Causative agents of Urinary Tract Infection in Diabetic Patients and their pattern of Antibiotic susceptibility.

by Hamid Bashir

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RAWALPINDI

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8

CAUSATIVE AGENTS OF URINARY TRACT INFECTION IN DIABETIC PATIENTS AND THEIR PATTERN OF ANTIBIOTIC SUSCEPTIBILITY.

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CAUSATIVE AGENTS OF URINARY TRACT INFECTION IN DIABETIC PATIENTS AND THEIR PATTERN OF ANTIBIOTIC SUSCEPTIBILITY.

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Short Title: Diabetics Uropathogens and antibiotic susceptibility.

ABSTRACT

Objective: Uropathogens vary in their susceptibility to antibiotics from place to place and time to time, hence constant screening of trendsand susceptibility pattern of predominant organisms against antimicrobials is essential.This study was planned to determine the etiologic agents of UTI and their antibiotic susceptibility patterns among diabetic patients.

Methodology: A Cross sectional observational study was undertaken for the period of 8months at Cantonment General Hospital Rawalpindi.Diabetic patients of both genders and age more than 18yrs were screened for UTI irrespective of their symptoms.Urine cultures were taken and uropathogen was isolated and tested for drug susceptibility. All samples and isolates were investigated by standard laboratory procedures.

Results: Out of 209 diabetics, 106 had culture positive UTI. Mean age was 49.9 ±9.80. 73.3% (n= 77) were females. 93.3% (n= 98) had type 2 diabetes.E coli was the most common uripathogen(80%) followed by Enterobacter(7.6%),citrobacter(6.7%), morganella(4.8%) and pseudomonas(1%). No gram positive bacteria was isolated. Fosfomycin was100% sensitive against all uropathogens.Meropenum, piperacillin/Tazobactum and cefoperazone/salbactum being 91.4%, 88.6% and 86.7% respectively. followed by amikacin that was 72.4% sensitive. Chloramphenicol, doxycycline and amoxicillin/culvunate showed sensitivity of 66.7%, 61% and 40% respectively. Cephalosporins and quinolones were least sensitive classes.

Conclusion: Continuous surveillance of sensitivity patterns among uropathogens is required to ensure appropriate recommendations for the treatment of these infections.

Key Words: Uropathogen, Diabetes mellitus, Urinary Tract Infection

Introduction:

Urinary tract infection (UTI) is one of the most common bacterial infections worldwide.[1] Infection ranges from uncomplicated cystitis to bacteremia with relevant morbidities.[1] Diabetes mellitus is the risk factor for urinary tract infection (UTI).[2] The exact reason for it is unclear; however, impaired immune system and inadequate bladder emptying predispose diabetics to UTI. [3,4,5]Moreover, glycusuric state creates a good culture medium for the growth of pathogenic microorganisms relating poor glycemic control to increase the risk of UTI.[6]

UTI in diabetics is asymptomatic initially, females are effected more than men and it leads to serious complications if not treated timely and adequately.[2,7,8]

Several studies have showed that Escherichia coli, Klebsiellaspp, Proteus spps, Group B Streptococcus, coagulase- negativeStaphylococci (CoNS), S. aureus, Enterococcus spp, Enterobacter spp., Citrobacter spp., Serratiaspp, pseudomonas aeruginosa and candidia spp. have been isolated among DM patients with a varying frequency in different regions.[2,7.-12]

Increasing antimicrobial resistance has been observed for common uropathogens in the Asia-Pacific as well as in global studies.[9-12]It leads to prolonged hospital stays and higher medical costs because of inappropriate antibiotic treatment.[1]

This is one of the big challenges in low-income countries like us, due to high Infection rates in poorly controlled diabetics, irrational use of antibiotics, over-thecounter availability of antibiotics and poor infection prevention practices.Empirical antibiotic treatment should be prescribed according to local epidemiologic data and antibiotic susceptibility results.

Uropathogens vary in their susceptibility to antibiotics from place to place and time to time, hence constant screening of trends and susceptibility pattern of predominant organisms against antimicrobials is essential. This study was planned to determine the etiologic agents of UTI and their antibiotic susceptibility patterns among diabetic patients.

Material and methods:

A Cross sectional observational study was undertaken for the period of 8months at Cantonment General Hospital Rawalpindi, it's a teaching hospital affiliated with Yusra Medical College.

All the diabetic patients of both genders and age more than 18yrs who came to the medical OPD were screened for UTI irrespective of their symptoms after taking informed consent. Patients with culture positive UTI were included in the study. Patients treated with antibiotics within the preceding 2 weeks, and known anatomic and neurologic urinary tract abnormalities, also diabetic pregnant women were excluded from the study.

Mid-stream urine sample was taken in a sterile container. Uropathogen was grown on clede plate media incubated at 37^0C for 24 hours. On the next day, the bacterial growth was controlled, and total colony count was calculated. Urine culture was considered significant bacteriuria (SB) when for a single isolated uropathogen colony forming units (CFUs) were $\geq 10^5$/mL of voided urine.Antibiotic susceptibility testing was performed on neutral agar.

The isolates were tested for amoxicillin-clavulanic acid, ceftriaxone, ciprofloxacin, norfloxacin, moxifloxacin, amikacin, tobramycin, doxycycline, fosfomycin, gentamicin, piperacillin-tazobactum,meropenum, cefoperazone-salbactum, cefixime, ceftazidime, cefepime, aztreonam and chloramphenicol. The result was interpreted accordingto the Clinical and Laboratory Standards Institute (CLSI)guideline as susceptible (S), intermediate (I) or resistant (R).

Data analysis:

Data was entered and analyzed using SPSS version 20. Descriptive statistic was calculated for both qualitative and quantitative variables. For qualitative variables like gender, uropathogen and their drug susceptibility % and frequency were calculated. For quantitative variables like age mean±SD will be calculated. Student T testand chi square test were employed to look for statistical difference where ever indicated. P value ≤ 0.05 was taken significant. All the results will be presented through charts and tables.

Results:

209 already diagnosed diabetic patients visiting medical OPD from 1st August 2016 to 28th Feb 2017 were screened for UTI. Urine for culture and sensitivity was sent for all these patients irrespective of their presenting complaints. 106 patients had culture proven UTI, they were included in the study.

Period prevalence of culture positive UTI in our study population was 50.7%. Mean age of patients was 49.9 ±9.80. 73.3% (n= 77) were females. 93.3% (n= 98) had type 2 diabetes. Mean HbA1c level was 9.63±2.001.

E coli was the most commonly isolated uropathogen accounting for 80% (n= 84) of all cases ofwhich 20% was ESBL. Enterobacter was next to it causing 7.6% (n= 8) infections, citrobacter was found in 6.7% (n=7) of patients. 4.8% (n=5) was due to morganella and pseudomonas was a culprit in only 1% (n=1) of the cases.(fig1)

Fosfomycin showed 100% drug sensitivity to all uropathogens. Meropenum, piperacillin/Tazobactum and cefoperazone/salbactum showed high sensitivities of 91.4%,88.6% and 86.7% respectively followed by amikacin that was 72.4% sensitive. Chloramphenicol, doxycycline and amoxicillin/culvunate showed sensitivity of 66.7%,

61% and 40% respectively. Cephalosporins and quinolones turned out to be the less sensitive classes. Details mentioned in fig 2.Organism wise drug susceptibility has been shown in table 1.

Discussion:

Our study showed that on routine screening, significant number of diabetics had UTI. Period prevalence of culture proven UTI was 50.7%. It is relatively high as compared to other studies showing 43%, 34% and 35% respectively.[9,11,12]

Reason for this can be geographic variation, ethnicity and also that our study population had poorly controlled diabetes that prone them to develop UTI.

Females are more prone to get UTI and same is true for diabetics. Our study also supported this fact.[9,12,13]

Our patients were relatively of younger age as compared to other studies,[3,11] the reason for this can be early diagnosis of diabetes, ethnic variation and attitude of general population for seeking medical attention.

9

Most common organism isolated in culture was E coli followed by citro, entero, morgenella. No doubt E coli remain universally the most common uropathogen but relevant studies documented e coli isolated in 41.5%(n=49), 48%(n=49), 58.3%(n=252),64.5% (n=31)[9-12] but in our study the figure was quite high ie 80%. Rest all organisms i.e citrobacter, Enterobacter,morgenella and pseudomonas were isolated in few cases ,this corroborates the findings of other authors who have reported less frequent isolation of these organisms in urine specimens of diabetic patients.[9-13]

20% of E coli were ESBL producing in our study, this is supported by the fact that diabetics especially with poor control are more prone to get ESBL positive UTI.[10,14]

We didn't report any gram positive organism or candida in any of the urine specimen, where as in a study staph was just next to e coli in causing UTI in diabetics followed by candida and streptococcus.[10] Even a study from India has revealed Staphylococcus as the second predominant isolates[15]which is absolutely absent in our findings. In this regard our study was supported by a study done in khatmandu that also showed no gram positive organism isolated in urine of diabetic patients.[11] Other studies showed less rate of gram positive and candida isolation in diabetic UTIs.[9,12]

There is wide variety of organisms being isolated at different frequencies in different studies, the reason being regional difference, diagnostic tools and expertise, geographic distribution of organisms, difference in sample size and patient related factors like previous h/o UTI, catheterization, diabetic control etc.

Regarding antibiotic susceptibility pattern, we found that our 100% organisms were sensitive to fosfomycin. This is never observed in any of the study before. Meropenum was next to fosfomycin giving more than 90% sensitivity, high sensitivity pattern of meropenum was consistent with other studies.[3,4,10]

Cefoperazone/salbactum and piperacillin/tazobactum were highly sensitive against all organisms in our study, high sensitivity of cefoperazone/salbactum is supported by one of the other study.[3] Regarding piperacillin/tazobactum previous studies have shown less sensitivity as compared to ours.[3]

Amikacin was moderately sensitive in our study population as documented in other studyaswel[9] but many studies have shown it highly sensitive to uropathogens.[3,12]

Amoxicillin/culvunate and quinolones demonstrated very high resistance profile against uropathogens.It's similar to other studies.[4,9,10,12] but its contrary to the study conducted in Ethiopia in 2016, that showed more than 80% sensitivity to norfloxacin and ciprofloxacin.[2]

The reason for this difference can be a small sample size of 11 in that study along with racial difference.

Regarding cephalosporins, we have documented very low sensitivity trend even with 4th generation drugs. Although many studies showed moderate sensitivity of cephalosporins[3,4]but in our case they were the least sensitive drugs.The probable explanation to this difference can be the irrational and/or over the counter use of cephalosporins in our setup.

Aztreonam had very low sensitivity against organisms; this finding was also supported in the study done in India.[3]

As a whole all studies including ours highlight the increasing resistance of uropathogens to antibiotics, this finding can be attributed to indiscriminate misuse of antibiotics among the general population, drug abuse and over the counter availability of drugs.

There were some limitations to our study. We didn't focus on the history in terms of urinary symptoms, prior episode of UTI or use of antibiotics. We didn't check for antibiotic sensitivity against nitrofurantoin that can be the good option for treatment.

Conclusion:

Our study showed high prevalence of UTI among diabetic patients in our setup, this led us to keep our threshold low to screen diabetic patients for UTI.

Gram negative organisms remain the common cause of UTI, E coli being the leading organism with significant number of ESBL. No gram positive uropathogen was isolated in our study population.

Fosfomycinwas 100% sensitive diverting our attention to it as it is fairly good option for treating UTI in terms of cost effectiveness and easy dosage.

It is the highly alarming situation that the broad spectrum antibiotics like ceftazidime, maxpime and aztreonam showed high rate of resistance for uropathogens in diabetes. These antibiotics are usually reserved for complicated UTIs but probably their irrational use has led to this devastating finding leaving us helpless in the situations where they are actually needed.

It's high time for physicians and pharmacists to identify the infection causing agents and the resistance pattern of antibiotics routinely at their setup to rationalize the use of antibiotics. Continued surveillance of sensitivity patterns among disease causing organisms is required to ensure appropriate recommendations for the treatment of these infections.

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Conflict of Interest:

We declare no conflict of interest and any financial support.

References:

1.Chiu C-C,Lin T-C, Wu R-X, Yang Y-S, Hsiao P-J,Lee Y, et al., Etiologies of community-onset urinary tract infections requiring hospitalizationand antimicrobial susceptibilities of causative microorganisms, Journal of Microbiology, Immunology and Infection (2016), http://dx.doi.org/10.1016/j.jmii.2016.08.008

2.Nigussie D, Amsalu A. Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients. Turkish Journal of Urology. 2017;43(1):85-92.

3.Aswani SM, Chandrashekar UK, Shivashankara KN, Pruthvi BC. Clinical profile of urinary tract infections in diabetics and non-diabetics.Australas Med J. 2014;7(1):29–34.

4. 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. Oman Medical Journal. 2010;25(4):282-285.

5. Mamuye Y. Antibiotic Resistance Patterns of Common Gram-negative Uropathogens in St. Paul's Hospital Millennium Medical College. Ethiopian Journal of Health Sciences. 2016;26(2):93-100.

6. Ramana BV, Chaudhury A. Prevalence of uropathogens in diabetic patients and their resistance pattern at a tertiary care centre in south India. Int J Biol Med Res 2012;3:1433-5.

7.Geerlings SE. Urinary tract infections in patients with diabetesmellitus: epidemiology, pathogenesis and treatment. Int J Antimicrob Agents 2008;31:54-7.

8. Sowmya S, Lakshmidevi N. Prevalence and incidence of urinarytract infection among diabetic patients in Mysore. Int J Recent SciRes 2013;4:1651-65.

9. Sharma V, Gupta V, mittal M. Prevalence Of Uropathogens In Diabetic Patients And Their Antimicrobial Susceptibility Pattern. National Journal of Laboratory Medicine. 2012;1(1): 26-28.

10.Longdoh N A, Assob J C N, Nsagha S D, Nde P F, Kamgo H L F, Nkume A F,et al.,Uropathogens from diabetic patients with asymptomatic bacteriuria and urinary tract infections. The West London Medical Journal 2013;5(1): 7-14

11. Acharya D, Bogati B, Shrestha GT, Gyawali P. Diabetes mellitus and Urinary Tract Infection:

Spectrum of Uropathogens and their Antibiotic Sensitivity Pattern.JMMIHS.2015;1(4): 24-28.

12. Sewify M, Nair S, Warsame S, et al. Prevalence of Urinary Tract Infection and Antimicrobial Susceptibility among Diabetic Patients with Controlled and Uncontrolled Glycemia in Kuwait. Journal of Diabetes Research. 2016;2016:6573215. doi:10.1155/2016/6573215.

13.Saleem M, Daniel B. Prevalence of Urinary Tract Infection among Patients with Diabetes in Bangalore City. Int J. Emerg. Sci2011;(2), 133-42.

14. S. H. MacVane, L. O. Tuttle, and D. P. Nicolau, "Impact of extended-spectrum β-lactamase-producing organisms on clinical and economic outcomes in patients with urinary tract infection," Journal of Hospital Medicine.2014:9(4);232–238.

15.Sibi G, Aheibam PD, Fouzia K, Patil, BR. Prevalence,microbiologic profile of urinary tract infectionand its treatment with trimethoprim in diabetespatients. Res. J. Microbiol 2011; 1-8.

Fig1: Organisms causing UTI.

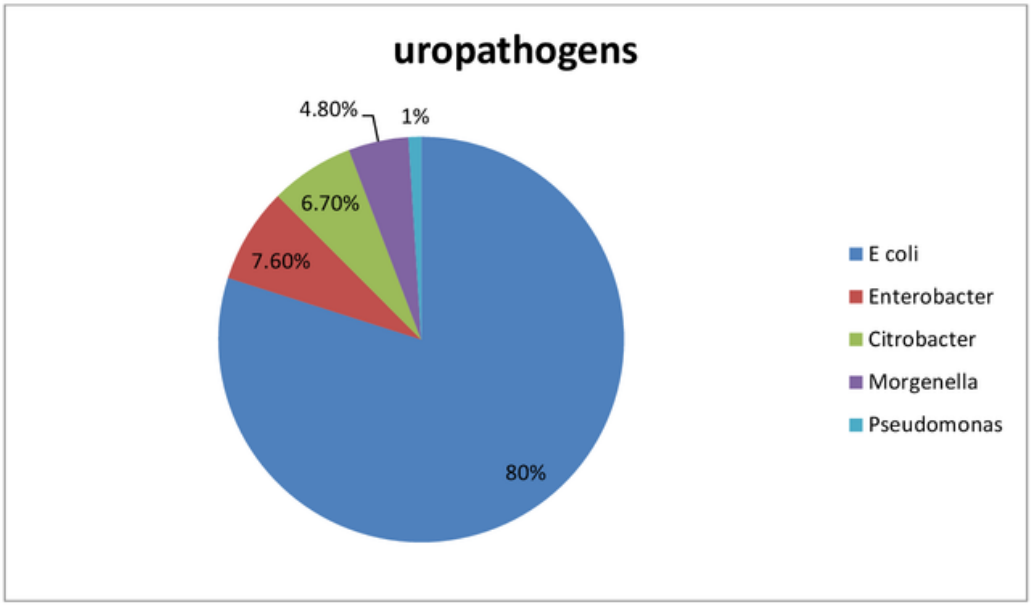

Fig 2: Antibiotic susceptibility pattern

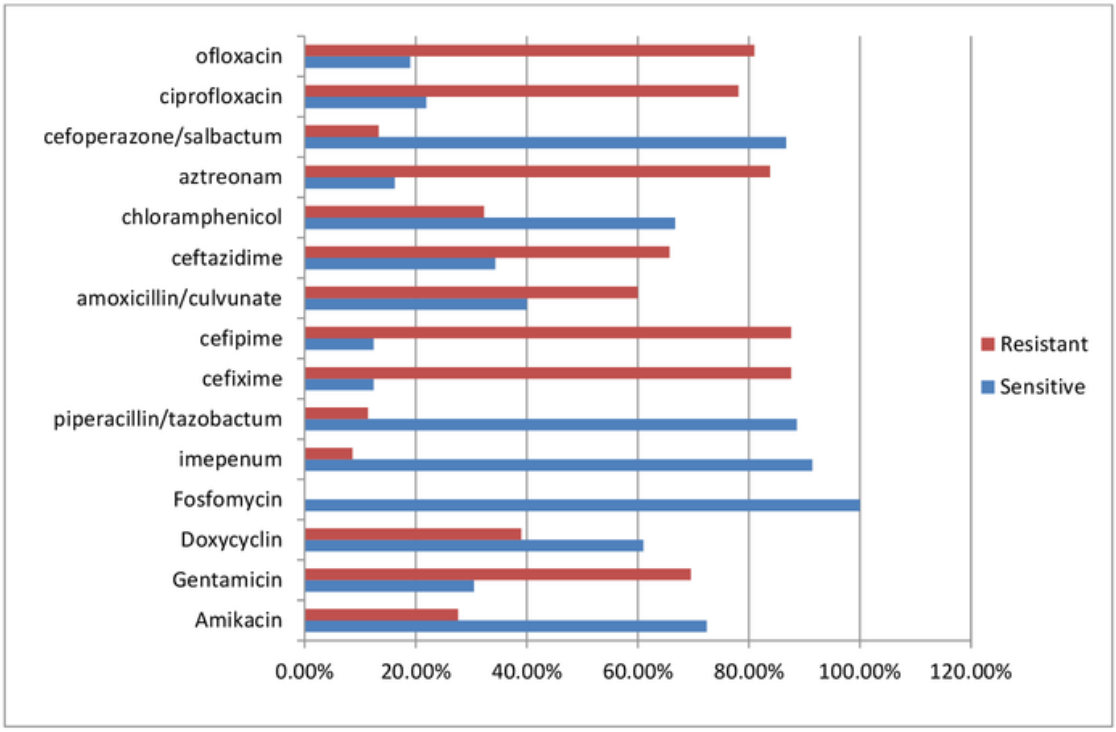

Table 1: Drug susceptibility of each organism.

Organisms	E coli Sensitivity	Enterobacter Sensitivity	Citrobacter Sensitivity	Morganella Sensitivity	Pseudomonas Sensitivity
Amikacin	73%	57.1%	62.5%	80%	100%
gentamicin	29.8%	42.9%	37.5%	20%	0%
Doxycyclin	61.9%	57.1%	62.5%	40%	100%
Fosfomycin	100%	100%	100%	100%	100%
Norfloxacin	11.9%	14.3%	50%	80%	100%
Ciprofloxacin	13.1%	28.6%	50%	100%	100%
Amoxiclave/culvunate	39.5%	57.1%	25%	60%	0%
Piperacillin/sulbactum	89.5%	57.1%	100%	100%	100%
Meropenum	95.2%	71.4%	100%	100%	100%
Aztreonam	13.1%	14.3%	37.5%	20%	0%
Cefixime	11.9%	14.3%	25%	100%	0%
Cefoperazone/sulbactum	88.1%	71.4%	87.5%	80%	100%
Ceftazidime	34.9%	28.6%	50%	100%	100%
Cefipime	11.9%	14.3%	25%	100%	0%
chloramphenicol	71.4%	57.1%	50%	20%	100%

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