Bacterial Etiologies, Antimicrobial Susceptibility Patterns and Associated Risk Factors of Urinary Tract Infection among Diabetic Patients Attending Diabetic Clinics in Harar, Eastern Ethiopia

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Abstract

Background: People with Diabetes Mellitus or problems with the body's natural defense mechanism are more likely to get Urinary Tract Infections (UTIs). The successful management of patients suffering from urinary tract infections in diabetic patients depends upon the identification of the types of organisms that cause the disease and the selection of an effective antibiotic against the organism in question.

Objective: To assess the prevalence of urinary tract infections, antimicrobial susceptibility patterns and associated risk factors among diabetic patients in Harar, Eastern Ethiopia.

Methods: A facility-based cross-sectional study was conducted among diabetic patients visiting diabetic clinics of five hospitals in Harar town from July 2014 to September, 2014. A structured questionnaire was used for collection of data on socio-demographic and associated risk factors. Mid-stream clean catch urine samples were collected using sterile containers. Culture and antimicrobial susceptibility testing were performed using the standard protocol. The data was entered into Epi-data version 3.15 and analyzed using SPSS version 16. Multivariate logistic regression analysis was conducted to determine the presence of an association between variables using odds ratio with 95% confident intervals and association was declared at P-value <0.05.

Results: A total of 240 diabetic patients participated in this study. Of these 95 (39.6%) of them presented with symptomatic urinary tract infection and the remaining 145 (60.4%) were asymptomatic. Significant bacteriuria was detected in 20% (19/95) and 12.4% (18/145) of symptomatic and asymptomatic diabetic patients respectively. The overall prevalence of urinary tract infection was 15.4% (37/240). The majority of the isolates (70 %) were Gram-negative bacteria. The most frequently isolated bacteria was Escherichia coli (45%) followed by Coagulase-Negative Staphylococci (15 %) and Pseudomonas aeruginosa (10.3%). All bacterial isolates were resistant to at least one antibiotic, and 92.5% of the isolates were resistant to multiple drugs. Previous history of urinary tract infections and female sex were significantly associated with urinary tract infection.

Conclusion: The prevalence of urinary tract infections among diabetic patients attending diabetic clinics in Harar is relative higher when compared to the findings of other studies conducted in different parts of the country and most of the isolates were resistant to multiple antimicrobial agents. Treatment of urinary tract infection among diabetic patients should be based on the result of culture and antimicrobial sensitivity tests.

Key Words: Urinary tract infection, Diabetic, Antimicrobial susceptibility test, Harar

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Introduction

Urinary tract infections (UTIs) are one of the most common microbial diseases affecting the urinary system of all ages (Dulawa, 2003). The risk of developing patients have a higher incidence of UTI than their non-diabetic counterparts (de Lastours and Foxman, 2014) and infection in diabetic patients is higher and the urinary tract is the most common site for infections. Diabetic infections can be more severe leading to complications, ranging from dysuria to organ damage and sometimes even death due to pyelonephritis (Saleem and Daniel, 2011). Changes in host defense mechanisms, the presence of diabetic cystopathy and micro-vascular

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disease in the kidneys may play a role in the higher incidence of UTI in diabetic patients. Moreover, diabetic patients encounter further urinary urgency and incontinence during the night, a condition often manifested by painful urination and retention of urine in the bladder (Bonadio *et al*., 2006).

A study showed that 20% of women who had Type 1 or Type 2 Diabetes developed UTIs (Geerlings *et al*., 2000). Different studies conducted in different parts of the world, including Ethiopia, have isolated *Escherichia coli, Pseudomonas aeruginosa, Enterococcus species, Staphylococcus aureus, , Klebsiela, Acinetobacter, Proteus and Coagulase Negative Staphylococci (CONs)* as common causes of UTI among diabetic patients (Feleke *et al*., 2007 ; Gizachew *et al*., 2010; Yeshitela *et a*l., 2012; Pragash *et.al*., 2014; Hamdan *et al*., 2015; and Demiss and Anteneh, 2016).

There are many intrinsic and extrinsic risk factors which are the leading causes of urinary tract infection such as stone/calculi, enlarged prostate, catheterization, pregnancy, tumor in the kidney, non-functional kidney, kinking of ureter, kidney transplant, myxoedema , lack of circumcision, those who have CD4 T cell counts of less than 200/ml and diabetics . These groups are at risk of bacteriuria and symptomatic UTI (Ramzan *et al*., 2004)

In general factors that have been proposed as constituting an enhanced risk for UTIs in diabetes include age, metabolic control, duration of diabetes, more frequent hospitalization and instrumentation of the urinary tract, recurrent vaginitis and vascular complications (Gizachew *et al*., 2010; de Lastours and Foxman, 2014).The successful management of diabetic patients suffering from urinary tract infections depends up on the identification of the types of organisms that cause the disease and the selection of an effective antibiotic against the organism in question. The emergences of resistant bacterial strains in hospitals poses a continued challenge to treat and control the spread of infections. Moreover, the indiscriminate use of antibiotics often results in the increased resistance of urine pathogens to most commonly used antimicrobial drugs (Gizachew *et al*., 2010).

Microbial drug resistance is a major problem in treating infectious diseases worldwide. It is aggravated due to increased use of empirical treatments or erratic use of antimicrobials (Gupta *et a*l., 2001) mainly in low income countries, which do not have laboratory facilities to isolate pathogens and determine their drug susceptibility patterns.

Some hospital-based studies conducted in the central, northwest and southern part of Ethiopia reported a varying prevalence of UTI ranging from 10.4% to 17.8% and a high rate of multidrug resistance varying between 59.8%, and 93.9% among diabetic patients (Feleke *et a*l., 2007; Gizachew *et al*., 2010; Yeshitela *et a*l., 2012 and Demiss and Anteneh, 2016). However, there is no study on the prevalence, antimicrobial susceptibility pattern and associated factors of UTIs among diabetic patients in the study area. Therefore, this study was conducted to identify bacterial etiologies, antimicrobial susceptibility patterns and associated risk factors of urinary tract infection among diabetic patients attending diabetic clinics in Harar, Eastern Ethiopia.

Materials and Methods

Study Area, Design, and Period

A cross-sectional study was conducted at the diabetic clinics of Hiwot Fana Specialized University Hospital, Jegula Hospital, Police Hospital, Army Hospital and Yemaje Hospital in Harar, Eastern Ethiopia between July, 2014 and September, 2014.

Source Population

The source population of this study was all diabetic patients attending diabetic clinics in all hospitals in Harar.

Study Population

Diabetic patients who visited diabetic clinics in five Hospitals in Harar during the study period were the study population.

Sample Size and Sampling Technique

The sample size was determined using a single population proportion formula considering the overall 17.8% prevalence of significant bacteriuria from a study conducted on diabetic patients in Gondar (Gizachew *et al*., 2010) and in this study we used 95% confidence level and 5% margin of error. The final sample size after adding 10% non-response was 247. Diabetic patients with symptoms (n=95) and without symptoms (n=145) of urinary tract infection who visited diabetic clinics of five hospitals in Harar during the study period were included in the study with response rate of 97%. The number of participants were 97, 97, 21, 13, and 12 from

Hiwot Fana specialized University Hospital, Jugula Hospital, Police Hospital, Army Hospital and Yemage Hospital respectively.

Total sample size was proportionally allocated to the diabetic clinics of five hospitals in Harar by considering total number of diabetic patients visiting the clinics of the respective hospitals. Systematic sampling technique was used to select the study subjects from each of the five hospitals. Since our study sample size was about half of the number of diabetic clients in all hospitals every other patient visiting the respective hospitals within the study period was included in the study and the first study participant was selected by the lottery method. The distribution of the number of study subjects was based on the proportions of diabetic clients in the respective health institutions.

Inclusion and Exclusion Criteria

All diabetic patients aged 18 years and above were included in the study. Those participants who took antibiotics during the last two weeks were excluded.

Data Collection

Information about the patient's demographic characteristics such as age, educational status, occupation and other variables including a history of urinary frequency, abdominal pain, history of sexually transmitted infections (STIs) and additional previous infections was collected using the interview method.

Collection, Handling and Transport of Specimens

Diabetic patients were instructed about the proper collection of urine specimen to avoid contamination. Clean voided 10-20 milliliters of midstream urine specimen was collected in a sterile container with the assistance of a medical laboratory technologist at the respective hospitals. Afterward the specimen was transported to the Microbiology Laboratory of the Department of Medical Laboratory Sciences, College of Health and Medical Sciences, Haramaya University, within 2 hours of collection for further analysis (Cheesebrough, 1998).

Identification of Uropathogens

The urine sample was inoculated on MacConkey and blood agar (Oxoid Ltd, Basingstoke and Hampshire, England) by using a calibrated wire loop and incubated at 37^0C for 48 hours. Significant bacteriuria was defined as urine cultures growing >105 colony-forming unit /ml midstream urine. All positive urine cultures showing significant bacteriuria were further identified by their characteristic appearance on their respective media and confirmed by the pattern of biochemical reactions using the standard procedures.

Antimicrobial Susceptibility Testing

Antimicrobial susceptibility testing was performed for isolates using agar disc diffusion method on Muller Hinton agar (Oxoid Ltd, Basingstoke, and Hampshire, England) as described by the National Committee for Clinical Laboratory Standards (NCCLS, 2002). Pure culture was transferred into a tube containing 5 ml sterile normal saline (0.85 % NaCl) and mixed gently until it formed a homogenous suspension. The turbidity of the suspension was then adjusted to the optical density of McFarland 0.5 tubes in order to standardize the inoculums size. A sterile cotton swab was then dipped into the suspension and the excess was removed by gentle rotation of the swab against the surface of the tube. The swab was then used to distribute the bacteria suspension evenly over the entire surface of Mueller-Hinton agar (Oxoid Ltd, Basingstoke, and Hampshire, England). The inoculated plates were left at room temperature to dry for 3 minutes. Using sterile forceps the antibiotic discs were placed on the inoculated plates and incubated at 36^0C for 24 hours. The diameter of the zone of inhibition around the disc was measured to the nearest millimeter using a metal caliper and the isolates were classified as sensitive and resistant (NCCLS, 2002).

The antimicrobials for disc diffusion testing for both gram positive and negative bacteria were obtained from Oxoid Ltd, Basingstoke, and Hampshire, England in the following concentrations amoxicillin-clavulanic acid (AMC) (30µg), ceftriaxone (CRO) (30 µg), ampicillin (AMP) (10 µg), penicillin G (10IU), chloramphenicol (C) (30µg), ciprofloxacin (CIP) (5 µg), trimethoprimsulphamethoxazole (SXT) (25µg), norfloxacin(NOR) (10µg) and tetracycline (TTC) (30 µg).

Quality Control

Reference strains of E. coli (ATCC 25922), S. aureus (ATCC 25923) and P. aeruginosa (ATCC 27853), sensitive to the antimicrobial agents tested obtained from Harari Regional Laboratory were used as a control throughout the study.

Operational Definitions

Asymptomatic Bacteriuria: defined as the presence of at least 10^5 colony-forming units (cfu)/ml of 1 or 2 bacterial species in a clean-voided midstream urine sample from an individual without symptoms of a UTI

Symptomatic Bacteriuria: defined as the presence of at least 10^5 colony-forming units (cfu)/ml of 1 or 2 bacterial species in clean-voided midstream urine sample from patients with at least two of the following complaints: dysuria, urgency, frequency, incontinence, suprapubic pain, flank pain or cost vertebral angle tenderness, fever (temperature of 38°C) and chills.

Low Level Resistance: when less than 50% of isolated bacteria are resistant to a given drug.

Intermediate Level Resistance: when 50-75% of isolated bacteria are resistant to a given drug.

Multi Drug Resistant: when the isolated bacteria are resistant to two or more drugs.

Data Processing and Analysis

Data were entered and cleaned using Epi-Data version 3.15, and analyzed using SPSS version16. Frequency and percentages were calculated and presented using tables and charts. Association between dependent and independent variable was assessed using chi-square and bi-variate analysis. Multi-variate regression analysis was employed to control confounders. A p-value <0.05 was considered statistically significant with 95% confident intervals (CI).

Ethical considerations

Ethical clearance was obtained from Haramaya University, College of Health and Medical Sciences, Institutional Health Research Ethical Review Committee. Written and signed consent was obtained from each study participant before initiation of data collection. 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 to the responsible health professional assigned to the diabetic clinic and managed accordingly.

Results

Characteristics of Study Participants

A total of 240 study participants were involved in this study. Out of these, 124 (51.7%) were male. Female to male ratio was 0.9:1. The mean age of the study participants was 49.2 years (+SD 15.8) with a range from 18 to 86 years. Urban residents comprised 72.5% of the sample. The majority, 174 (72.4%) of the participants were married, 72 (30%) of the participants were illiterate, and 66 (27.5%) were unemployed. A total of 63 (26.2%) had a history of urinary tract infection and 131 (54.6%) had been diabetic for less than five years (Table 1).

Table 1: Socio-demographics and clinical characteristics of diabetic patients investigated for urinary tract infection in diabetic clinics of Harar, eastern Ethiopia from July 2014 to September, 2014, (n=240).

Variable	Freq.	(%)
Sex		
Male	124	51.7
Female	116	48.3
Age (in years)		
18-35	55	22.9
36-45	47	19.6
46-55	47	19.6
>55	91	37.9
Residents		
Urban	174	72.5
Rural	66	27.5
Duration of diabetes (in year)		
<5	131	54.6
>5	109	45.4
History of UTI		
Yes	63	26.2
No	177	73.8
History of antibiotics use		
Yes	64	26.7
No	176	73.3
Marital status		
Single	66	27.6
Married	174	72.4
Educational status		
Illiterate	72	30
Read and write	36	15
Primary school	56	23.3
Secondary school and more	76	31.7
Occupational status		
Unemployed	66	27.5
Governmental employee	50	20.8
Private	77	32.1
House wife	47	19.6

Significant Bacteriuria

Out of 240 diabetic patients, 95 (39.6%) presented with symptomatic UTIs whereas, 145 (60.4%) had no symptoms. Significant bacteriuria was detected in 19/95 (20%) and 18/145 (12.4%) of symptomatic and asymptomatic diabetic patients, respectively. The overall prevalence of significant bacteriuria in both groups was 37/240 (15.4%).

Etiologic Agents

A total of 40 bacterial uropathogens were isolated from 240 diabetic patients investigated for UTIs. Of these, 22/40 (55 %) were from symptomatic diabetic patients and the remaining 18/40 (45%) were from asymptomatic diabetic patients. E. coli (18 (47.5%)) was the most common isolated bacteria followed by Coagulase Negative Staphylococci (CONs) (6 (15%)) and Pseudomonas (4(10%)). Mixed infections (two pathogenic bacteria) were detected in three diabetic patients. Co-infection of Proteus species and Escherichia coli were isolated from two diabetic patients and, Staphylococci saprophyticus and Enterococci were isolated from one diabetic patient (Figure1).

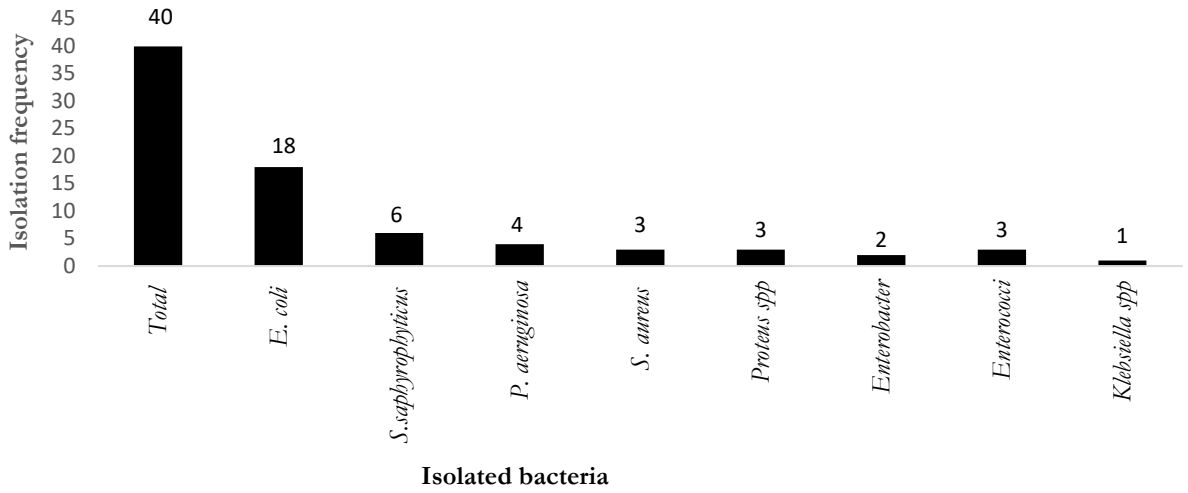

Figure 1: Frequency and type of bacterial species isolated from diabetic patients investigated for urinary tract infections at diabetic centers in Harar, Eastern Ethiopia from July 2014 to September, 2014(n=40).

Factors Associated With Significant Bacteriuria

Significant bacteriuria was detected among 19.2% and 10.1% of female and male study participants respectively. In bivariate logistic regression analysis, bacteriuria was significantly associated with sex, duration of diabetes and previous history of urinary tract infection. Other factors such as age, previous antibiotic usage, marital status, residence, educational status and occupational status were not associated with UTI. Bivariate analysis showed that female sex had a 3.5 (1.591-7.520) times more chance of getting urinary tract infection than male sex. Study participants who were diabetics for less than five years had 1.88 (1.25-6.12) times more chance of getting urinary tract infections than those who were diabetics for more than five years. Diabetic patients with previous history of UTI had 1.24 (1.11-3.84) times more chance of getting urinary tract infections than those without a previous history of UTI (Table 2). Those variables (previous history of UTI, sex and duration of diabetes) associated with UTI in bivariate analysis were analysed using multivariate logistic regression analysis.

In multivariate logistic regression analysis, previous history of UTI and sex were statistically significantly associated with UTI. Diabetes patients with a previous history of UTI [AOR=2.23; 95% CI=1.330 6.520] were 2.23 times more likely to develop a UTI compared to those who had no previous history of UTI. Similarly, female diabetic patients [AOR=2.51; 95% CI=1.520 6.104] were 2.51 times more likely to develop UTI compared to male diabetic patients (Table 2).

Table 2. Risk factors associated with urinary tract infection among diabetic patients visiting diabetic clinics in Harar, Eastern Ethiopia from July 2014 to September, 2014.

Variables	UTI		**COR (95% CI)**	**AOR (95% CI)**
	Yes No (%)	No No (%)		
Sex				
Female	27(19.2)	114(80.8)	3.458(1.591-7.520)	2.51(1.52-6.14)
Male	10(10.1)	89(89.9)	1	1
Age group (in years)				
18-35	6(11)	49(89)	1.485(0.535-4.123)	
36-45	8((17)	39(83)	0.886(0.343-2.292)	
46-55	9(19)	38(81)	0.768(0.305-1.932)	
>55	14(15.4)	77(84.6)	1	
Marital status				
Single	14(21.2)	52(78.8)	0.580(0.278-1.210)	
Married	23(13.2)	151(86.8)	1	
Residence				
Rural	28(16)	146(84)	1.215(0.540-2.733	
Urban	9(13.6)	57(86.4)	1	
Educational status				
Illiterate	12(16.7)	60(83.3)	0.672(0.265-1.705)	
Read and write	8(22.2)	28(77.8)	0.470(0.165-1.343)	
Primary school	8(14.3)	48(85.7)	0.806(0.290-2.239)	
Secondary school and above	9(11.5)	69(88.5)	1	
Occupational status				
Unemployed	10(15.2)	56(84.8)	1.920(0.750-4.913)	
Governmental employee	5(10)	45(90)	3.086(0.994-9.580)	
Private	10(13)	67(87)	2.297(0.903-5.842)	
House wife	12(25.5)	35(74.5)	1	
History of UTI				
Yes	13(20.6)	50(79.4)	1.24 (1.11-3.84)	2.23(1.330-6.520)
No	24(13.5)	153(86.5)	1	1
History of antibiotics use				
Yes	13(20.3)	51(79.7)	0.624(0.296-1.315)	
No	24(13.6)	152(86.4)	1	
Duration of diabetes(in years)				
<5	24(18.3)	107(81.7)	1.88 (1.25-6.12)	1.51(0.950-4.310)
>5	13(11.9)	96(88.1)	1	1

Antimicrobial Susceptibility

Antimicrobial susceptibility testing was performed for 40 bacterial isolates identified from the patients. All isolates showed 100% resistance to penicillin and ampicillin, >60% resistance to amoxicillin-clavulanic acid, gentamicin and trimethoprim-sulphamethoxazole and less than 55 % resistance to chloramphenicol, norfloxacin, ciprofloxacin and ceftriaxone. All gram-negative isolates showed 100% resistance to trimethoprim sulphamethoxazole and > 75% resistance to amoxicillin-clavulanic and chloramphenicol. But ceftriaxone and Ciprofloxacin had <50% resistance. Multi-drug resistance was found in 92.5% of the isolatesof both gram positive and gram negative bacteria (Table 3).

Table 3: Antimicrobial susceptibility pattern of bacterial uropathogens isolated from diabetic patients with urinary tract infections attending diabetic centers in Harar, Eastern Ethiopia from July 2014 to September, 2014.

Organism		Antibiotics							
		Nor	**AMC**	**CRo**	**C**	**SXT**	***CIP***	**K**	**TTC**
Proteus spp(n=3)	S* N0	2	1	2	0	0	1	2	0
	R* N0	1	2	1	3	3	2	1	3
Klebsiella spp(n=1)	S* N0	0	0	0	1	1	1	0	1
	R* N0	1	1	1	0	0	0	1	0
E.coli(n=18)	S* N0	6	5	9	9	4	8	4	
	R* N0	12	13	9	9	14	10	14	15
P. aeruginosa(n=4)	S* N0	4	0	1	1	1	1	0	2
	R* N0	0	4	3	3	3	3	4	2
Enterobacter	S* N0	1	1	1	0	2	0	1	1
	R*N0	1	1	1	2	0	2	1	1
Total(n=28)	S* N0	13	7	13	11	8	11	7	7
	R* N0	15	21	15	17	20	17	21	21
CONS(n=6)	S* N0	2	0	2	1	1	1	4	1
	R* N0	4	6	4	5	5	5	2	5
S. aureus(n=3)	S* N0)	0	0	2	1	1	1	2	1
	R* N0	3	3	1	2	2	2	1	2
Enterococci=3	S* N0	1	0	2	1	1	2	0	1
	R* N0	2	3	1	2	2	1	3	2
Total(n=12)	S* N0	3	0	6	3	3	0	6	3
	R* N0	9	12	6	9	9	12	6	9

CONS= Coagulase negative Staphylococci; AMC=Amoxicillin-clavulanic acid; CRO=Ceftriaxone; CIP=Ciprofloxacin; C=Chloramphenicol; SXT= Trimethoprim-sulphamethoxazole; TTC= Tetracycline Nor= Norfloxacin; S=Sensitive R*=Resistant*

Discussion

In this study, the overall prevalence of significant bacteriuria (SB) in both symptomatic and asymptomatic diabetic patients was 15.4%. Similar findings have been reported in previous studies conducted in some parts of Ethiopia such as Gondar University Hospital (17.8%) (Gizachew *et al*., 2010), Tikur Anbessa Specialized University Hospital, Addis Ababa (14%) (Feleke *et al*., 2007), Hawassa University Referral Hospital (13.8%) (Demiss and Anteneh, 2017) and other countries including Uganda (13.3%) (Ampaire *et al*., 2015) and Sudan (19.5%) (Hamdan *et al*., 2015).However, it is much lower than reports from different parts of world such as a study in Libya which reported 57% UTIs among diabetic patients (Ghenghesh *et al*., 2009), Kuwait which reported 35% (May *et al*., 2015), Nepal which reported 54.76 % (Kumar *et al*., 2014), and rural South India which reported 58% (Pragash *et al*., 2014). The variation in prevalence might be explained by differences in geography, the host factor and practices such as, social habits of the community, standards of personal hygiene and health education practices. In this study gram-negative bacteria were predominantly isolated with a rate of 60.6% (refer to Figure 1). Similar findings were reported from previous studies in Libya, Nepal, Khartoum, Sudan, rural South India, Kuwait and Gondar University Hospital in which all studies isolated gram negative bacteria as the dominant causative agent of UTIs (Ghenghesh *et al*., 2009; Gizachew *et al*.,2010; Hamdan *et al*., 2015; Kumar *et al.,* 2014; Pragash *et al*., 2014; and May *et al*., 2015).

Our study found *E. coli* to be the most frequently isolated bacteria from diabetic patients with UTI similar to previous international studies (Ghenghesh *et al*., 2009; Gizachew *et al*.,2010; Kumar *et al.,* 2014; Pragash *et al*., 2014; Hamdan *et al*., 2015 and May *et al*., 2015). In general, the relatively high number of Enterobacteriaceae isolated in this study as well as different previous studies may be indicative of faecal contamination and a reflection of poor personal hygiene. This group of organisms tends to be endemic in hospital environments and in the community as they are easily transferred from object to object. They also tend to be resistant to common antiseptics making them difficult to eradicate in the long term and increasingly responsible for the many hospital acquired infections.

In this study bacterial mixed infections were isolated from only three diabetic patients unlike a study conducted in Gondar University Hospital which isolated mixed infection from seven diabetic patients (Gizachew *et al*., 2010).

In this study, bacteriuria was significantly associated with female sex in which more infections were reported in females (23%) than males (8%) ($p<0.05$) in line with reports from previous studies in Kuwait, Nepal and rural South India which also showed higher infection rates in females than males (Kumar *et al.,* 2014: May *et al*., 2015 and Pragash *et al*., 2014), but in contrast to a previous study in Gondar University Hospital which reported no statistical association between sex and bacteriuria (UTI) ($p<0.05$) (Gizachew *et al*., 2010). The higher infection rate of UTI among females in our study may be due to decrease of normal vaginal flora (Lactobacilli), less acidic pH of vaginal surface, poor hygienic condition, short and wide urethra and proximity to anus.

In our study significant bacteriuria was strongly associated with a history of previous UTI similar to a previous study in conducted in Gondar University Hospital ($p<0.05$) (Gizachew *et al*., 2010). This higher infection rate among diabetic patients with a previous history of UTI may due to inappropriate treatment of previous infections which in turn results in recurrence.

In this study a large number of the isolates were resistant to amoxicillin, tetracyline, norfloxacin ,ciprofloxacin, ceftriaxone and trimethoprim-sulphamethoxazole which is consistent with reports of different studies conducted in different areas (Kumar *et al.,* 2014; Pragash *et al*., 2014 and May *et al*., 2015).The remarkably higher prevalence of resistance to the commonly prescribed antibiotics noticed in the present study may be due to the easily availability and indiscriminate use of the drugs without prescription. It was reported that amoxicillin-clavulanic acid was effective for more than 90% of gram-positive and 59% of gram-negative isolates in Gondar (Gizachew *et al*., 2010), however, in the present study amoxicillin-clavulanic acid was found to be effective for only 25% of gram-negative bacteria and none of the gram-positive bacteria isolates. This sharp fall in effectiveness may be due to overuse of it as an empiric treatment option.

In the present study, *P. aeruginosa* was not appreciably susceptible to most antibacterial agents and it was 100% resistant to amoxicillin-clavulanic acid which was in line with study in Gondar University Hospital (Gizachew *et al*., 2010). In this study the only effective antibacterial agent was ceftriaxone; which was effective for more than 50% of gram-positive and gram-negative isolates.

The high frequency of multiple antibiotic resistance might be a reflection of inappropriate use of antimicrobials, lack of laboratory diagnostic tests and the lack of guidelines for the selection of antibiotics. Most of the isolates were resistant to these antibiotics. This finding is relatively higher as compared to the other study in Gondar (Gizachew *et al*., 2010). This may be explained by irrational use of antibiotics for conditions that may not be clinically indicated, over-the-counter sale of antibiotics, and some new drug formulations which may be of poor quality and dumping of banned products into the market where the public may get access to them, thus producing antimicrobial-resistant strains.

Conclusion and Recommendations

The overall prevalence of urinary tract infections in diabetes mellitus in this studied population was 15.4% and the predominant uropathogen was *Escherichia coli*. Bacteriuria is significantly associated with female sex and a previous history of UTI ($P<0.05$). Most isolates showed 100% resistance to penicillin and ampicillin whereas ceftriaxone and ciprofloxacin showed <50% resistance against both gram-negative and gram-positive bacteria among our study population. We found that 92.5% bacteria isolates had resistance to multiple antimicrobial agents. Therefore, early screening of diabetics for UTI and determining their antibiotic susceptibility pattern is an important intervention to prevent complications due to UTI among diabetic patients. Empirical treatment for UTIs may not be effective, therefore treatment should be based on the results of culture and sensitivity tests. But in the absence of laboratory facilities for drug sensitivity tests we recommend ceftriaxone and ciprofloxacin for treatment of UTIs, but not penicillin and ampicillin since most isolates showed 100% resistance. The authors also recommend improvement of personal hygiene, maintaining acidic pH of vaginal surface and appropriate use of prescribed antibiotics.

Limitation of the Study

The antibiotic susceptibility testing did not include all the currently recommended antibiotics for treatment of UTIs.

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Competing Interests

The authors would like to declare that we have no competing interests in this study.

Authors' Contributions

DA: was responsible for selection of the topic, write up of the proposal, data collection, statistical analysis and also responsible for the final write up. GK: was responsible for designing the methodology of the study and also involved in the selection of the topic, data collection and statistical analysis. FU and DM: Participated in the revision of the design of the study, data collection and the statistical analysis.

References

Ampaire, L., Butoto,A., Orikiriza,P. and Muhwezi,O. 2015. Bacterial and Drug Susceptibility Profiles of Urinary Tract Infection in Diabetes Mellitus Patients at Mbarara Regional Referral Hospital, Uganda. *British Microbiology Research Journal*, *9*(4), pp.1-5.

Bonadio, M., Costarelli, S., Morelli, G., and Tartaglia, T. 2006. The influence of diabetes mellitus on the spectrum of uropathogens and the antimicrobial resistance in elderly adult patients with urinary tract infection. *BMC infectious diseases*, *6*(1), p.54

Cheesebrough, M. 1998 .Medical laboratory manual for tropical countries, *Microbiology* Volume II, Cambridge University Press, London UK, pp. 251-260.

de Lastours, V. and Foxman, B. 2014. Urinary tract infection in diabetes:epidemiologic considerations. *Current infectious disease reports*, *16*(1), p.389.

Demiss, N., Anteneh, A. 2017. Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients. *Turk J Urol* 2017; 43(1): 85-92.

Dulawa, J. (2003). Urinary tract infections. *Annals of Academic Medical Bialostoc.*, 49, 182-184

Feleke, Y., Mengistu, Y., Enquselassie, F. 2007. Diabetic infections: clinical and bacteriological study at Tikur Anbessa Specialized University Hospital, Addis Ababa, Ethiopia. *Ethiop Med J*; 45:171-9.

Geerlings, S.E., Stolk, R.P., Camps, M.J., Netten, P.M., Hoekstra, J.B., Bouter, K.P., Bravenbour, B.E.R.T., Collet, J.T., Jansz, A.R., Hoepelman, A. I. 2000. Asymptomatic bacteriuria may be considered a complication in women with diabetis. Diabetes Mellitus Women Asymptomatic Bacteriuria Utrecht Study Group. *Diabetes Care*, *23*(6), pp.744-749.

Ghenghesh, K.S., Elkateb, E., Berbash, N., Abdel, R., Ahmed, S.F., Rahouma, M.A., Belresh, T., Klena, J.D., Seif-EnnasseElkhabrounr, N. 2009. Uropathogens from Diabetic Patients in Libya: virulence factors and phylogenetic groups of isolated Escherichia coli. *.J Med Microbiol.*, 58(8):1006-14 DOI: 10.1099/jmm.0.007146-0

Gizachew, Y., Daniel, A., Yimtubezinash,W., Chandrashekhar, U. 2010. Urinary Tract Infection: Bacterial etiologies, drug resistance profile and associated risk factors in diabetic patients attending Gondar University Hospital, Gondar, Ethiopia, *Euro. J. Exp. Bio.*, 2012, 2 (4):889-898

Gupta, K., Hooten, T.M., Stamm, W.E., 2001. Increasing antimicrobial resistance and the Management of uncomplicated community-acquired urinary tract infections. *Ann Int Med.* 135:41-50.

Hamdan, Z,.,Eman, K., Amar, M., Onab, S., Sarah, O., Ishag, A. 2015. Urinary tract infections and antimicrobial sensitivity among diabetic patients at Khartoum, Sudan. *Journal of Annals of Clinical Microbiology and Antimicrobials*, 14:26 DOI 10.1186/s12941-015-0082-4

Kumar, Jha, P., Baral, R. and Khanal, B., 2014. Prevalence of uropathogens in diabetic patients and their susceptibility pattern at a tertiary care center in Nepal-A Retrospective study. *Int J Bio Lab Sci*, *3*, pp.29-34.

May, S., Shinu, N., Samia,W., Mohamed, M., Asma, A., Kazem, B., Faisal, Al. , Ali, T. 2015. Prevalence of Urinary Tract Infection and antimicrobial susceptibility among Diabetic Patients with controlled and uncontrolled glycemia in *Kuwait. Journal of Diabetes Research*,Volume 2016 (2016).

National Committee for Clinical Laboratory Standards (NCCLS). 2002. Performance standards of antimicrobial susceptibility, NCCLS approved standards M 100-59 National Committee for Clinical Laboratory Standards.

Pragash, D.S., Girija, S., Shekar, U., Rayapu, V. 2014. Study of uropathogens among Type II Diabetic patients and their antimicrobial resistance pattern among Rural South Indian Population. *Sch. J. App. Med. Sci.*, 2(2B):58

Ramzan, M., Bakhsh, S., Salam, A., Khan, G.M. and Mustafa, G., 2004. Risk factors in urinary tract infection. *Gomal Journal of Medical Sciences*, *2*(1).

Saleem, M. and Daniel, B., 2011. Prevalence of urinary tract infection among patients with diabetes in Bangalore city.*International Journal of Emerging Sciences*, *1*(2), p.133.

Yeshitela, B., Gebre-Selassie, S., Feleke, Y., 2012. 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*; 50:239-49.