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Clinico-bacteriological Profile of Urinary Tract Infection in Selected Patients of Type 2 Diabetes Mellitus in a Tertiary Care Hospital, Eastern India: An Observational Study

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ABSTRACT

Background: The incidence of diabetes mellitus (DM) throughout the world is increasing strikingly and is becoming a serious public health problem especially in the developing countries. Infections are important cause of death in diabetes and remain a very important cause of morbidity and mortality in people with diabetes. Most common type of diabetes in Indian population is type 2 DM. Most common infection associated with DM found to be urinary tract infections (UTI). **Objective:** The main objectives of this study were to isolate, identify and to determine antimicrobial susceptibility pattern of microbiological agents of UTI in type 2 DM patients and assess prognosis of these patients with prescribed antimicrobial treatment regimen. **Results and Discussions:** We conducted the study from December 2013 to December 2018 in the department of microbiology from the patients attending the outpatients department of a tertiary care hospital. In this study, total 774 non-repetitive patients' samples were included but 14 samples were contaminated and lost from follow-up. Thus, available data for analysis were 760 samples. Total 254 samples showed significant growth (32.82%). Most common isolated pathogen was *Escherichia coli.* In our study, 17.82% patients were asymptomatic but culture positive. The asymptomatic patients with positive urine culture turn up with symptomatic UTI, often with complications. **Conclusion:** UTI with multidrug-resistant organism in outpatients has emerged; limiting the treatment options in the high-risk groups. The need for an antibiotic policy based on adequate and continuous monitoring of susceptibility patterns in the institutions is recommended.

Keywords: Antimicrobial resistance, Diabetes mellitus, Urinary tract infections

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Introduction

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. People with diabetes develop infections more often than those without diabetes and the course of the infections is also more complicated. Historically, infections have been well recognized as an important cause of death in diabetes and remain a very important cause of morbidity and mortality in people with diabetes. Most common type of diabetes in Indian population is type 2 DM.[1] Most common infection associated with DM found to be urinary tract infections (UTIs).[2,3] The incidence of DM throughout the world is increasing strikingly and is becoming a serious public health problem especially in the developing countries.[4] It has a long-term effect on the incidence of UTI and it has been reported to be around four times higher in diabetics compared to non-diabetic patients.[5] Diabetes is also a risk factor for multidrug-resistant UTI, perhaps related to recurrent or increased exposure to antibiotics.[6] In community and hospital settings the etiology of UTIs and the antimicrobial susceptibility of uropathogens have been changing over the years. Factors such as the changing patient population, extensive use, and misuse of antimicrobial agents could all contribute to changes in the microbial profile of UTI. Knowledge of the antimicrobial resistance pattern of common uropathogens according to local epidemiology is essential for providing clinically appropriate and cost-effective therapy for UTI.

Objectives

The objectives of the study were to isolate and identify the etiological agents of UTI in type 2 DM patients, to determine their antimicrobial susceptibility pattern, and assess prognosis of these patients with prescribed antimicrobial treatment regimen.

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Methods

The study was conducted from December 2013 to December 2018 in the department of microbiology from the patients attending the outpatients department of a tertiary care hospital. Necessary clearances from the institutional ethical committee were obtained before the study. The informed consents were obtained from all the patients include in the study before collection of the specimen. Mid-stream clean catch urine samples were collected from selected type 2DM patients as cases and were analyzed by wet mount, cultures and stained smears, biochemical reactions, and other microbiological methods. The semi-quantitative culture was

performed by inoculating urine on Blood agar and CLED media by standard loop method. Colony count was performed on blood agar. On culture of urine, a colony count of ≥10^5/ml organisms was considered significant. Only a single positive culture per patient was included in the analysis. In addition, a pure culture of *Staphylococcus aureus* was considered significant regardless of the number of colony-forming units.[7] Cultures showing insignificant growth were considered as no growth and in cases of mixed growth of three or more pathogens or growth of non-pathogens were asked to send repeat sample for culture and sensitivity after proper collection of urine. The isolates were subjected to identification by conventional phenotypic methods including the antimicrobial susceptibility testing by modified Kirby-Bauer disk-diffusion technique as per the recommendations of Clinical and Laboratory Standards Institute.[8] The control strains used were *Escherichia coli* American Type Culture Collection (ATCC) 25922, *Pseudomonas aeruginosa* ATCC 27853, and *S. aureus* ATCC 25923. For ESBL test control strain used was *Klebsiella* ATCC 700603

Results

In this study, total 774 non-repetitive patients' samples were included but 14 samples were contaminated and lost from follow-up. Thus, available data for analysis were 760 samples. Total 254 samples showed significant growth (32.82%). The mean age of type 2 diabetic patients' was 49.57 ± 12.27 years. Majority of patients were between 41 and 50 years age group. The overall culture positivity of urine samples was 32.82%. Females were more susceptible for UTI with an overall male:female ratio 1:2.23. In our study, among women with type 2 DM patients 17.82% of asymptomatic and 46.60% of symptomatic patients showed positive culture. Among the symptomatic patients, 55.21% presented with dysuria as the most common presenting symptom. Among the 45 asymptomatic culture positive patients, 42 (93.54%) were female patients. Out of the 254 culture positive cases, 152 (59.85%) cases were isolated from patient being treated with OHA and 90 (35.43%) cases were isolated from patient being treated with insulin. Twelve (4.72%) cases were isolated from patient being treated with insulin and OHA. In the present study, average duration of treatment of type 2 DM is 5.35 years. Significant association was found between a positive urine culture and longer duration of treatment for type 2 DM. In this study, *E. coli* were the predominant uropathogen, accounted for approximately 35% (89) of all clinically significant urinary isolates Figure 1. For Gram-positive isolates linezolid and vancomycin showed excellent *in vitro* sensitivity found. For Gram-negative organisms, there was aminoglycosides, nitrofurantoin, and doxycycline, respectively, found sensitive *in vitro*. Fluoroquinolone resistance is being encountered regularly. Drug resistance is emerging among the clinical isolates. Among the total 254 urinary isolates from type 2 DM patient 30 cases (11.82%) showed to produce extended spectrum beta-lactamase enzyme. Patients with urine culture positive report were given antimicrobial based on AST and they responded well. Only 6 (2.36%) patients showed positive urine culture after 2 weeks of antimicrobial treatment. *In vitro,* drug susceptibility results corroborated with good clinical responses.

Discussion

The present study was undertaken to determine the distribution and antibiotic susceptibility pattern of microbial species isolated from urine samples of selected type 2 DM patients in a tertiary care hospital. Out of 774 samples obtained, 14 cases (1.8%) showed growth of contaminants and they could not be processed. Rest 760 samples were processed and results were analyzed. 254 cases showed culture positivity with significant colony count, giving the outcome percentage of 32.82%. This result was similar to a study in the Philippines by Alcantara *et al.* they obtained 33.6% culture positivity with similar groups. Boyko *et al.* also demonstrated 30.69% positive culture among 215 diabetic patients.[9] However, it was dissimilar from a study of Saudi Arab by Al-Rubeaan *et al.* in where they found out 25.3% positive cultures.[10] Proportion of positive urine culture was more common in higher age group it was similar to Astra Zeneca trial in 2010.[11] In our study, mean age of type 2 diabetic patients' was 49.57 ± 12.27 years. Majority of patients were between 41 and 50 years age group. Recent studies have demonstrated an increased risk of symptomatic UTIs primarily in women with type 2 DM.[12] In postmenopausal women, type 2 diabetes has been associated with a two-fold increased risk for UTIs.[9,13] Symptoms associations were also studied. In our study, among women with type 2 DM patients 17.82% were asymptomatic and 46.60% symptomatic patients showed positive urine culture. However, in an Iranian study on women with type 2 DM researchers found out lower prevalence of UTI; 1.8% in asymptomatic patients and 6.2% in symptomatic patients[14] and also Geerlings *et al.* in Netherlands found that total of 81 of the 348 women (23%) with type 2 diabetes developed a UTI.[15] This is similar to the results of the previous studies that showed occurrences of positive urine culture in different geographical locations 21% in Karachi (Baqai *et al.*, 2003), 26% in Nigeria (Alebiosu *et al.*, 2003), and 19% in

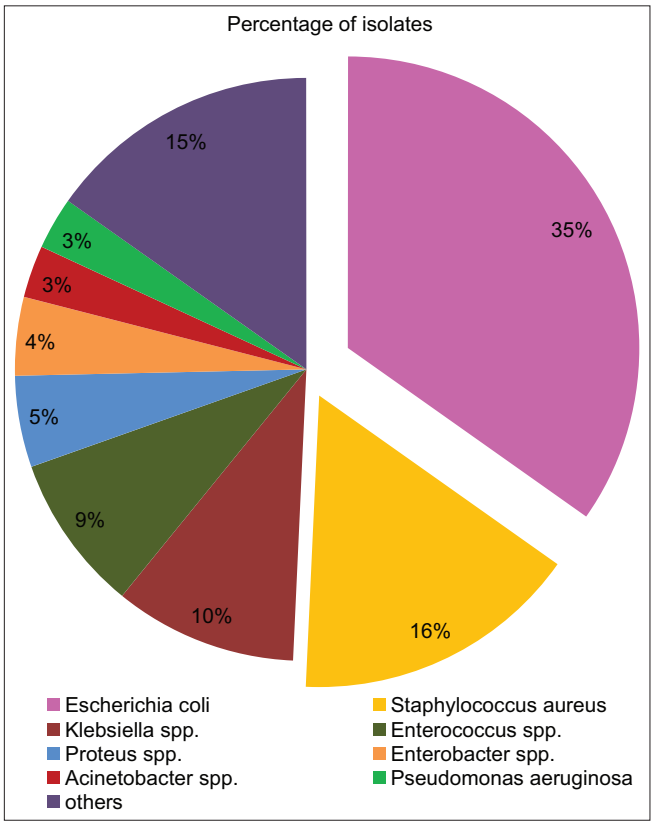

Figure 1: Distribution of culture positive cases according to microbial species in urine

Bahrain (Hajeri, 2008). This is higher than 9.3% in Ethiopia (Uncu *et al*., 2002), in Ghana (Turpun *et al*., 2007), and lower than 36.15% in Benin (Ophori *et al*., 2010) with type 2 DM.[16] In our study, culture positive cases found to be 31 in number out of 174 (17.8%) asymptomatic type 2 diabetic patients. It was similar to a study by Bonadio *et al*. they found among 176 asymptomatic outpatients 18.8% were positive for urine culture.[17] However, dissimilar results obtained from an outpatient study of type 2 diabetic females by Sotiropoulos *et al*. they found out only 9.6% culture positivity but in lesser number of patients were included in that study.[18] Our study demonstrated 17.82% positive urine culture among female asymptomatic outpatients In an Italian study in Pisa 1321 out of 10221 (12.9%), an Iranian study[14] 22 out of 202 (10.9%) type 2 diabetic women were asymptomatic and urine culture positive. This is comparable with studies of Kayima *et al.* (11.2%) and Zhanel *et al*.[19] (7.9%). However, prevalence of asymptomatic culture positive in diabetic women was reported 26% in Geerlings *et al*. study[15] and 26.6% in Alebiosu *et al*. report.[20] We are imposing stress on asymptomatic culture positivity because large share of them presented with symptomatic UTI during and after study period. This observation was supported by Ribera *et al*. as symptomatic UTI occurred in 69.2% of patients with ASB (67.6% female and 76.5% male) versus 9.8% without ASB (14.9% female and 2.6% male).[4] Among symptomatic patients, 46.6% showed positive urine culture. The most common symptoms were dysuria (43.69%), followed by frequency (38.35%). All the symptoms were significantly associated with positive urine culture. Reason of symptom with negative yield of urine culture could be the causative organisms are parasites or fastidious organisms, which could not be grown in this study.

Our study findings show that patients who had prior history of UTI are more likely to have a positive urine culture ($P < 0.001$). It suggests that DM is a risk factor for recurrence of UTI. Schneeberger *et al*. found out that women with type 2 DM are more likely to have a recurrence.[21] Out of the 254 culture positive cases, 152 (59.85%) cases were isolated from patients being treated with oral hypoglycemic agents and 90 (35.43%) cases were isolated from patients being treated with insulin. 12 (4.72%) cases were isolated from patients being treated with combinatorial therapy of insulin and OHA. Boyko *et al.* demonstrated that insulin has a three- to four-fold higher risk of UTI, possibly indicating an association with severity of diabetes.[9] Women taking insulin were mainly those at higher risk, possibly because of more severe diabetes, since the use of insulin may be a marker for disease severity. DM is a chronic disease. Average duration of treatment is also prolonged. Prolonged duration of treatment of diabetes often associated with complications. In the present study, average duration of treatment of type 2 DM was 5.35 years. Significant association was found between a positive urine culture and longer duration of treatment for type 2 DM ($P = 0.04$). However, in Iranian diabetic women no evidence of a significant relation between bacteriuria and the duration of diabetes ($P = 0.09$) was found.[14] It supports that longer duration of diabetes damages the host immunity severely and enhances chance of acquiring an UTI.[22] In our study, we defined HbA1C levels as the parameter for glycemic control and HbA1C ≤7% were marked as good control and 7.1–8.9% as poorly controlled and ≥9% very poorly controlled glycemic status; significant association of positive urine culture was seen with very poorly controlled glycemic status ($P < 0.001$) Table 1. However, it differs from the study of Gerrlings *et al*.[4] where they did not find any association of urine culture positivity with glycemic control status. It could be due to the fact they did not take into account the very poorly controlled diabetic patients in that study. In this study, *E. coli* was the predominant uropathogen, accounted for approximately 35% of all clinically significant urinary isolates. This was consistent with the findings of previous studies, in which *E. coli* was the predominant pathogen isolated from patients with community acquired UTIs.[22,23] Similar results were obtained by Ghenghesh *et al.* in Libya.[24] Goswami *et al*. observed that *E. coli* was the most commonly grown organism (64.3%), followed by *S. aureus* (21.4%) and *Klebsiella pneumoniae* (14.3%)[25] which was very similar to our study.

Antibiotic resistance is a major clinical problem in treating infections caused by these microorganisms. Our study demonstrated that *E. coli* isolated from the urine showed increasing resistance to trimethoprim/sulfamethoxazole, norfloxacin, and cefuroxime Table 2. *E. coli* was highly sensitive to polymyxin B, cefoperazone-sulbactam and that were commonly used in our patients studied it was similar to study of Janifer *et al.*[26] *S. aureus* was sensitive to linezolid and vancomycin but resistant to ampicillin and penicillin this was similar top study by Alcantara *et al.*[27] in the Philippines. We stressed on these two microorganisms as they comprise 51% of the total isolates of this study. The frequency of resistance in the study has been attributed to a complex interaction of various factors that influence the host, microorganism, and/or the environment. These include the use of broad spectrum antimicrobial drugs, an increase in the number of susceptible hosts; technological changes that lead to increased exposure to resistant organisms; and breakdown in hygiene, infection control practices, or disease control programs that lead to increased transmission of resistant organisms.[28] The increasing antimicrobial resistance is often a result of poor patient compliance and/or physicians poor adherence to recommended treatment guidelines.[29] This is now a very important medical problem in the treatment among diabetic patients with infections. From our study, we could suggest that cefoperazone-sulbactam and vancomycin/linezolid could be the best choice as empirical therapy for the uncontrolled symptomatic type 2 DM indoor patients, as often they have a complicated course of disease. Among the total 254 urinary isolates from type 2 DM patient, 30 cases shown to produce extended spectrum beta-lactamase enzyme by phenotypic method. Of those *E. coli and K. pneumoniae* were the only isolates. Among those isolates all of the cases were from outpatients. Majority (66.67%) were females, among females 80% were postmenopausal. It signifies that drug resistance is emerging in community among high-risk groups. Out of 114 isolates of *E. coli* and *K. pneumoniae* 30 (26.31%) shown to produce ESBL. It was much lower than found in a Bangladesh study by Saber *et al.* where they found out 47.8% ESBL producers, they also found out *E. coli* and *K. pneumoniae* as the only ESBL producers.[30] The difference could be attributed to the fact that our study populations were mostly outpatients and these drug resistant strains are not so

Table 1: Distribution of cases and glycemic control status

HbA_1C	*Culture positive (%)*	*Culture negative (%)*	*Total P=0.0004*
≤7%	130 (17.11)	256 (33.68%)	396
7.1–8.9%	34 (4.47)	146 (19.21%)	180
≥9%	90 (11.84)	104 (13.68%)	194
Total	254	506	760

HbA_1C: Glycated hemoglobin. HbA1c≤7%: Good glycemic control, HbA1c 7.1–8.9%: Poor glycemic control, ≥9%: Very poor glycemic control

Table 2: Distribution of gram negative bacilli and their susceptibility pattern

Organism	*Susceptibility*	*GM* (%)	*CM* (%)	*MP* (%)	*PB* (%)	*CP* (%)	*CAC* (%)	*FG* (%)	*FD* (%)	*NX* (%)	*BA* (%)	*CB* (%)	*NA* (%)	*DX* (%)
E. coli (*n*=88)	S	44	75	74	94	34	59	34	87	27	25	38	8	35
	R	52	16	26	6	66	39	66	13	73	75	62	92	61
K. pneumoniae (*n*=26)	S	71	63	79	86	36	43	36	36	43	21	20	29	78
	R	29	37	21	14	64	57	64	64	57	79	80	71	22
Proteus spp.(*n*=13)	S	67	100	100	NA	100	100	100	NA	83	50	50	0	NA
	R	33	0	0	NA	0	0	0	NA	17	50	50	100	NA
Enterobacter spp.(*n*=11)	S	25	25	25	100	0	25	0	50	0	50	0	0	0
	R	75	75	75	0	100	75	100	50	100	50	100	100	100

S: Sensitive, R: Resistant, GM: Gentamicin, CM: Cefoperazone-sulbactam, MP: Meropenem, PB: Polymyxin-B, CP: Cefoperazone, CAC: Ceftazidime-clavulinic acid, FG: Ceftazidime, FD: Nitrofurantoin, NX: Norfloxacin, BA: Cotrimoxazole, CB: Cefuroxime, NA: Nalidixic acid, DX: Doxycycline. *E. coli*: *Escherichia coli*, *K. pneumoniae*: *Klebsiella pneumoniae*

widespread in the community. However, it is also reflecting that the drug-resistant strains are emerging in the community. Amongst 774 patients of type 2 DM in the study, 254 (32.82%) patients showed positive urine culture. Among those only 8 (3.15%) isolates showed to produce carbapenemase enzymes. All of them were isolated from inpatients. The carbapenemase producers were mostly *K. pneumoniae*, only one case of *Enterobacter spp.* was carbapenemase producer. No AmpC β lactamase producers were phenotypically detected in this study. Methicillin resistances were detected significantly among *S. aureus* isolates. About 41% of the *S. aureus* isolates were detected to be Methicillin-resistant *S. aureus* (MRSA) phenotypically. Among MRSA isolates majority were from outpatients (77.8%) indicating high proportion of CA-MRSA. Inducible clindamycin resistance was not so common, only 14% showed inducible Clindamycin resistance; concurrently all of them were methicillin resistant phenotypically. Clinicians following antimicrobial susceptibility testing instituted antimicrobials. Patients with urine culture positive report were given antimicrobial and they responded well. Only 6 (2.36%) patients showed positive urine culture after 2 weeks of antimicrobial treatment. Here, *in vitro* responses were different from clinical response. They were treated with different antimicrobial based on AST of second occasion and during follow-up they showed favorable clinical response. A prospective study of diabetic patients can be done to determine whether associations of urinary symptoms influence the long-term outcome.

Conclusion

UTI is common in type 2 DM. With the high occurrence of infection, there is a need to increase the surveillance of infections among diabetic patients. The asymptomatic patients with positive urine culture turn up with symptomatic UTI, often with complications. UTI with multidrug-resistant organism in outpatients have emerged; limiting the treatment options in the high-risk groups. The need for an antibiotic policy based on adequate and continuous monitoring of susceptibility patterns in the institutions is recommended.

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Conflicts of Interest

There are no conflicts of interest.

References

1. Sandeep S, Ganesan A, Mohan V. Development and updation of the diabetes atlas of India Report. Chennai: Madras Diabetes Research Foundation; 2007.
2. Shah BR, Hux JE. Quantifying the risk of infectious diseases for people with diabetes. Diabetes Care 2003;26:510-3.
3. Carton JA, Maradona JA, Nuno FJ. Diabetes mellitus and bacteremia: A comparative study between diabetic and non-diabetic patients. Eur J Med 1992;1:281-7.
4. Ribera MC, Pascual R, Orozco D, Barba CP, Pedrera V, Gil V. Incidence and risk factors associated with urinary tract infection in diabetic patients with and without asymptomatic bacteriuria. Eur J Clin Mic Inf Dis 2006;25:389-93.
5. Adeyeba OA, Adesiji YO, Omosigho PO. Bacterial Urinary tract infections in patients with diabetes mellitus. Int Trop J Med 2007;2:89-92.
6. Cockram CS, Lee N. Infection in DM. In: Holt RI, Cockram CS, Flyvbjerg A, Goldstein BJ, editors. Textbook of Diabetes. 4th ed. United Kingdom: Wiley-Blackwell; 2010. p. 846.
7. Collee JG, Marr W. Specimen collection, culture containers and media. In: Collee JG, Marimon BP, Fraser AG, Simmons A, editors. Mackie and McCartney Practical Medical Microbiology. 14th ed. United Kingdom: Churchill Livingstone; 2010. p. 699-700.
8. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; Twenty Fourth Informational Supplement CLSI Document M100-S26. Wayne, PA: Clinical and Laboratory Standards Institute; 2016.
9. Boyko EJ, Fihn SD, Scholes D, Chen CL, Normand EH, Yarbro P. Diabetes and the risk of acute urinary tract infection among postmenopausal women. Diabetes Care 2002;25:1778-83.
10. Al-Rubeaan KA, Osama M, Al-Naqeb D, Hasan A, Rafiullah MR. Prevalence of urinary tract infection and risk factors among Saudi patients with diabetes. World J Urol 2013;31:573-8.
11. Hammar N, Farahmand B, Gran M, Joelson S, Andersson SW. Incidence of urinary tract infection in patients with Type 2 diabetes. Experience from adverse event reporting in clinical trials. Pharmacoepidemiol Drug Saf 2010;19:1287-92.
12. Hakeem LM, Bhattacharyya DN, Lafong C, Januja KS, Serhan JT, Campbell IW. Diversity and complexity of Urinary Tract Infection in Diabetes. Br J Diabetes Vasc Dis 2009;9:119-25.
13. Moore EE, Hawes SE, Scholes D, Boyko EJ, Hughes JP, Fihn SD. Sexual intercourse and risk of symptomatic urinary tract infection in post-menopausal women. J Gen Intern Med 2008;23:595-9.
14. Boroumand MA, Sam L, Abbasi SH, Salarifar M, Kassaian E, Forghani S. Asymptomatic bacteriuria in Type 2 Iranian diabetic women: A cross-sectional study. BMC Womens Health 2006;6:4.
15. Geerlings SE, Stolk RP, Camps MJ, Netten PM, Collet TJ, Hoepelman AI. Risk factors for symptomatic urinary tract infection in women with diabetes. Diabetes Care 2000;23:1737-41.
16. Ophori EA, Imade EP, Johnny J. Asymptomatic bacteriuria in patients

with Type-2 diabetes mellitus. J Bacteriol Res 2010;2:14-7.
17. Bonadio M, Boldrini E, Forotti G, Matteucci E, Vigna A, Mori S, *et al*. Asymptomatic bacteriuria in women with diabetes: Influence of metabolic control. Clin Infect Dis 2004;38:e41-5.
18. Sotiropoulos A, Skourtis S, Merkouris P, Peppas T, Apostolou O, Kontela E, *et al*. Incidence and outcome of asymptomatic bacteriuria in females with Type 2 diabetes mellitus over a 1-year follow-up period and association with risk factors. Diabet Med 2005;22:1625-6.
19. Godfrey K, Harding M, Zhanel GG, Nicolle LE, Cheang M. Prevalence of asymptomatic bacteriuria and associated host factors in women with diabetes mellitus. N Engl J Med 2002;347:1576-83.
20. Alebiosu CO, Osinupebi OA, Olajubu FA. Significant asymptomatic bacteriuria among Nigerian Type 2 diabetics. J Natl Med Assoc 2003;95:344-51.
21. Schneeberger C, Stolk RP, Devries JH, Schneeberger PM, Herings RM, Geerlings S. Differences in the pattern of antibiotic prescription profile and recurrence rate for possible urinary tract infections in women with and without diabetes. Diabetes Care 2008;31:1380-5.
22. Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, editors. Urinary Tract Infections, Pyelonephritis, and Prostatitis Harrison's Principles of Internal Medicine. 18th ed. New York: McGraw-Hill; 2012.
23. Sobel JD, Kaye D. Urinary tract infections. In: Mandell GL, Bennett JE, Dolin R, editors. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010. p. 964.
24. Ghenghesh KS, Elkateb E, Berbash N, Nada RA, Ahmed SF, Rahouma A, *et al*. Uropathogens from diabetic patients in Libya: Virulence factors and phylogenetic groups of *Escherichia coli* isolates. J Med Microbiol 2009;58:1006-14.
25. Goswami R, Bal CS, Tejaswi S, Punjabi GV, Kapil A, Kochupillai N. Prevalence of urinary tract infection and renal scar in patient with diabetes mellitus. Diabetes Res Clin Pract 2001;53:181-6.
26. Janifer J, Geethalakshmi S, Satyavani K, Viswanathan V. Prevalence of lower urinary tract infection in South Indian Type 2 diabetic subjects. Indian J Nephrol 2009;19:107-11.
27. Alcantara AS, Araza LA, Mercadoasis LB, Tan-Alora A. Bacterial infections among filipino diabetics at the Santo Tomas university hospital. Phil J Microbiol Infect Dis 1999;28:91-7.
28. Cohen M. Emerging problems of antimicrobial resistance. Ann Emerg Med 1994;24:454-6.
29. Dy EE. Inappropriate antibiotic use in the Philippines. Phil J Microbiol Infect Dis 1997;26:77-87.
30. Saber MH, Barai L, Haq JA, Jilani MS, Begum J. The pattern of organism causing urinary tract infection in diabetic and non-diabetic patients in Bangladesh. Bangladesh J Med Microbiol 2010;4:6-8.