Prevalence of Uropathogens in Diabetic Patients and Their Corresponding Resistance Pattern: Results of a Survey Conducted at Diagnostic Centers in Dhaka, Bangladesh

Manik C. Shill,[1] Naz H. Huda,[2] Fahad B. Moain,[3]
Utpal K. Karmakar[4]

Abstract:

Objectives: Urinary tract infection is the second most common clinical indication for empirical antibiotic treatment in primary and secondary health care settings. The incidence of diabetes mellitus throughout the world is increasing strikingly and in the long run, it has some major effects on the genitourinary system which makes diabetic patients more liable to urinary tract infection. This study is designed to reveal the distribution of uropathogens in diabetic patients according to age and sex, and corresponding resistance patterns.

Methods: A six-month retrospective review of urine culture assay data from August 2009 to January 2010 from randomly selected 85 patients who suffered from both urinary tract infection and diabetes was conducted. Relevant information was retrieved and analyzed statistically using Microsoft® Excel 2002 software.

Results: The study showed that females are more vulnerable to pathogenic attack than males throughout a wide age distribution. In terms of pathogenic distribution, *Escherichia coli* was the highest followed by *Streptococcus sp.*, *Acinetobacter*, *Klebsiella pneumoniae* and few others. Though Meropenem showed no resistance with *E. coli*, *Acinetobacter* and *Klebsiella pneumoniae*, in the case of *Streptococcus sp.* it exhibited resistance of 25%. Amikacin exhibited only 3% resistance with *E. coli*, whereas no resistance with *Acinetobacter* and *Klebsiella pneumoniae*, and most interestingly showed 75% resistance with *Streptococcus sp.* Gentamicin exhibited no resistance with *Acinetobacter* while 26.9%, 50% and 87.5% resistance with *E. coli*, *Klebsiella pneumoniae* and *Streptococcus sp.* respectively. Hence, Nitrofurantoin exhibited less resistance 11.9% compared to 12.5% resistance with *E. coli* and *Streptococcus sp.* Nitrofurantoin was highly prone to resistance with *Acinetobacter* and *Klebsiella pneumoniae* (100%, 50% respectively). Cephalosporins (cephradine, cefixime, ceftriaxone, cefepime etc.) showed moderate resistance (avg. 50%), whereas amoxicillin and ciprofloxacin showed the highest resistance in all these cases.

Conclusion: Pathogens are mostly resistant to antibiotics including amoxicillin, ciprofloxacin, cephalosporins and nitrofurantoin, with few exceptions including gentamicin, amikacin and meropenem.

From the [1]Department of Pharmacy, Square Hospitals Ltd, Dhaka, Bangladesh; [2]Department of Pharmacy, Stamford University Bangladesh; [3]Department of Pharmacy, North South University, Dhaka, Bangladesh; [4]Pharmacy Discipline, Khulna University, Khulna, Bangladesh.

Received: 27 Jul 2010
Accepted: 06 Sep 2010

Address correspondence and reprint request to: Naz Hasan Huda, Department of Pharmacy, Stamford University Bangladesh, 51, Siddeswari Road, Dhaka-1217, Bangladesh.
E-mail: nazhasan@gmail.com

doi:10.5001/omj.2010.82

Introduction

Urinary tract infection (UTI) is the second most common clinical indication for empirical antibiotic treatment in primary and secondary health care settings, and urine samples constitute the largest single category of specimens examined in most medical microbiological laboratories.[1] 34% of self-reported adults had at least one occurrence of UTI in the United States within the period of 1988 and 1994.[2] Diabetes mellitus is a complex metabolic syndrome caused by lack of insulin resulting in inappropriate high blood glucose levels.[3] 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.[4] Diabetes mellitus is associated with many complications and in the long run it has some major effects on the genitourinary system which makes diabetic patients more liable to UTI and particularly to upper urinary tract infections.[5] 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.[6] Although the exact reasons for this trend remains unclear, a few studies have shown that the reason could be the presence of static pools of urine due to dysfunctional bladders contracting poorly, which serves a favorable media for bacterial growth while others suggest that hyperglycemic urine promotes rapid bacterial growth and colonization.[7,8] A series of studies from 1959-2005 have also provided evidence that UTI is distinctly more common among female diabetics compared to healthy females.[9]

The most common organisms causing UTI are *E. coli* while *Proteus*, *Klebsiella*, *Streptococcus* and *Staphylococcus* epidermis also commonly the causative agents.[9] Both in community and hospital settings, antimicrobial resistance among uropathogens causing urinary tract infections is also increasing.[10] *E. coli* is the most frequently found bacteria in UTI patients from both these settings which accounts for 80-90% of UTI cases.[11-13]

A study of the susceptibility of the host and the prevalence of the different strains of UTI pathogens are of primary importance in the development of infections. Therefore, the aim of this study is to determine the prevalence of different kinds of uropathogens in diabetic patients and the resistance pattern of antibiotics in various pathogens.

Methods

This was a retrospective study where the retrospective urine culture assay data from 85 patients who suffered from both UTI and diabetes were randomly studied. Data was collected from log and register book of Popular Diagnostic Center and Medinova Diagnostic center in Dhaka for a six months period between August 2009 and January 2010. The data was analyzed statistically using Microsoft® Excel 2002 (10.6854.6845) SP3 software.

The age of all patients included in this survey was above 18. Subjects were included only when they were clinically diagnosed to be diabetic patients and had a blood sugar level greater than 7.8 mmol/l and exhibited glycosouria. All of the subjects were clinically diagnosed as UTI patients with a corresponding uro-culture showing a bacterial count of more than 10^5 cfu/ml.

Results

The distribution of the infections according to the age and sex of the diabetic patients is summarized in Table 1. Out of the 85 patients randomly reviewed within the 6 months period, 25.9% (22 patients) were males and 74.1% (63 patients) were females. Overall, all the females were aged between 26-83 years while the males were aged between 43-70 years. Among the population infected with *E. coli*, the number of male patients was 18 while that of females was 49 with the age range of 43-70 years and 26-83 years respectively. In case of *Streptococcus sp*. the number of females infected was 7 with just a single male patient in the group and age ranged between 30-70 and 60 years respectively. The occurrences of other pathogenic infections were higher among females compared to male patients.

The prevalence of the uropathogens in diabetic patients is shown in Fig 1. The results from the reviewed reports of the patients showed an extremely high prevalence of *E. coli* infections (78.8%, 67 cases) whereas *Streptococcus sp*. were found in 8 cases (9.4%) which was the second highest causative pathogen. The proportion of *Acinetobacter* and *Klebsiella pneumoniae* were 3.5% and 2.4% respectively while of the other pathogens accounted for 5.9% of infections.

Table 1: Frequency distribution of patients according to pathogen, sex and age range.

Microorganism responsible for infection	Number of Patients	Sex	Number of Patients	Percentages (%)	Age Range
E. coli	67	M	18	21.2	43-70
		F	49	57.6	26-83
Streptococcus sp.	8	M	1	1.2	60
		F	7	8.2	30-70
Klebsiella pneumoniae	2	M	1	1.2	46
		F	1	1.2	56
Acinetobacter	3	M	0	0.0	N/A
		F	3	3.5	57-72
Others*	5	M	3	3.5	49-55
		F	2	2.4	61-78
Total	**85**	**M**	**22**	**25.9**	**43-70**
		F	**63**	**74.1**	**26-83**

F: Female; M: Male; Others = Enterobacter sp., Hafnia alvei, Pseudomonas sp., Staphylococcus aureus*

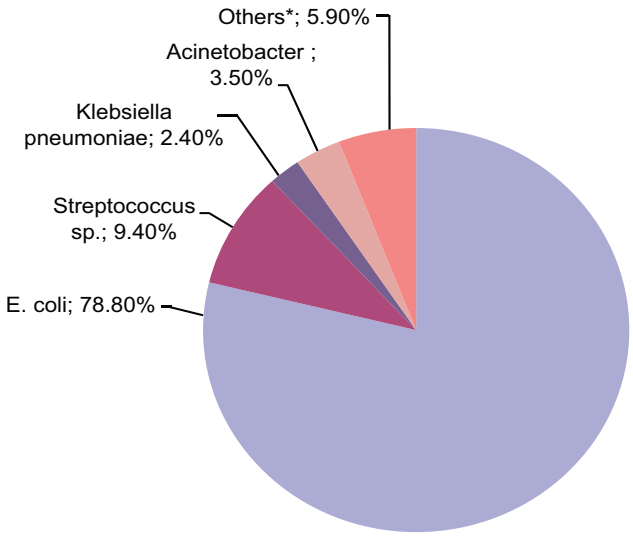

Figure 1: Prevalence of various pathogens responsible for UTI of diabetic patients in Dhaka, Bangladesh.

The resistance pattern of the discussed antibiotics is summarized in Fig 2. *E. coli* exhibited high resistance with amoxicillin and ciprofloxacin with 94% and 79% resistance respectively. All the cephalosporins showed moderate activity against the *E. coli* infection; cephradine, cefixime, ceftriaxone, and cefepime exhibited 68.7%, 62.7%, 61.2%, and 46.3% resistance respectively. Gentamicin demonstrated only 26.9% resistance while meropenem showed no resistance at all. Amikacin also proved to be very active against *E. coli* with only 3% resistance and so did nitrofurantoin with just 11.9% resistance.

Streptococcus sp. on the other hand, showed an overall greater resistance than *E. coli*. *Streptococcus sp. exhibited* most resistance with gentamicin (87.5%), amikacin (75%) and ciprofloxacin (75%). Average resistances were observed with amoxicillin (62.5%) and the cephalosporins which were cephradine (50%), cefixime (50%), ceftriaxone (50%) and cefepime (37.5%). Though meropenem was very effective against *Streptococcus sp*, showing only 25% resistance. The lowest resistance was observed with nitrofurantoin which exhibited only 12.5% resistance.

Both *Acinetobacter* and *Klebsiella pneumoniae* showed moderate resistance with amoxicillin (33.3% and 100% respectively) and all the cephalosporins with cephradine (33% *vs.* 50%), cefixime (33.3% *vs.* 50%), ceftriaxone (33.3% *vs.* 50%), and cefepime (33.3% *vs.* 50%). Stronger resistance was observed with nitrofurantoin (100% vs. 50%). Meropenem and Amikacin showed no resistance among these two strains while the resistance for gentamicin was 0% *vs.* 50%. It was also revealed that *Acinetobacter* is very susceptible to ciprofloxacin with no resistance at all; however the drug is completely useless for *Klebsiella pneumoniae* infections.

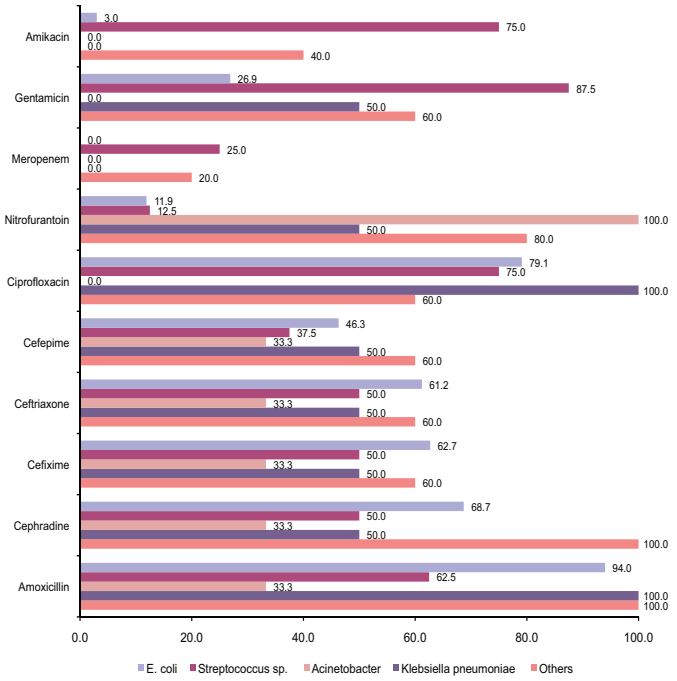

Figure 2: Pattern of antibiotic resistance of various pathogens found in urine culture of diabetic patients. Overall resistance pattern in decreasing order of various commonly used antibiotics is Amoxicillin (78.0%)>Ciprofloxacin (62.8%)>Cephradine (60.4%) >Cefixime (51.2%)>Ceftriaxone (50.9)>Nitrofurantoin (50.9%)> Cefepime (45.4%)>Gentamicin (44.9%)>Amikacin (23.6%)> Meropenem (9%).

Discussion

This study confirmed that overall, UTI is more common in females than males (3 times more) agreeing with other previous studies.[9,14] *E. coli* and *Streptococcus sp.* were found to be the major group of pathogens responsible for the infections which also support other research reports from other countries.[15-18] In the diabetic group of patients, the age range of infected females (26-83 years) was also much broader compared to that of males (43-70 years). *E. coli* was the most prevalent pathogen among the UTI patients as confirmed by other studies.[14] This study revealed that after *E. coli* and *Streptococcus sp.* were the most prevalent pathogens followed by *Acinetobacter* and *Klebsiella pneumoniae*.

When the effectiveness of various antibiotics was studied for UTI based on the resistance patterns, it pointed out that the most effective antibiotic overall is meropenem followed by amikacin. The once blockbuster antibiotics such as amoxicillin, ciprofloxacin,

cephradine showed most resistance with 78.0%, 62.8%, 60.4% resistance respectively and cephalosporins such as cefixime, cefepime and ceftriaxone showed around 50% resistance. These findings are clearly alarming as our country could be running out of effective antibiotics if this trend continues.

E. coli exhibited a 94% resistance to amoxicillin and a striking 79% resistance to ciprofloxacin, which should be a matter of consideration. Resistance to cephalosporins was also well above 60% in most cases. *E. coli* was most inhibited by meropenem, amikacin and nitrofurantoin. Streptococcus showed similar patterns but it exhibited a profound resistance of 87.5% to gentamicin and also an alarming 75% to amikacin. *Acinetobacter* and *Klebsiella pneumoniae* also showed similar resistance patterns to that of *E. coli*. Other pathogens, including *Enterobacter sp.*, *Hafnia alvei*, *Pseudomonas sp.* and *Staphylococcus aureus* exhibited complete resistance to amoxicillin, cephradine. Resistance to nitrofurantoin was also 80%. Most other commonly used antibiotics including the cephalosporins showed more than 50% resistance. Hence, the best acting antibiotic was found to be meropenem.

Conclusion

The significance of the study lies in the determination of common pathogens in diabetic patients with UTI and the resistance pattern of antibiotics so that physicians and pharmacists get the proper information rationalizing the use of antibiotics. This study also demonstrated that antibiotics including amoxicillin, ciprofloxacin, cephalosporins (1st generation, 2nd generation, 3rd generation in some cases) and nitrofurantoin are mostly resistant to pathogens with few exceptions including gentamicin, amikacin and meropenem (most effective one). Thus this study should provoke policy makers to formulate an antibiotic policy for rational use of antibiotics.

Acknowledgements

The authors are kind enough to show their gratitude to the microbiologists and technicians of Popular and Medinova Diagnostic center who helped a lot in different ways. The authors reported no conflict of interest and no funding was received on this work.

References

1. Morgan MG, McKenzie H. Controversies in the laboratory diagnosis of community-acquired urinary tract infection. Eur J Clin Microbiol Infect Dis 1993 Jul;12(7):491-504.
2. Weighted Analysis of 1988-1994 NHANES, 2003, NIDDK.
3. O'Sullivan DJ, Fitzgerald MG, Meynell MJ, Malins JM. Urinary tract infection. A comparative study in the diabetic and general populations. Br Med J 1961 Mar;1(5228):786-788.
4. Ribera MC, Pascual R, Orozco D, Pérez Barba C, Pedrera V, Gil V. Incidence and risk factors associated with urinary tract infection in diabetic patients with and without asymptomatic bacteriuria. Eur J Clin Microbiol Infect Dis 2006 Jun;25(6):389-393.
5. Patterson JE, Andriole VT. Bacterial urinary tract infections in diabetics. Infect Dis Clin North Am 1997;11(3):735-750.
6. Adeyeba OA, Adesiji YO, Omosigho PO. Bacterial Urinary tract infections in patients with Diabetes Mellitus. International Tropical Journal of Medicine 2007;2:89-92.
7. Andriole VT. Asymptomatic bacteriuria in patients with diabetes–enemy or innocent visitor? N Engl J Med 2002 Nov;347(20):1617-1618.
8. King H, Reiwers M. Performance Standardized for Antimicrobial Disk Susceptibility Testing, 1993, 5th Edn. approved Standard NCCLS Document M2-A5. Villanova Pa:NCLLS.
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 Infect Dis 2006;6:54. doi:10.1186/1471-2334-6-54.
10. Bonadio M, Meini M, Spitaleri P, Gigli C. Current microbiological and clinical aspects of urinary tract infections. Eur Urol 2001 Oct;40(4):439-445, discussion 445.
11. Grüneberg RN. Changes in urinary pathogens and their antibiotic sensitivities, 1971-1992. J Antimicrob Chemother 1994 May;33(Suppl A):1-8.
12. MacGowan AP, Brown NM, Holt HA, Lovering AM, McCulloch SY, Reeves DS. An eight-year survey of the antimicrobial susceptibility patterns of 85,971 bacteria isolated from patients in a district general hospital and the local community. J Antimicrob Chemother 1993 Apr;31(4):543-557.
13. Delzell JE Jr, Lefevre ML. Urinary tract infections during pregnancy. Am Fam Physician 2000 Feb;61(3):713-721.
14. Jha N, Bapat SK. A study of sensitivity and resistance of pathogenic micro organisms causing UTI in Kathmandu valley. Kathmandu Univ Med J (KUMJ) 2005 Apr-Jun;3(2):123-129.
15. Leigh D. Urinary Tract Infections. In: Smith GR, Easma Charles SF,eds. Topley and Wilson's principles of bacteriology, virology and immunity, volume 3. Bacterial disease. 8th edition. Frome and London: Butler and Tanler Ltd, 1990. p. 197-214.
16. Obi CL, Tarupiwa A, Simango C. Scope of urinary pathogens isolated in the Public Health Bacteriology Laboratory, Harare: antibiotic susceptibility patterns of isolates and incidence of haemolytic bacteria. Cent Afr J Med 1996 Aug;42(8):244-249.
17. Tsunoda K, Goya N, Miyazaki Y, et al. Bacterial flora of the urinary tract and their drug sensitivity: 2 years clinical statistics in Sanskinkai Hara Hospital, Japan Nishinihon. J Urol 1979;41(2):337-345.
18. Manandhar S. Microbiology of urinary tract infection: A hospital based study. A dissertation presented to the Central Department of Microbiology, Tribhuwan University 1995.