Original Article

Diabetes mellitus and Urinary Tract Infection: Spectrum of Uropathogens and their Antibiotic Sensitivity Pattern

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Abstract

The incidence of urinary tract infections (UTIs) is common in both diabetic and non diabetic patients. Since the microorganisms causing UTI vary in their susceptibility to antimicrobials from place to place and time to time, hence constant screening of trends and susceptibility pattern of predominant organisms against antimicrobials is essential. The study aims to determine the spectrum of uropathogens and antibiotic sensitivity pattern in both diabetic and non diabetic patients with clinically suspected UTI .A prospective cross sectional study was conducted during period of February 2013 to July 2013 among 90 diabetic and 90 non diabetic patients attending Dhulikhel Hospital-Kathmandu University Hospital, Dhulikhel, Kavre (DH-KUH). All samples and isolates were investigated by standard laboratory procedures. A total of 55 (30.5%) samples showed significant growth. No significant difference among culture positivity rate was noted between diabetic and non diabetic patients (34.5% Vs 26.7%). Escherichia coli was the most frequent organism (64.5% in diabetic and 66.7% non diabetic) followed by Klebsiella sps (22.6% in diabetic and 12.5% in non diabetic). Gentamycin and nitrofurantoin were highly sensitive to E. coli isolated in diabetic patients among the tested antimicrobials followed by cotrimoxazole, norfloxacin and ciprofloxacin. Least sensitivity rate was observed with ampicillin and cephalexin. However, no difference was noted on the sensitivity pattern of the antimicrobials among E. coli isolated between diabetic and non diabetic patients.In this study high proportion of gram negative bacilli with predominant uropathogen being E. coli was noted. Irrespective of the status of diabetes, Staphylococcus sps and Pseudomonas sps were not isolated from UTI patients in our study. The isolation of organisms and their resistance pattern was almost similar between diabetic and non diabetic patients.

Key words: Antibiotic Susceptibility Test, Diabetes mellitus, Urinary Tract Infection

Introduction:

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action or both and has been estimated that 347 million people worldwide have diabetes, and Nepal with the mortality rate of ?300[1,2]. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction, and failure of various organs especially the eyes, genitourinary system, nerves, heart, and blood vessels [3].Over time, patients with diabetes may develop cystopathy, nephropathy, and renal papillary necrosis, complications that predispose them to urinary tract infections (UTIs). Susceptibility increases with the longer duration and great severity of diabetes. The high urine glucose content and defective host immune factors predispose to infection. Hyperglycemia causes neutrophil dysfunction by increasing intracellular calcium levels and interfering with actin and, thus, diapedesis and phagocytosis [4].

UTI which is defined as the presence and active multiplication of microorganisms within the urinary tract is one of the commonest bacterial infections seeking

treatment in clinical practice. Although a variety of etiology is involved with UTI,ÊE. coliÊand other coliforms account for large majority of naturally acquired urinary tract infections [5].

Evidences suggest that the incidence of UTI in diabetes patients is four times higher comparing to non diabetes patients [6]. It has been reported elsewhere that the occurrence of UTI in diabetic patients is more in people with low socioeconomic status and the resistant pattern of antibiotic agents against organisms isolated in diabetic patients were different to the non diabetic patients [7]. However, previous studies also have reported that there was no influence of diabetes in the isolation rate of different uropathogens and their susceptibility patterns to antimicrobials [8].

Microorganisms causing UTI vary in their susceptibility to antimicrobials from place to place and time to time. Resistant to newer and more potent antimicrobials are making the therapeutic options very limited in case of UTI. In Nepal, there have been several studies focusing on antibiotic susceptibility patterns of uropathogens[9,10]. But the studies on spectrum of uropathogens and the profile of antibiotic resistance in UTI patients with and without diabetes are limited, at least as a scientific publications.

Thus the screening of UTI in diabetic patients is essential and has no alternative so far. Hence, this study was undertaken to understand the incidence of spectrum of uropathogens and antibiotic sensitivity pattern in both diabetic and non diabetic patients with clinically suspected UTI.

Methods

A prospective cross sectional study with a total number of 180 patients (90 with DM and 90 without DM) with clinically diagnosed UTI, attending both outpatients and inpatients of Dhulikhel Hospital-Kathmandu University Hospital (DH-KUH) were studied. The study was approved by Institute Review Committee (IRC). Study was conducted during period of February 2013 to July 2013 in the Department of Microbiology and Department of Clinical Biochemsitry, DH-KUH. The diagnosis of diabetes was based on WHO-2003 glucose based criteria [11].

Clean voided midstream urine samples were collected in sterile containers after giving proper instructions and samples were processed in the laboratory within 2 hours of collection. Urine cultures were done by inoculating urine samples on Blood agar and MacConkey agar plates using a calibrated loop (0.001ml) and incubated at 37oC for 18-24 hours. Those culture reports were considered positive who had colony forming units more than 105/mL of voided urine. The presence of yeast in any number was considered to be significant. The pathogens were isolated and specific biochemical tests were done for identifying the species of the pathogens. Antimicrzobial sensitivity was done by Kirby-Bauer disc diffusion method according to CLSI guidelines [12].

Data were entered in Microsoft Office Excel and analyzed using SPSS version 17.0 (SPSS Inc; Chicago, IL, USA) and interpreted according to frequency distribution and percentage.

Results

Out of 180 urine samples, 90 patients (50 females and 40 males) were diabetic and 90 (60 females and 30 males) were non diabetic patients. The mean ages of diabetic and non diabetic patients were 56±1.5 years and 52±1.4 years respectively. The overall culture positivity rate in diabetic patients was 34.5% and in non diabetic patients was 26.7%. A total of 55 (30.5%) samples showed significant growth. The study showed that UTI is more common in females than in males. Rate of culture positivity in different category of population is given in Table 1.

Table 1: Rate of culture positive UTI in different category of population

Category of patients	Diabetic			Non-Diabetic		
	Total	Male	Female	Total	Male	Female
Culture positive n (%)	31 (34.5)	14 (35)	17 (34)	24 (26.7)	8 (26.7)	16 (26.6)
Culture Negative n (%)	59 (65.5)	26 (65)	33 (66)	66 (73.3)	22 (73.4)	44 (73.4)
Total No. of suspected UTI	90	50	40	90	30	60

Escherichia coli was the most frequent organism isolated in UTI patients accounting 64.5% in diabetic and 66.7% non diabetic patients followed by Klebsiella sps accounting 22.6% in diabetic and 12.5% in non diabetic

patients. The pattern of all the organisms isolated from patients with both diabetic and non diabetic are shown in Table 2.

Table 2: Isolation rate of uropathogens isolated in patients with and without diabetes

Organisms	Diabetic n=31 (%)	Non-Diabetic n=24 (%)
E. coli	20 (64.5)	16 (66.7)
Klebsiella sps.	7(22.6)	3 (12.5)
Enterococcus sps.	2(6.5)	1 (4.2)
Enterobacter sps.	0	1 (4.2)
Citrobacter sps.	1(3.2)	0
Proteus sps.	0	2 (8.4)
Candida albicans	1(3.2)	1 (4.2)

Gentamycin and nitrofurantoin were found to be highly sensitive to E. coli isolated in diabetic patients among the tested antimicrobials followed by cotrimoxazole, norfloxacin and ciprofloxacin. Least sensitivity rate was observed with ampicillin and cephalexin. However, we found no difference on the sensitivity pattern of the antimicrobials among E. coli isolated between diabetic and non diabetic patients as shown in Table 3. No associations of the antibiotic sensitivity pattern were shown among other microorganisms because of the low isolation rate.

Table 3: Antimicrobial sensitivity pattern of urinary E. coli in patients with and without diabetes.

Antimicrobial agents	Diabetic		Non-Diabetic	
	E. coli (n=20)		E. coli (n=16)	
	Sensitive	%	Sensitive	%
Ampicillin	1	5	2	12.5
Cephalexin	8	40	5	31.3
Co-trimoxazole	12	60	5	31.3
Gentamycin	17	85	12	75
Nitrofurantoin	15	75	15	93.8
Norfloxacin	11	55	7	43.8
Ciprofloxacin	11	55	7	43.8

Discussion

In this study we have tried to determine whether there are differences in the microbiological patterns of UTI and in the antibiotic sensitivity patterns of the pathogens concerned with diabetic and non-diabetic patients. The overall prevalence of UTI in diabetic and non diabetic patients was 34.5% and 26.7% respectively. The bacteria causing UTI in diabetic patients are the same as in non diabetic patients and the predominant of pathogens isolated in our study were gram negative enteric organisms that commonly cause UTI. Regarding the antimicrobial susceptibility pattern of the uropathogens, we observed that the isolated gram negative enteric organisms were sensitive at similar rates in both diabetic and non diabetic patients.

The age and the gender were almost comparable in both study populations. It is stated that UTI is predominantly a disease of the female due to a short urethra and proximity to the anal opening. The majority of the study all over the world has concluded female predominance to UTI over male [8,13]. Our finding of female predominance is not in accordance with the results from a study [14] where male were more infected than female among diabetic patients. Evidence from various epidemiological studies showed that UTI is more common in female with diabetes than in non diabetes female as a consequence of debilitated immune system [15]. However our study did not revealed the differences among diabetic and non diabetic female patients. This differences might have been attributed to factors such as geographical variations, ethnicity of study participants and variation in the screening tests used [16,17].

The overall culture positivity rate in our study among diabetic patients was found to be 34.5% and among non diabetic patients was 26.7%. This is in accordance with the study done in a hospital in Bangladesh where the sample population was almost similar to our study [18]. The diabetic patients are more prone to infectious diseases. A similar study [19] reported 20 % UTI in diabetic patients in their study. However, a study on a large series of diabetic and non diabetic patients from a hospital in Italy, the culture positivity rate was 15% and 14% in diabetic and non diabetic population respectively [8]. This could be due to the differences in the sample size in these different studies.

UTIs are caused by variety of microorganisms, including both gram positive and gram negative ones. The etiology of UTI has been regarded as well established and reasonably consistent. The predominant numbers of pathogens isolated in our study were gram negative bacilli rather than gram positive pathogens. The rate of E. coli isolation we found in both diabetic and non diabetic patients are almost similar, which predominant organism is constituted 65% and 67% among diabetic and non diabetic patients respectively. This is similar with the data obtained by various studies indicated that gram negative bacteria mostly E. coli and Klebsiella are the predominent pathogen isolated in patients with UTI irrespective of risk factors associated with it [7,9,20,21]. This was followed by Klebsiella sps (Diabetic 23%; Non diabetic 13%) and Enterococcus sps (Diabetic 7%; Non diabetic 4%). In another study from Nepal, it was found that E. coli was most commonly grown organism (68.7%) followed by Enterococcus sps (13.92%) [10]. Even a study from India has revealed Staphylococcus sps as the second predominant isolates which is absolutely absent in our findings [14]. There was no difference between the rate of isolation of organisms in diabetic and non diabetic patients in our study which is in accordance with the study done in Bangladesh [18]. It is noted that in a clinical setting different from ours, urinary isolates of symptomatic post menopausal women did not show a significant difference in the bacterial species when compared to the matched group of women without diabetes mellitus [22].

Pseudomonas sps is another gram negative bacterium that is associated with UTI [8]. Irrespective of the status of diabetes, Staphylococcus sps and Pseudomonas sps were not isolated from UTI patients in our study. However other studies from other regions of Nepal have shown the involvement of these organisms as a urinary isolates in UTI patients [9, 10,26]

Regarding the antimicrobial resistant profile of the uropathogens, in our study, 65% of the isolates were E. coli among gram negative pathogens, and were sensitive at similar rates to all the antibiotics used in this study in both diabetic and non diabetic patients. The low rate of E. coli sensitivity to ampicillin and cephalexin we found in our study precludes, at least in our area, the choice of these or similar drugs in the empirical initial treatment of patients with UTI. The significant differences between diabetic and non diabetic patients to the sensitivity to gentamycin, ciprofloxacin and nitrofurantoin was noted in a study from Bangladesh [18].Ciprofloxacin resistant E. coli was noted significantly higher in diabetic patients than the control group in a study done in Iraq [23].An association was found in a study done in emergency department between the presence of cortimoxazole resistance and diabetes and but in an outpatient setting no correlation was found between E. coli resistance to cotrimoxazole [24,25]. Moreover this difference in sensitivity pattern of isolates could be attributed to time difference between the two studies or environment factors such as practices of self medications, the drug abuse and indiscriminate misuse of antibiotics among the general population which has favored the emergence of resistance strains.

The limitations of our study were, first information regarding type and duration of diabetes was lacking and second was we could not elaborate the correlation of all the uropathogens among various age groups, regions and socioeconomic status due to low sample size and isolation rate.

Conclusion

We found high proportion of gram negative bacilli with predominant uropathogen being E. coli in both diabetic and non diabetic patients. The sensitivity of uropathogens to the antibiotics was similar in study participants. Both diabetic and non diabetic patients are at high risk of development of UTIs, so laboratories should encourage accurate bacteriological record keeping of urinary isolates. Therefore, continued surveillance of sensitivity rates among uropathogens is needed to ensure appropriate recommendations for the treatment of these infections.

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