Urinary Tract Infection: Antibiotic Resistance Profiles of Bacterial Etiologies and Associated Risk Factors in Diabetic Patients Attending Debre Tabor Hospital, Northwest Ethiopia

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Research Article

Keywords: Bacterial Pathogen, UTI, Diabetes Mellitus, Antimicrobial Susceptibility, Ethiopia

Posted Date: February 11th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1316717/v1

Abstract

Background: Urinary tract infection is a major health problem especially in developing countries. Information about bacterial pathogens isolated from urinary tract infection in diabetic patients and their antimicrobial susceptibility patterns are limited in Ethiopia. Therefore, this study aimed at to isolate bacterial pathogens and their antimicrobial susceptibility patterns.

Methods: A hospital based cross sectional study was conducted at Debre Tabor. Urine sample was inoculated on to cysteine lysine electrolyte deficient (CLED) medium. Bacterial pathogens were identified using standard bacteriological methods. The data were cleaned and entered in to SPSS version 20. P-Value less than 0.05 is considered statistically significant.

Result: A total of 250 study participants were included in the study. Of them, 28 (11.2%) bacterial pathogens were isolated. Gram positive bacteria were commonly isolated 19 (67.8%) than Gram negatives 9 (32.1%). The commonly isolated bacterial species were *Staphylococcus aureus*8 (28.6%),*Escherichia coli*5 (19.1%), Coagulase negative *Staphylococci* 8 (28.6%),*Kelebsllapneumoniae*4(14.3%), and *Entrococcus*(9.5%).Gram positive isolates were resistant to cotrimoxazole 10 (58.8%).

Conclusion: Bacteriuria was significantly associated with sex and type of diabetes**.** Multidrug resistance to two or more antibiotics was observed in 56.7% of bacterial isolates. Rational use of antimicrobial agent should be thought to prevent the emergency of multidrug resistance.

Introduction

Diabetes mellitus (DM) is a worldwide public health problem considering its high prevalence and extremely high economic and social costs. In developing countries, incidence of DM is becoming a serious public health problem (3).The risk of developing infection in diabetic patients is higher and urinary tract infection (UTI) is a major problem and urinary tract is the most common site for infection. Diabetes mellitus is a chronic metabolic disorder characterized by hyperglycaemia resulting from impairments in insulin secretion, defects in insulin action, or both which in turn damage many of the body's systems and also cause several abnormalities of the host defense system that might increase the risk of certain infections (1). Based on pathogenic process diabetes mellitus have two broad categories. Type 1 diabetes is the result of complete or near-total insulin deficiency. Type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production (2).

Urinary tract infections (UTIs) are caused by growth of microorganisms anywhere in the urinary tract. It is usually due to bacteria from the digestive tract which climb the opening of the urethra and begin to multiply to cause infection (4). Urinary tract infections have been the major problem in the tropics and also a common problem seen in community as well as in hospitals (5) and the most common conditions causing individuals to seek medical care and results in a significant morbidity and high medical costs. It

is occur in all age groups, in both genders and usually require urgent treatment (6). Globally the prevalence of UTI is high in healthy populations during the last 25 years and the morbidity and mortality due to UTI have remained static. It is most common particularly in females, about 10-20 % of women have UTI in their life and a significant number have recurrent infections at young age (7). In developing countries, UTIs are commonly encountered diseases by clinicians with an estimated annual global incidence of at least 250 million and also has been estimated that globally symptomatic UTIs result in as many as 7 million visits to out patient's clinics, 1 million visits to emergency departments and 100,000 hospitalizations annually (8).

Both gram positive and gram negative bacteria are implicated as common causes of UTI. *Escherichia coli* is the most common causative agent of UTIs in both DM patients. Other organisms reported include members of the family Enterobacteriaceae (i.e. *Proteus*, *Klebsiella, Enterobacter* and *Citrobacter species*), *Pseudomonas* species*, Enterococcus* species, *streptococci, staphylococci* and *Candida albicans* (9). The emergences of resistant bacterial strains in hospitals pose 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 (10). Antimicrobial resistance is becoming an important public health problem in diabetic urinary tract infection. Information about the etiologies of UTI in diabetic patients is limited in Ethiopia.

For appropriate therapy, current knowledge of the organisms that cause UTI and their antibiotic susceptibility is mandatory. Since patterns of antibiotic resistance in a wide variety of pathogenic organisms may vary even over short periods and depend on type of isolation and on different environments, periodic evaluation of antibacterial activity is necessary (15).

Therefore, this study we aimed to assess the prevalence of UTI in diabetic patients as well as the type of microbiologically confirmed UTI bacterial pathogen and pattern of the antimicrobial drugs susceptibility in relation to diabetes mellitus patients

Materials And Methods

Study area and period

The study was conducted in Debre tabor town, which is located 666 km far from Addis Ababa, in South Gondar Zone of the Amhara Region. It is 100 km from Bahir Dar the capital city of Amhara regional state. In the town there are three Governmental Health Centers, 3 private clinics and one hospital. Based on figures from 2007 Central Statistical Agency of Ethiopia (CSA), Debre Tabor town has a total population of 55,596. The hospital serves as a teaching as well as patient-care providing center for the region. There are about 172 health professionals and 105 administration staff, who provide care for about 6600 outpatients per month. The hospital has a 91 bed capacity. Close to 192 patients visit the hospital every day. Debre Tabor Hospital has diabetic treatment centre which gives serves for about 2149 diabetic patients. The study
was conducted from September 20 to January 20, 2016.

Study design and populations

A hospital based cross-sectional study was conducted among those Diabetic patients who attend at Debre Tabor Hospital during study period who fulfill criteria was included and patient who had treatment with antibiotics in the last 14 days, unconscious patient, pregnant women, HIV positive patients and any patient who had treatment with steroid drug was excluded.

Sample size and sampling technique

The sampling technique was systematic sampling and the sample size (n) was calculated by taking highest prevalence of urethral tract infection (UTI) in previous study 17.8 % (15).

The expected margin of error (d) was 0.05 and the confidence interval (Zα/2) was 95%. Contingency for the unknown circumstance was 10%.

$$n = \frac{(1.96)^2 \times 0.18 \times o.82}{(0.05)^2} = \frac{0.56702}{0.0025} = 226.8 \approx 227 + 10\% = 250$$

Data collection and laboratory methods

Socio-demographic and clinical data were collected from each study participant by using structured questionnaire by trained nurses.

Specimen collection

Each diabetic patient was instructed how to collect a ‘clean-catch’ mid-stream urine specimen by laboratory personnel or staff. About 10 to 20 ml urine specimen was collected in a sterile screw-capped and wide-mouthed container. The container was labeled with unique sample number, date and time of collection. Following collection, it was delivered to the bacteriology laboratory of Debre Tabor University for culture and drug susceptibility testing.

Isolation and identification of bacteria

For the detection of pathogenic bacteria, collected urine specimens were inoculated onto cysteine lysine electrolyte deficient agar (CLED)(Oxoid, Ltd., Basingstoke, Hampshire, England) using calibrated loop (0.001ml).The inoculated plate was incubated in aerobic atmosphere at 37oC for 18 -24 hours (hrs). Then, the plate was inspected for growth. Significant bacteriuria was defined as colony count $\geq 10^5$cfu/ml; sub-culture on to maconkey and blood agar. The inoculated plate was incubated at 37^0c for 18-24 hrs. After obtaining pure colonies, further identification was done by using the standard

microbiological technique, which includes gram stain, colony morphology and biochemical tests (Oxoid, LTD). Preliminary identification of bacteria was based on gram reaction, colony characteristics of the bacteria like hemolysis on blood agar and enzyme activities of the bacteria on different substrates.

Biochemical tests: Biochemical tests were performed on colonies from pure cultures for final identification of the isolates. Gram-negative rods were identified after performing a series of biochemical tests, which includes gas production, sugar fermentation, H_2S production, indoleproduction, citrate utilization, lysine decarboxylase production, hydrolysis of urea and motility tests. The bacterial isolates were identified by combination of different biochemical tests. Gram-positive cocci were identified based on their gram reaction, catalase, coagulase, bacitracin and optochin test results (11).

Antimicrobial susceptibility testing: Antimicrobial susceptibility testing was carried out on each identified organism by disc diffusion method on Muller Hinton agar (MHA) (11). After a pure culture was obtained, a loop full of bacteria was taken from a colony and was transferred to a tube containing 5 ml sterile normal saline (0.85 % NaCl) and mixed gently until it formed a homogenous suspension. The turbidity of suspension was determined in comparison with 0.5 Mac-Farland standard (11). A sterile swab was dipped in the broth suspension and excess suspension was removed by pressing the swab against the wall of the tube. The swab was used to distribute the bacteria suspension evenly over the entire surface of MHA (Oxoid). For antimicrobial testing of *streptococci*, 5% defibrnated sterile sheep blood was aseptically added to Mueller-Hinton medium. The inoculated plates were left at room temperature until dry. The antimicrobial impregnated disks were placed with sterile forceps on the agar surface at least 24 mm away from each other to avoid the overlapping zone of inhibition. After placed the disk the plate was allowed to stand for 30 minutes to dissolve the antibiotic in the media. Then, the plates were inverted and incubated at 37for 24 hrs and was read for the diameter of zone of inhibition. Grades of susceptibility pattern were recognized as sensitive, intermediate and resistant by comparison of zone of inhibition as indicated in the manufacturer's guide (12).The antimicrobial agents tested were obtained from Oxoid in the following concentrations: For gram-negative ampicillin (AMP) (10µg), amoxicillin-clavulanic acid (AMC) (30µg), ceftriaxone (CRO) (30 µg), ciprofloxacin (CIP) (5µg), gentamycin (CN) (10µg), cotrimoxazole (25µg) and Tetracycline (TTC) (30 µg) and for gram-positive Ampicillin (AMP) (10µg), amoxicillin-clavulanic acid (AMC) (30µg), ceftriaxone (CRO) (30 µg), chloramphenicol (C) (30µg), ciprofloxacin (CIP) (5 µg), erythromycin (E) (15µg), gentamycin (CN) (10µg), penicillin (P) (10 IU), cotrimoxazole (25µg) and tetracycline (TTC) (30 µg) (10).

Quality control

All specimens were collected and tested according to the standard operating procedure of each phase. The sterility of culture media was ensured by incubating 5% of each batch of the prepared media at 37°c for 24 hours. Performance of all prepared media was also checked by inoculating international standard-strains such as *Escherichia coli* (ATCC 25922), *S. aureus* (ATCC 25923). To standardize the

inoculum density of bacterial suspension for the susceptibility test, 0.5 MacFarland standard was used (11). To ensure the accuracy of data, double data entry method was used.

Data analysis

Data were entered, clean and edited, using EPI info version 3.7 and were exported in to SPSS version 20 for data analysis. Frequencies and cross tabulations were used to summarize descriptive statistics. Tables were used for data presentation. Odd ratio and adjusted odds ratio were used in the analysis. Both bivariate and multiple logistic regression were employed to assess the association between outcome and explanatory variables. P-values < 0.05 were considered statistically significant

Results

Socio-demographic and clinical characteristics of study participants

Of the total study participants, 250, included in the study, 133 (53.2%) were males and 117 (46.8%) were females. The age of the study participants ranged from 10 to 86 years for diabetic with a mean age of 39.8 ±17.3 years. Among the diabetic patients 148 (59.2%) lived in rural areas, of whom 102 (40.8%) were farmers (Table 1).

Among the diabetic patients who were culture positive 5(17.9%) had symptomatic urinary tract infection and 23(82.1%) had asymptomatic urinary tract infection. Majority, 222 (88.8%) of the diabetic patients were asymptomatic and culture negative.

The relation between individual risk factors and bacteriuria among diabetic and non- diabetic patients were assessed using multivariate logistic regression. Statistically significant associations were observed between patient status (p=0.024) and sex (p=0.002) and urinary tract infection among diabetic and non-diabetic patients. Diabetic patients were 2.5 times as likely to develop UTI during the follow-up period as were non-diabetic patients (p = 0.026).

Statistically significant associations were observed between sex (p=0.002) and urinary tract infection among diabetic (Table 3).

Antibiotic sensitivity patterns of the isolates of bacteria were determined following the Kirby-Bauer disk diffusion technique. The antimicrobial susceptibility patterns of the gram positive and gram negative bacterial isolates were presented, in Table 4 & 5 respectively. The predominant isolate, *Staphylococcus aureus,* revealed intermediate level of resistance to cotrimoxazole 6 (75%), and low level resistance to penicillin 4 (50%), oxacillin 4 (50%), tetracycline 5 (62.5%), doxycycline 4 (50%), erythromycin 4 (44.4%), cephalothin 2(25%) and nitrofurantoin 1(12.5%). Most isolates of *Staphylococcus aureus* were sensitive to ceftriaxone 6 (75%).

The other predominant gram positive isolate, *S. saprophyticus* also showed low level of resistance to oxacillin 4 (50%), cotrimoxazole 4 (50%), nitrofurantoin and cephalothin to 1(12.5%) and tetracycline 3 (37.5%). All of the isolates of *S. saprophyticus* were sensitive to doxcicyclin, erythromycin and ceftriaxone 8 (100%).

The first predominant gram negative isolate, *Escherichia coli,* showed high resistance to amoxicillin 5(100%) and low level resistant to tetracycline 2 (40%), ampicillin 2(40%), nitrofurantoin 1 (20%), and cotrimoxazole 1 (20%). All of the isolates of *Escherichia coli* were 100% sensitive to ciprofloxacin, gentamicin, chloramphenicol, ceftriaxone. *Kelebsilla pneumonia* showed high resistance to amoxicillin 4 (100%), intermediate level of resistance to tetracycline 3 (75%) and ampicillin 3(75%), and low level resistant to ciprofloxacin 1 (25%). All of the isolates of *Kelebsilla pneumonia* were sensitive to gentamicin and ceftriaxone, nitrofurantoin, cotrimoxazole, and chloramphenicol 4 (100%).

Of the 8 (28.2%) *Staphylococcus aureus* isolates 5 (62.5%) showed multi-drug resistant strain while two of them was sensitive to all antimicrobial agents tested. The eight isolates of *S. saprophyticus* showed 5 (62.5%) of multi-drug resistant isolates. The overall multiple drug resistance patterns were 17 (56.7%). Among three isolates of *Enterococci* spp. only two were found to be resistant to one antibiotic. Of the five *Escherichia coli* isolates one isolate showed multi-drug resistant and the other three were resistant to only one antibiotic (Table 6).

Discussion

In this study, the overall prevalence of significant bacteriuria (SB) in both symptomatic and asymptomatic diabetic patients was 11.2%.It was similar to the findings of a study conducted in Addis Ababa (10.9%& 11.6%) (13, 14).In this study the isolation rates of bacterial pathogens among diabetic patients were found lower than previous studies done in Gondar (17.8%) (10) and India (37%) (7).

In the present study the isolation rates of bacterial pathogens were (6%) and (16.3%) in male and female diabetic patients these findings were consistent with the previous reports in Gondar (14%) (10) and (21.2%) (10) in males and females diabetic patients. The prevalence of UTI among female is high this may be due to low acidic pH of vaginal surface, poor hygienic conditions, short and wide urethra and proximity to anus (10).The present finding showed that the isolation rates of gram positive bacteria were found to be higher than the previous study done in Gondar (36.1%), Cameroon (41.2%) (15) and in Gondar (42.7%) (10).

In the present study, *Staphylococcus aureus* was the predominant isolate among diabetic patients. This finding was similar with a study in Nigeria (26.03%) (16) However, this finding is higher as compared with previous report from Gondar University Hospital (8.5%) (10). This discrepancy might be poor personal hygiene condition.

The isolation rate of *S. saprophyticus* (28.6%)in this study was consistent with a study finding from Gondar University Hospital (22%) (10). However, it is lower than a report from Cameroon (36.3%) (14).

This could be due to the appropriate use of antibiotics that may reduce the proliferation of *S. saprophyticus* bacteria or good personal hygiene practice.

The current study finding showed 33.4% of the isolates were gram negative bacteria which was lower than the previous report in Gondar (57.3%) (10). This inconsistency would be probably due to study design or sample size deference. On the other hand, this study was consistent with the previous report in Cameroon (45.1%) (15.)

The second predominant bacterial isolate next to *Staphylococcus aureus* was *Escherichia coli* (Table 2) in diabetic patients. This findings was higher than the study done in Libya (13%) (13). However, it was lower than a study findings reported from Italy (54.1%) (19).In addition, the isolation rates of *Kelebsilla pneumonia* in the present study were (14.3%) that was similar to those reported from Cameroon (15.9%) (15) and Libya (13%) (13).

In the present study significant bacteriuria was detected in symptomatic diabetic patients (80%) which was higher than reports from Gondar (51.4%) (10) and Addis Ababa (13.6%) (17).

The finding of this study also showed that diabetic patients were more likely prone to UTIs than non-diabetic patients (10.9% vs. 4.7%). This could be due to diabetes affects many systems that protect against infection in general, and against urinary tract infections specifically.

In the present study, significant bacteriuria was detected in asymptomatic diabetic patients (9.1%) which were consistent with the reports in Addis Ababa (10.4%) (18) and Gondar (14.7%) (10). However, the finding was lower than the report from Cameroon (33.2%) (14).

Urinary tract infection appears to be multi-factorial in subjects with diabetes and various diabetes-related risk factors. In this study being becoming female sex, and diabetic patient was four times more likely to be infected with bacteriuria [AOR: 4.011; 95% CI: 1.669-9.636] (Table 3).Similar findings have been reported in studies conducted elsewhere (10, 18). In this study the susceptibility pattern of *Staphylococcus aureus* isolates demonstrated low and intermediate level of resistance to the commonly used antimicrobial agents (Table 4).

Most of the gram negative isolates (Table 5) were resistant to amoxicillin. This showed as sensitivity was decreased in contrast with the report from Gondar (59.6%) (10). Decreased susceptibility to this drug might be due to self-medication and indiscriminate use of antibiotics in the study area.

In this investigation, *Escherichia coli* isolates were 100% sensitive to ciprofloxacin, gentamicin, chloramphenicol and ceftriaxone which was higher than the report from Addis Ababa (85%) (17). On the other hand, in the present study *E .coli* isolates were resistant to amoxicilin 100%thatwas also similar with a study done in Gondar: have shown increased the resistance of *E .coli* to amoxicillin -clavulanic acid is the result of hyper production of TEM-β lactamase, production of pencillinase resistant to inhibitors and production of cephalosporinase (10), ampicillin and tetracycline 40% (Table 5).

In the present study *K. pneumonia* isolates were 100% sensitive to chloramphenicol, gentamicin, nitrofurantoin, ceftriaxon and cotrimoxazole for diabetic patients. This result depicted similar finding with the report from Addis Ababa (17) and Gondar. However, inconsistent report was reported from Libya more than (20%) of *Kelebsilla pneumonia* isolates were resistant to ciprofloxacin (13) (Table 5). This discrepancy could be study setting, geography, and population difference.

Multidrug resistance (MDR) to two or more drugs was observed in (53.6%) of the isolates in this study (Table 6). This was consistent with the previous report from Gondar (59.8%) (10).However, lower than the previous report from Addis Ababa (71.7%) (17).The lower multidrug resistance rate from the isolates could be rational use of antimicrobial agents.

Conclusion

In conclusion, significant bacteriuria was detected in 17.9% and 82.1% of symptomatic and asymptomatic diabetic patients, respectively. Based on this, UTI in asymptomatic diabetic patients should not be neglected and follow up studies are required to supplement the present findings for appropriate management of asymptomatic UTI's in diabetic patients. As a complication of diabetes, UTI may be preventable with better glucose control and unnecessary use of antimicrobials. Gram-positive and gram-negative organisms were the commonest organisms isolated; among which *Staphylococcus aureus and Escherichia coli* were the principal urinary pathogen from gram- positive and gram-negative *respectively*. Statistically significant UTI was observed between sex differences. Most of the isolates showed intermediate to low level of resistance to one or more antimicrobials tested. This indicates that regular monitoring is required to establish reliable information about resistance pattern of urinary pathogens for optimal empirical therapy of diabetic patients with UTI. Nitrofurantoin, gentamicin and ceftriaxone were the choice of antimicrobial agents against gram positives and ciprofloxacin, gentamicin and ceftriaxone were relatively sensitive for most of gram negative isolates.

Abbreviations

ASB Asymptomatic Bacteriuria

ATCC American Type Culture Collection

BMI Body Mass Index

CLED Cysteine Lysine Electrolyte Deficient

DM Diabetes Mellitus

MHA Muller Hinton Agar

OPD Out Patient Department

SPSS Statistical Packages for Social Sciences

UTI Urinary Tract Infection

Declarations

Acknowledgments:

We are gratefully to Debre Tabor University who provided for financial support for the research project. We are grateful to Debre Tabor laboratory staffs especially Abay Teshager study and participants.

Authors' contributions

SW: was the primary researcher, conceived the study, data collection, analysis, interpretation of the findings, drafting the manuscript and write up. **AG**: drafting the manuscript and write up.

AB: participated in the design of the study, analysis and interpretations of the findings, drafting the manuscript and write up and AA: Participated in analysis and interpretations of the findings, drafting the manuscript and write up. All authors read and approved the final manuscript.

Funding
This study was sponsored by Debre Tabor University, Ethiopia.

Availability of data and materials
The data sets generated during and/or analyzed during the current study are available from the corresponding authors on reasonable request.

Ethics approval and consent to participate

Ethical clearance and approval was obtained from the institution review board (IRB) of Debre Tabor University.

Above all the data were collected after full informed and written consent was obtained from each participant.

Consent for publication
Not applicable

Competing interests: We authors declare that no competing interest.

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References

1. Sibi G, Devi AP, Fouzia K, Patil BR . Prevalence, microbiologic Profile of UTI and its treatment with Trimethoprim in Diabetic patient . *J Mic*. 2011 ; 6(6) : 543-551.
2. Fauci AS, Longo DL, Braunwald E, Kasper DL, Hauser SL, Jameson JL, *et al*. *Harisson's Principles of Internal Medicine*.17thUSA:TheMcGraw-Hill Companies Inc; 2008 : 325-328.
3. Vlad I, Popa AR. Epidemiology of Diabetes Mellitus: *A Cur. Rev*. 2012 ; 19(4) : 433-440.
4. Okonko IO, Ijandipe LA, Ilusanya OA, Donbraye-Emmanuel OB, Ejembi J, Udeze AO, *et al*.Incidence of urinary tract infection (UTI) among Pregnant women in Ibadan, South-Western Nigeria. *J Bio*. 2009 ; 8(23) : 6649-6657.
5. Chukwuocha UM, Emerole CO, Njokuobi TN, Nwawume IC. Urinary Tract Infections (UTIs) Associated with Diabetic Patients in the Federal Medical Center owerri, Nigeria. *Adv .Res. J Mi .* 2012 ; 1(5) : 062-066.
6. Aiyegoro OA, Igbinosa OO, Ogunmwonyi IN, Odjadjaro E, Igbinosa OE, Okoh AI. Incidence of urinary tract infections (UTI) among children and adolescents in Ile–Ife, Nigeria. *Afr . J Mic. Res.* 2007; 1: 13-19.
7. Pargavi B, Mekala T, Selvi AT, Moorthy K. Prevalence of Urinary Tract Infection (UTI) among Diabetics patients in Vandavasi, Tamil Nadu, India. *J Bio. Tec.* 2011; 2(2): 42-45.
8. Wilson ML, Gaido L. Laboratory diagnosis of urinary tract infections in adult patients*. Clin Inf. Dis*.2004; 38: 1150-1158.
9. 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 Inf. Dis.* 2006; 6(54): 1471-2334.
10. 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. *J Exp. Bio.* 2012; 2 (4): 889-898.
11. Geerlings SE .Urinary tract infections in patients with diabetes mellitus: epidemiology, pathogenesis and treatment. *Int J Ant. Age.* 2008; 31: 54-57.
12. Mnif MF, Kamoun M, Kacem FH, Bouaziz Z, Charfi N, Mnif F, *et al*. Complicated urinary tract infections associated with diabetes mellitus: Pathogenesis, diagnosis and management. *J End. Met.*

2013 ; 17(3) : 442-445.

13. Hakeem LM, Bhattacharyya D, Lafong C, Janjua KS, Serhan J, Campbell I. Diversity and complexity of urinary tract infection in diabetes mellitus . *Bri. J Dia. Vas. Dis*. 2009 ; 9 : 119-1
14. Saleem M, Daniel B . Prevalence of Urinary Tract Infection among Patients with Diabetes in Bangalore. *J Eme. Sci*. 2011 ; 1(2) : 133-142.
15. 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. *J Exp. Bio.* 2012 ; 2 (4) : 889-898.
16. Yeshitela B, Gebre-Selassie S, Feleke Y. Asymptomatic bacteriuria and symptomatic urinary tract infections (UTI) in patients with diabetes mellitus in Tikur Anbessa Specialized University Hospital, Addis Ababa, Ethiopia. *Med. J* 2012 ; 50(3) : 239-49.
17. AL-Rubeaa KA, Moharram O, Al-Naqeb D, Hassan A, Rafiullah MR. Prevalence of urinary tract infection and risk factors among Saudi patients with diabetes. *J Urol*. 2013; 31(3): 573-8.
18. Rawat V, Singhai M, and Goyal R. Bacteriological and Resistance Profile in Isolates from Diabetic Patients. N Am J Med Sci. Nov 2012; 4(11): 563–568.
19. Shill MC, Huda NH, Moain FB, Karmakar UK. Prevalence of Uropathogens in Diabetic Patients and Their Corresponding Resistance Pattern: Results of a Survey Conducted at Diagnostic Centers in Dhaka, Bangladesh. *Oma . Cal. J* 2010; 25(4): 282-285.
20. Hasan MK, Nazimuddin H, Ahmed AS, Sarke RS C, Haque M, Musa A . Differences in bacteriological and antibiotic sensitivity patterns in UTI among hospitalized diabetic and non-diabetic patients. *J Med*. 2007; 8: 10-13.
21. Ramana BV, Chaudhury Prevalence of uropathogens in diabetic patients and their resistance pattern at a tertiary care centre in south India. *Int. J Biol. Med .Res*. 2012; 3(1): 1433 – 1435.
22. Bissong MEA, Fon PN, Tabe-Besong FO, Akenji TN. Asymptomatic bacteriuria in diabetes mellitus patients in Southwest Cameroon. *Hea. Sci.* 2013; 13(3): 661 - 666.
23. **Hamdan Z H,Eman K, Amar M A, Onab S H, Sarah O S,**Urinary tract infections and antimicrobial sensitivity among diabetic patients. *AC Microbiology and Antimicrobials* 2015**; 14** (26):12941-015-0082-4.
24. Cheesbrough M. Biochemical tests to identify bacteria. In: *District Laboratory Practice in Tropical Countries Part II*. 2nd United States of America, New York: Cambridge University Press; 2006: 45-58.
25. Clinical and Laboratory Standards Institute (CLSI).*Performance standards for antibiotic susceptibility testing tewenty first informational supplement*. CLSI document M100-S21.Wayne, Penssylavia USA:Clinical and Laboratory StandardsInstitute. 2011 ; 42-76.

Tables

Table 1. Socio demographic characteristics of diabetic patients attending Debre Tabor Hospital, Northwest Ethiopia

Characteristic	Diabetic
	Number (%)
Age in (year)	
10-20	44 (17.7)
21-35	65 (26.0)
36-45	47(18.8)
46-55	46 (18.2)
≥56	48 (19.3)
Sex	
Male	133 (53.1)
Female	117 (46.9)
Residence	
Rural	148 (59.4)
Urban	102 (40.6)
Educational status	
Illiterate	143 (57.3)
Literate	107 (42.7)
Occupation	
Civil servant	52 (20.8)
Housewife	46 (18.0)
Student	10 (4.1)
Farmer	86 (34.3)
Merchant	18 (7.2)
Daily labor	22 (8.8)
Other*	16 (6.3)

*jobless, driver

Table 2. Frequency and types of bacterial species isolated from symptomatic and asymptomatic Diabetic patients' urine culture attending Debre Tabor Hospital Northwest Ethiopia, Northwest Ethiopia

Bacterial isolates	**Diabetic patient (No (%)**		**Total**	**P-value**
	Symptomatic	**Asymptomatic**	No (%)	
E .coli	1(25.0)	4 (75.0)	5 (19.1)	0.030
S. aureus	0 (0.0)	8 (28.6)	8 (28.6)	0.999
S.saprophyticus	3 (33.3)	5 (66.6)	8 (28.6)	0.011
Enterococcus spp	1 (25.0)	2 (75.0)	3 (9.5)	0.011
K. pneumoniae	0 (0.0)	4 (100.0)	4 (14.3)	0.999
Total	5 (17.9)	23 (82.1)	28 (100.0)	

Table 3.Univariate and bivariate analysis of urinary tract infection among diabetic patients attending Debre Tabor, Northwest Ethiopia

Characteristic	**Bacterial Isolation**		**Crude-OR(95%CI)**	**Adjusted-OR(95%CI)**	**P-value**
	Yes n (%)	**No n (%)**			
Patient status					
Diabetic	28 (11.2)	222 (88.8)	4.00(0.178-0.899)	2.562(1.130-5.809)	0.024
Non-Diabetic	2 (4.7%)	(95.3%)	1	1	
Sex					
Male	10 (4)	240 (96)	1	1	
Female	21 (8.4)	229 (91 .6)	3.939(1.648-9.416)	4.011(1.669-9.636)	0.002

Table 4.Antimicrobial resistance patterns of gram-positive bacteria isolated from urine of diabetic patients attending Debre Tabor Hospital, Northwest Ethiopia

Antibiotics tested	**Gram positive isolates**			**Total**
	S. aurues(N= 8) n (%)	CON (N=8) n (%)	*Enterococcus spp*(N=3) n (%)	n (%)
Oxacillin	4 (50)	4(50.0)	0(0.0)	8(42.1)
Nitrofurantoin	1(12.5)	1(12.5)	2(67.0)	4(21)
Doxycycline	4 (50)	0(0.0)	0(0.0)	4(21)
Ampicillin	0 (0.0)	-	0(0.0)	0(0.0)
Cotrimoxazole	6 (75)	4(50.0)	0(0.0)	10(52.6)
Tetracycline	5 (62.5)	3 (37.5)	0(0.0)	8(42.1)
Chloramphenicol	0(0.0)	-	0(0.0)	0(0.0)
Penicillin	4 (50)	1(12.5)	0(0.0)	5(26.3)
Erythromycin	4 (50)	0(0.0)	0(0.0)	4(21)
Ceftriaxone	2 (25)	0(0.0)	0(0.0)	2(10.5)
Cephalothin	2 (25)	1(12.5)	0(0.0)	3(31.5)

Table 5. Antimicrobial resistance patterns of gram-negative bacteria isolated from urine of diabetic patients attending Debre Tabor Hospital, Northwest Ethiopia

Antibiotics tested	Total n (%)	
	Escherichia coli (N= 5) n (%)	*K. Pneumoniae* (N= 4) n (%)
Amoxicillin	5(100)	4(100)
Ampicillin	2(40.0)	3(75.0)
Ciprofloxacin	0(0.0)	1(25.0)
Chloramphenicol	0(0.0)	0(0.0)
Gentamicin	0(0.0)	0(0.0)
Nitrofurantoin	1(20.0)	0(0.0)
Cotrimoxazole	1(20.0)	0(0.0)
Tetracycline	2(40.0)	3(75.0)
Ceftriaxone	0(0.0)	0(0.0)

Table 6. Multiple antimicrobial resistance patterns of bacterial isolates from urine of patients attending Debre Tabor Hospital, Northwest Ethiopia

Bacterial isolates	Number (%)	**Antibiogram patterns n (%)**					
		R_0	R_1	R_2	R_3	R_4	$\geq R_5$
S.aureus	8 (28.2)	2 (25)	1(12.5)	1(12.5)	0(0.0)	2 (25)	2 (25)
S.saprophyticus	8 (28.2)	1(12.5)	2 (25)	1(12.5)	0(0.0)	2 (25)	2 (25)
Enterococcus spp.	3 (10.7)	1 (33.3)	2(66.6)	0(0.0)	0(0.0)	0(0.0)	0(0.0)
Escherichia coli	5 (17.9)	1 (20)	3 (60)	1 (20)	0 (0.0)	0 (0.0)	0(0.0)
K. pneumoniae	4 (14.2)	1(25.0)	0(0.0)	1(25.0)	1(25.0)	0(0.0)	1(25.0)
Total	**28 (100.0)**	**6 (21.4)**	**7 (25)**	**5 (17.9)**	**2 (7.1)**	**5 (17.9)**	**3 (10.7)**

Keys: $R_{0=}$ No antibiotic Resistance $R_{1=}$Resistant to one antibiotic, R2=Resistant to two antibiotic, R3= resistant to three antibiotic, R4=Resistant to four antibiotic, R5=Resistant to five and more than five