95.7)
History of antibiotic Rx			
Yes	17 (7.1)	9 (17.3)	8 (4.3)
No	223 (92.9)	43 (82.7)	180 (95.7)
Duration of diabetes			
<5 years	135 (56.2)	24 (46.2)	111 (59.0)
≥5 years	105 (43.8)	28 (53.8)	77 (41.0)
Blood glucose level (mg/dL)			
<126	88 (36.7)	17 (32.7)	71 (37.8)
≥126	152 (63.3)	35 (67.3)	117 (62.2)

Rx: treatment; UTI: urinary tract infection; n: number of patients

Turk J Urol 2017; 43(1): 85-92
DOI:10.5152/tud.2016.86155

(33.3%) followed by CoNS in 8 (24.2%), *Staphylococcus aureus* in 6 (18.2%), *Klebsiella spp* in 3 (9.1%), *Citrobacter spp* and β-hemolytic streptococci in 2 (6.1%) patients. The least prevalent bacterium was *Pseudomonas aeruginosa* in 1 (3%) which was isolated only in asymptomatic diabetic patients. *E. coli* was the most commonly isolated bacteria in both asymptomatic 6 (28.6%) and symptomatic 5 (41.7%) diabetic patients, followed by CoNS in 5 (23.8%) and in 3 (25%) patients, respectively (Table 3). Four urine samples out of 240 (1.7%) demonstrated candidial growth.

Antibiotic resistance pattern

Antibiotic resistance patterns of Gram- negative bacteria to various antibiotics was shown in Table 4. Gram- negative isolates showed 100% resistance against ampicillin and high percentage (82.4%), of resistance to trimethoprim-sulphamethoxazole, ceftriaxone (64.7%), gentamicin (58.8%) and amoxicillin-clavulanic acid (41.2%). However, 100% of the isolated Gram-negative bacteria were susceptible to nitrofurantoin. Among Gram-negative bacteria, the predominant isolate was *E. coli*, (64.7% of Gram- negatives, 33.3% of all isolates) which showed 100 % re-

Table 2. Association of independent variables with UTI among diabetic patients by logistic regression analysis

	UTI				
Variables	**Yes n (%)**	**No n (%)**	**COR (95% CI)**	**AOR (95% CI)**	**p**
Age (years)					
15-20	5 (19.2)	21 (80.8)	1		
21-40	11 (14.9)	63 (85.1)	1.364 (0.425-4.380)		
41-60	10 (9.2)	99 (90.8)	2.357 (0.730-7.612)		
61-86	7 (22.6)	24 (77.4)	0.816 (0.225-2.961)		
Sex					
Male	14 (9.6)	132 (90.4)	1	1	
Female	19 (20.2)	75 (79.8)	0.419 (0.199-0.883)*	0.582 (0.255-1.332)	0.200
Education					
Literate	20 (10.8)	168 (89.4)	1	1	
Illiterate	13 (25.0)	39 (75.0)	2.800 (1.283-6.110)*	2.510 (1.052-5.989)	0.038
Current symptom of UTI					
Yes	12 (23.1)	40 (76.9)	1		
No	21 (11.2)	167 (88.8)-	2.386 (1.084-5.250)*	1.479 (0.598-3.660)	0.397
History of UTI					
Yes	8 (36.4)	14 (63.6)	1	1	
No	25 (11.5)	193 (88.5)	4.411 (1.683-1.561)*	3.547 (1.186-10.611)	0.024
History of antibiotic Rx					
Yes	2 (11.8)	15 (88.2)	1		
No	31 (13.9)	192 (86.1)	0.826 (0.180-3.789)		
Type of diabetes					
Type I	10 (14.9)	57 (85.1)	1		
Type II	23 (13.3)	150 (86.7)	1.144 (0.513-2.553)		
Duration of diabetes					
<5 years	17 (12.6)	118 (87.4)	1		
≥5 years	16 (15.2)	89 (84.8)	0.801 (0.384-1.673)		
Blood glucose level (mg/dL)					
<126	7 (8.0)	81 (92.0)	1		
≥126	26 (17.1)	126 (82.9)	0.419 (0.174-1.010)**	0.402 (0.161-1.001)	0.050

Rx: treatment; UTI: urinary tract infection; COR: crude odds ratio; AOR: adjusted odds ratio; n: number of patients;*p<0.05; **p=0.05

sistance to ampicillin, followed by trimethoprim-sulphamethoxazole (81.8%), gentamicin (72.7%), ceftriaxone (63.6%), amoxicillin-clavulanic acid (36.4%) and ciprofloxacin (18.2%). Low resistance to norfloxacin (9.1%) was observed. However, 100% of the isolated *E. coli* was susceptible to nitrofurantoin (Table 4). The antibiotic resistance pattern of Gram- positive bacteria to various antibiotics was shown in Table 5. Similarly, Gram-positive isolates were 100% resistant to ampicillin and 100% sensitive to nitrofurantoin. High percentage of resistance to penicillin (87.5%) norfloxacin (62.5%), ciprofloxacin (50.0%), trimethoprim-sulphamethoxazole (43.75%) and a nearly 25% resistance to ceftriaxone, amoxicillin-clavulanic acid and oxacillin were observed. However, 87.5% of Gram- positive bacteria were sensitive to gentamicin. Coagulase- negative staphylococci were the most predominant isolate among Gram-positive bacteria in 8 (50%) and the second most predominant pathogen of all isolates in 8 (24.2%) patients which showed 100% resistance to ampicillin and penicillin followed by norfloxacin 6 (75%), and ciprofloxacin 4 (50.0%). However, 100% of the isolated CoNS were sensitive to nitrofurantoin and gentamicin (Table 5).

Table 3. Distribution of the causative agents of asymptomatic and symptomatic UTI among diabetic patients

Uropathogen Isolated	Asymptomatic UTI No (%)	Symptomatic UTI No (%)	Total No (%)
E. coli	6 (28.6)	5 (41.7)	11 (33.3)
CoNS	5 (23.8)	3 (25.0)	8 (24.2)
S. aureus	5 (23.8)	1 (8.3)	6 (18.2)
Klebsiella spp,	1 (4.8)	2 (16.7)	3 (9.1)
β.H. streptococci	2 (9.5)	0	2 (6.1)
Citrobacter spp	1 (4.8)	1 (8.3)	2 (6.1)
P. aeruogenosa	1 (4.8)	0	1 (3.0)
Total	21 (63.6)	12 (36.4)	33 (100)

CoNS: Coagulase- negative *Staphylococci* β.HS: *Beta Hemolytic streptococci*

The overall multidrug resistance (MDR ≥two antimicrobial agents) was observed in 31 out of 33 (93.9%) bacterial isolates. While, 2 (6.1%) of the isolates were resistant to one antibiotic. There was no isolate sensitive and resistant to all the antibiotic agents tested (Table 6).

Discussion

The risk of developing antibiotic resistance in diabetes -associated UTI is a major concern in developing countries where urine culture is not routinely performed. In this study, overall prevalence of diabetic UTI was 13.8%. DM patients without any previous history of UTI had higher odds of contracting UTI compared with those who had previous history of UTI. Similarly, illiterate patients had higher odds of getting UTI compared with those who are literate. *E. coli* was the commonest isolated uropathogen and all the isolated bacteria were 100%, resistant to ampicillin and 100 % sensitive to nitrofurantoin.

In this study, the prevalence of diabetic-associated UTI was 13.8%. This finding is comparable with other findings in Addis Ababa (10.4-14%)[10,11] and Gondar (17.8%)[9], Ethiopia and Nigeria (17.3%).[22] However, this finding was lower as compared to the studies conducted in Nepal (21%)[23] and Germany (22.5%).[12] The variation in prevalence might be explained by difference in geography, the host factor and practices such as, social habits of the community, standards of personal hygiene and health education practices.

Table 4. Antimicrobial resistance patterns of gram-negative bacteria isolated from urine cultures of diabetic patients

Bacterial Isolates	Total No	S/R	AMP	AMC	CRO	CIP	NOR	NIF	CN	SxT
E. coli	11	S	0	7 (63.6)	4 (36.4)	9 (81.8)	10 (90.9)	11 (100)	3 (27.3)	2 (18.2)
		R	11 (100)	4 (36.4)	7 (63.6)	2 (18.2)	1 (9.1)	0	8 (72.7)	9 (81.8)
Klebsiella spp	3	S	0	1 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)	3 (100)	2 (66.7)	0
		R	3 (100)	2 (66.7)	2 (66.7)	2 (66.7)	2 (66.7)	0	1 (33.3)	3 (100)
Citrobacter spp	2	S	0	2 (100)	1 (50)	2 (100)	2 (100)	2 (100)	2 (100)	1 (50)
		R	2 (100)	0	1 (50)	0	0	0	0	1 (50)
P. aeruogenosa	1	S	0	0	0	1 (100)	1 (1000	1 (100)	0	0
		R	1 (100)	1 (100)	1 (100)	0	0	0	1 (100)	1 (100)
Total	17	S	0	10 (58.8)	6 (35.3)	13 (76.5)	14 (82.4)	17 (100)	7 (41.2)	3 (17.6)
		R	17 (100)	7 (41.2)	11 (64.7)	4 (23.5)	3 (17.6)	0	10 (58.8)	14 (82.4)

AMP: ampicillin; AMC: amoxicillin-clavulanic acid; CRO: ceftriaxone; CIP: ciprofloxacin; NIF: nitrofurantoin; NOR: norfloxacin; CN: gentamicin; SxT: trimethoprim-sulphamethoxazole

Turk J Urol 2017; 43(1): 85-92
DOI:10.5152/tud.2016.86155

Table 5. Antimicrobial resistance patterns of Gram- positive bacteria isolated from urine culture of diabetic patients

Bacterial Isolates	Total no	S/R	AMP	AMC	CRO	CIP	NOR	NIF	CN	SXT	PG	OX
CoNS	8	S	-	6 (75)	5 (62.5)	4 (50)	2 (25)	8 (100)	8 (100)	5 (62.5)	0	5 (62.5)
		R	8 (100)	2 (25)	3 (32.5)	4 (50)	6 (75)	0	0	3 (32.5)	8 (100)	3 (32.5)
S. aureus	6	S	-	4 (66.7)	5 (83.3)	3 (50)	3 (50)	6 (100)	6 (100)	4 (66.7)	0	5 (83.3)
		R	6 (100)	2 (33.3)	1 (17.7)	3 (50)	3 (50)	0	0	2 (33.3)	6 (100)	1 (17.7)
β.HS	2	S	-	2 (100)	2 (100)	1 (50)	1 (50)	2 (100)	0	0	2 (100)	2 (100)
		R	2 (100)	0	0	1 (50)	1 (50)	0	2 (100)	2 (100)	0	0
Total	16	S	-	12 (75)	12 (75)	8 (50)	6 (37.5)	16 (100)	14 (87.5)	9 (56.25)	2 (12.5)	12 (75)
		R	16 (100)	4 (25)	4 (25)	8 (50)	10 (62.5)	0	2 (12.5)	7 (43.75)	14 (87.5)	4 (25)

AMP: ampicillin; AMC: amoxicilin + clavulanic acid; CRO: ceftriaxone; CIP: ciprofloxacin; NIF: nitrofurantoin; NOR: norfloxacin; CN: gentamicin; SxT: trimethoprim-sulphamethoxazole; PG: penicillin; OX: oxacillin CoNS: *Coagulase- negative Staphylococci β.HS: Beta Hemolytic streptococci*

Table 6. Multiple antibiotic resistance patterns of bacterial isolates from urine culture of diabetic patients

		Antibiogram patterns						
Organisms	**No (%)**	**R1**	**R2**	**R3**	**R4**	**R5**	**R6**	**R7**
S. aureus	6 (18.2)	0	2 (33.3)	1 (16.7)	0	1 (16.7)	2 (33.3)	0
CoNS	8 (24.2)	0	1 (12.5)	2 (25)	1 (12.5)	1 (12.5)	1 (12.5)	2 (25)
β.HS	2 (6.1)	0	0	1 (50)	0	1 (50)	0	0
E. coli	11 (33.3)	1 (9.1)	1 (9.1)	2 (18.2)	2 (18,2)	3 (27.3)	2 (18.2)	0
Klebsiella spp	3 (9.1)	0	0	0	1 (33.3)	1 (33.3)	1 (33.3)	0
Citrobacter spp	2 (6.1)	1 (50)	0	1 (50)	0	0	0	0
P. aeruogenosa	1 (3)	0	0	0	0	1 (100)	0	0
Total	33 (100)	2 (6.1)	4 (12.1)	7 (21.2)	4 (12.1)	8 (24.2)	6 (24.2)	2 (6.1)

R1, R2, R3, R4, R5, R6,R7 resistance to one, two, three, four, five, six, seven antimicrobials tested, CoNS: *Coagulase- negative Staphylococci β.HS: Beta Hemolytic streptococci*

In this study, DM patients with no previous history of UTI had higher odds of contracting UTI compared with those who had previous history of UTI which showed contradictory results relative to previous studies conducted within the country[9] and other parts of the world.[8] The possible reason might be due to recall bias of patients. But it needs future advanced research to corroborate these findings. In addition, illiterate study participants had higher odds of getting UTI compared with those who are literate. Although, the association was borderline significant, patients with fasting blood glucose level of ≥126 mg/dL were less likely to have significant bacteriuria compared with patients who have <126 mg/dL. However, the previous study in Gondar[9] reported a significant correlation between hyperglycemia, and UTI. This indicates instataneous determination of fasting blood glucose level may not be associated with bacteriuria. Further large scale and glucose level follow-up studies are needed to conclude whether fasting blood glucose level is associated with significant bacteriuria or not.

The predominant uropathogen detected both in asymptomatic and symptomatic UTIs in this study was *E. coli* concordant with studies done in Ethiopia[9-11] and elsewhere.[12,13,22-25] This may be due to much stronger adherence of virulent type 1-fimbriated *E. coli* to the uroepithelial cells of diabetic patients.[26] The second most common isolated uropathogen was CoNS in conformity with a study conducted in Gondar.[9] However, this is in contrast to other studies; where *Klebsiella species* was the second most common isolated uropathogen.[11,22-25] High isolation rate of CoNS in this study might be explained by contamination during specimen collection or processing and/or a possible change in pattern of infection in DM patients.[9]

According to the Ethiopian standard treatment guideline[27], trimethoprim-sulphamethoxazole is the first- line drug while, norfloxacin or amoxicillin is an alternative drug for the empiric treatment of uncomplicated UTI. In this study, Gram-negative bacteria showed high resistance to ampicillin, trimethoprim-sulphamethoxazole, ceftriaxone, gentamicin and amoxicillin-

clavulanic acid. This result coincides with results reported from different part of the country[9,15,28,29] except the degree of resistance was higher in our cases. Even if the resistance rate and usage of drug is complicated; the cause of resistance for these drugs in this hospital might be deviation from the WHO standard prescription practices[30] which provide an environment or selection of resistant bacteria.

In this study, the higher resistance of Gram- negative bacteria to trimethoprim-sulphamethoxazole (82.7%) was demonstrated in agreement with a study conducted in Ethiopia[9,28,29] and elsewhere.[13,22] Studies had also proposed that due to emergence of high antimicrobial resistance and hypoglycemia, this antibiotic cannot be used as an empirical therapy for urinary tract infections among DM patients.[31] Indeed, emphasis should be given while developing treatment guideline. Although, Gram-negative isolates were susceptible to fluoroquinolones as ciprofloxacin and norfloxacin, more than half of the isolated Gram-positive bacteria were resistant to these antibiotics. This finding questions the usefulness of fluoroquinolone for the empiric treatment of UTI. However, all of isolated uropathogens were susceptible to nitrofurantoin. This is comparable with other studies.[5,29] Thus, nitrofurantoin can be used as drug of choice for empiric treatment of UTI in the study area.

In this study, 93.9% of the isolated uropathogens showed MDR against two and more antimicrobial agents tested. This finding is comparable with findings reported in Gondar (91.7%-95%) [15] and Addis Ababa (92.34%).[29] However, this incidence rate is higher than the findings of other studies conducted in Gondar (59.8%)[9] and Addis Ababa (71.7%).[10] The reason for high incidence of MDR might be patients' poor adherence to prescribed antibiotics, irrational use of antimicrobials, over-the-counter availability of antibiotics[16] and circulation of plasmid borne[32] high level drug resistant uropathogen in the study area.

Nevertheless, this study has some limitations regarding interpretation of its results. First, as a hospital- based study that used a non-probability sampling method, selection bias may be introduced that hinder the generalizability of the results to all DM patients in the study area. Second, because of lack of resource tests evaluating HBA1c and immunologic function like cytokine production and neutrophil function could not be performed.

In conclusion, the overall prevalence of diabetic UTI was 13.8%. DM patients with no previous history of UTI had higher odds of contracting UTI compared with those who had previous history of UTI. Similarly, those who are illiterate had higher odds of getting UTI compared with their counterparts. *E. coli* was the most common isolated uropathogen followed by CoNS. All isolated bacteria were 100% resistant to ampicillin and 100% sensitive to nitrofurantoin. Multidrug resistance to commonly used antibiotics in the study area is alarming. Therefore, performing urine culture and periodic surveillance of UTI on DM patients is necessary.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Hawassa University.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – D.N.; Design – D.N., A.A.; Supervision – A.A.; Resources – D.N.; Materials – D.N.; Data Collection and/or Processing – A.A; Analysis and/or Interpretation – A.A.; Literature Search – D.N., A.A.; Writing Manuscript – A.A.; Critical Review – D.N., A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received financial support Hawassa University.

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