Urinary Tract Infection in Diabetics - A Five Year Retrospective Study on the Prevalence of Bacterial Isolates and its Antibiotic Susceptibility Patterns in A Tertiary Care Hospital in South India

Jagadeeswaran G[1], Mohammad Zeya Ansari[2], Tolstoy Rajangam[3]

ABSTRACT

Introduction: Urinary tract infection (UTI) is almost most common seen infection in the diabetic patient due to various local and systemic immunopathogenetic reasons. This causes multiple renal and extrarenal complications and even death if not intervened early. We aimed to find out the prevalence of different bacteria in urine culture and the antibiotic susceptibility pattern amongst diabetic patients admitted in our hospital and to start empirical antibiotics for early recovery and to prevent complications.

Material and Methods: Retrospectively, 651 culture positive urine samples were taken for study with inclusion and exclusion criteria. We saw all the case records and investigations of every subject to correlate with criteria of selection. Our laboratory follows the standard protocols for urine sampling, timely transportation and microbiological study. Antibiotic susceptibly was tested by Kirby Bauer method and interpretations were done by clinical laboratory and standards institute (CLSI) guidelines.

Results: Out of total 651 patients most commonly affected age group was 51-60 years (30.26%).Here males (53.3%) dominated females (46.7%) in number with little difference. Most common Gram-negative bacteria were Escherichia coli (69.12%) and Klebsiella pneumoniae (8.60%) while most common Gram-positive bacteria were Enterococcus faecalis (10.90%) and Staphylococcus aureus (2.91%).Most of the gram-negative bacteria were having a good susceptibility to amikacin, piperacillin/tazobactam, cefoperazone/sulbactam and carbapenems while Gram-positive bacteria were mostly sensitive to nitrofurantoin, linezolid and vancomycin.

Conclusion: in our study, the occurrence of UTI among the diabetic is commoner in the sixth decade with a male predominance. We found E.coli, E.faecalis, and K.pneumoniae as the most commonly grown organisms in descending order. Most of the Gram-negative isolates were susceptible to amikacin, piperacillin/tazobactam, cefoperazone/sulbactam and carbapenems, while most of the Gram-positive cocci were sensitive to nitrofurantoin, linezolid, and vancomycin. Antibiotic resistance is seen very commonly in our setup. We cannot depend upon frequently used oral antibiotics and certain groups like fluoroquinolones and cephalosporin (except for sulbactam containing ones) and ampicillin for empirical treatment in UTI especially the complicated ones.

Keywords: Urinary Tract Infection, Diabetics, Prevalence, Isolates, Antibiotic Susceptibility

INTRODUCTION

The urinary tract is a principal site of infection in diabetics.[1] UTI (Urinary Tract Infection) encompasses a variety of clinical entities, including ABU (asymptomatic bacteriuria), cystitis, prostatitis, and pyelonephritis. There can be an increased risk of ABU or symptomatic UTI in diabetics.[2]

Urinary tract infection can be uncomplicated or complicated. Uncomplicated UTI can be asymptomatic bacteriuria, cystitis, pyelonephritis, in men and nonpregnant women, also prostatitis in men. Complicated UTI can be symptomatic episodes of cystitis or pyelonephritis in men or women with an anatomic predisposition to infection, with a foreign body in the urinary tract, or factors predisposing to a delayed response to therapy. There can be a relapse or reinfection. A relapse is a recurrent infection with an organism similar to the pretherapy isolate, usually following persistence of the organism in the genitourinary tract. A reinfection is a recurrent infection with a new organism. The quantitative criteria of at least 10^5 CFU (colony forming units)/mL are generally appropriate for the microbiological identification of complicated urinary infection. Bacteriuria is more common in diabetics than in non-diabetics due to a combination of host and local risk factors.[3] Some microorganisms become more virulent in a high glucose environment. Therefore, screening for UTI in diabetic patients is very important to enable bacteruria to be properly treated.[4] There is a significant correlation between duration of diabetes and UTI.[5] Changes in host defense mechanisms, the presence of diabetic cystopathy and of microvascular disease in the kidneys may play a role in the higher incidence of UTI in diabetic patients. As diabetics are more prone to UTI, it is necessary to pay special attention to early diagnosis and treatment.[6]

The aim of this study was to determine the causative bacteria, culture and sensitivity pattern in diabetics with Urinary tract infection in our setup. This will guide us to start an

[1]Associate Professor, Department of Medicine, [2]Assistant Professor, Department of Medicine, [3]Professor, Department of Medicine, PSG Institute of Medical Science And Research, Coimbatore, India

Corresponding author: Mohammad Zeya Ansari, S3, Staff Quarters, Psgimsr Campus, Peelamedu, Coimbatore-641004, India

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appropriate timely empirical antibiotic which will prevent the diabetic patients from the complications of UTI like pyelonephritis, urosepsis, renal failure etc. This can decrease the hospital stay, morbidity, and mortality.

MATERIAL AND METHODS

This was a 5 year (August 2010 to August 2015) study done in PSG Hospital, Peelamedu, Coimbatore and was based on the retrospective collection of data from case records of patients who were admitted under medicine department of PSG Hospital. Only those cases that fulfill the inclusion criteria were analyzed. To know the reliability of causative organism, we went through the case records and looked into the various clinical and laboratory parameters of the Diabetic patients who have culture positive UTI.

As per the standard protocol clean voided midstream urine samples were collected in sterile containers. In sampling procedure, all the patients were given proper information while collecting the urine sample. Urine culture reports that exhibited CFU of more than 10^5/ml were considered positive. Only single isolates were taken for study purpose and mixed growths were excluded. The pathogens were isolated and identified using phenotypic methods and biochemical testing. Antimicrobial susceptibility testing was performed using Kirby-Bauer disc diffusion method as described by the Clinical and Laboratory Standards Institute (CLSI). We took nine types of isolates and went through their susceptibility patterns to 26 antibiotics. Ethical clearance was obtained before the start of the study.

Inclusion criteria:

1. Diabetic patients
2. Sex: Both male and female
3. Age: 18 years and above
4. Urine culture positive cases

Exclusion criteria:

1. Nondiabetic
2. Pregnancy
3. Known congenital/acquired urogenital anomaly
4. Patients on chronic catheterization
5. Candiduria

STATISTICAL ANALYSIS

The data was descriptively analyzed using Microsoft Excel 2007 software.

RESULT

As per our finding depicted in Table 1 most of the patients were in the age range 51 to 60 years (30.26%) followed by 61 to 70 years (22.27%) and next 41 to 50 years (20.89%) while lower and higher of age groups are lesser affected.

In figure 1 regarding the gender predilection, males were more affected than females (53.3% vs 46.7%).

From the distribution pattern seen in figure 2, it is clear that most common Gram-negative bacteria were E.coli (69.12%) followed by Klebsiella pneumoniae (8.60%). Out of Gram-positive organisms most frequently seen bacteria (figure 3), were Enterococcus faecalis (10.90%) followed by Staphylococcus aureus (2.91%). So, the actual second most common bacteria seen were E.faecalis.

Age	No.of patients	Percentage
10-20	2	0.3
21 -30	18	2.76
31 – 40	39	5.99
41 – 50	136	20.89
51– 60	197	30.26
61– 70	145	22.27
71 – 80	87	13.36
81 – 90	27	4.14
90– 100	0	0
Total	651	100

Table-1: Distribution of patients by age

Age group	In male	In female
10-20	1	1
21-30	10	8
31-40	20	19
41-50	69	67
51-60	100	97
61-70	81	64
71-80	48	39
81-90	18	9
91-100	0	0

Table-2: Number of urine samples with single isolate in various age groups

S.N.	Bacteria	AK	GM	VCM	NA	LOX	NOX	COX	CPH	CTZ	CTX	CEP	CEF-S	AMP	PIP-T
1	E.coli	96	46	-	7	31	18	19	16	20	22	28	71	10	77
2	E.faecium	-	14	100	-	-	-	-	-	-	-	-	-	43	-
3	E. faecalis	75	28	100	17	11	11	-	-	-	-	-	-	54	-
4	K.pneumonaie	81	56	-	42	54	45	37	0	34	35	39	54	2	59
5	P. aeruginosa	72	69	-	-	-	50	40	-	68	-	61	67	-	82
6	Staph.aureus	-	86	100	-	-	20	33	-	-	100	-	-	-	-
7	Citrobacter spp	50	50	-	-	100	47	-	-	51	-	39	-	-	50
8	Proteus spp	91	80	-	20	60	82	40	50	89	67	78	80	-	100
9	Acinetobacter spp.	20	25	-	-	-	-	50	-	25	-	26	-	-	60

AK=amikacin, GM=gentamycin, VCM=vancomycin, LOX=levofloxacin, NOX=norfloxacin, COX=ciprofloxacin, CPH=cephalexin, CTZ=ceftazidime, CTX=ceftriaxone, CEP=cefipime, CEFS=cefoperazone/sulbactam, AMP=ampicillin, PIP-T, piperacillin/tazobactam

Table-3: (part-1) Antibiotic sensitivity in percentage

S.N.	Bacteria	MNM	INM	ENM	CTMX	NIT	TET	LNZ	COLI	RIF	TIGE	CLIND	AMXCL
1	E.coli	95	96	96	34	81	38	-	99	-	97	100	33
2	E. faecium	-	-	-	-	77	40	100	-	-	-	-	29
3	E. faecalis	-	-	-	-	82	47	100	-	-	-	-	-
4	K.pneumonaie	79	83	81	56	28	-	-	91	-	63	39	-
5	P.aeruginosa	50	78	-	0	20	-	-	82	-	-	-	0
6	Staph.aureus	-	-	-	57	100	-	100	-	10	-	50	40
7	Citrobacter spp.	54	59	-	-	-	-	-	-	-	-	-	-
8	Proteus spp.	88	71	75	50	20	-	-	-	-	-	-	50
9	Acinetobacter spp.	-	40	-	80	-	-	-	50	-	-	-	-

(MNM=meropenem, INM=imipenem, ENM=ertapenem, CTMX=cotrimoxazole, NIT=nitrofurantoin, TET=tetracycline, LNZ=linezolid, COLI=colistin, RIF=rifampicin, TIGE=tigecycline, CLIND=clindamycin, AMXCL=amoxicillin/clavulinic acid, CXIM=cefixime)

Table-3: (part-2) Antibiotic sensitivity in percentage

S.N.	Organisms	AK	GM	NA	CXIM	CTX	AMP	CTMX	AMXCL
1	E.coli	3	51	93	100	78	90	66	52
2	K.pneumonaie	16	44	58	100	65	98	44	56
3	P.aeruginosa	33	33	-	-	-	-	-	-
4	Citobacter spp.	50	50	100	-	-	-	100	-
5	Proteus spp.	9	20	80	-	33	30	50	50
6	E.faecalis	25	97	83	-	-	46	-	40
7	Staphylococcus aureus	-	14	-	-	0	100	43	60
8	E.faecium	-	80	-	-	-	57	-	71

Table-4: Resistance to commonly used antibiotics (in percentage)

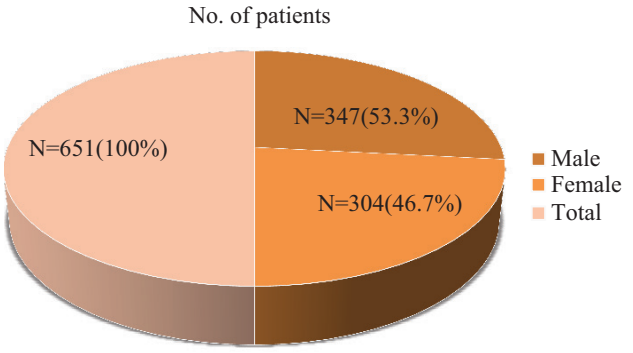

Figure-1: Distribution of patients by gender

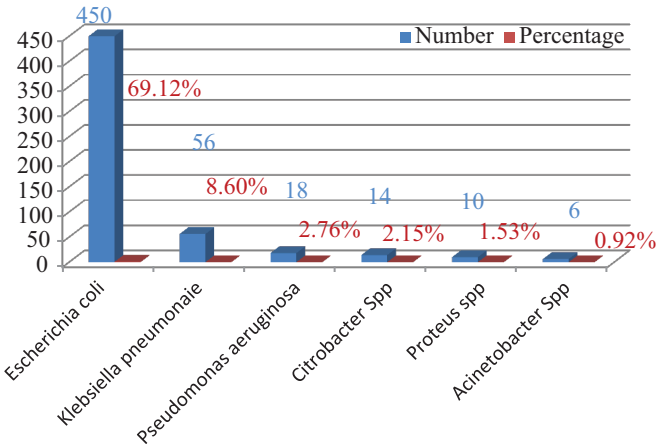

Figure-2: Distribution of Gram –negative bacteria

From table 2 we observed that males had higher prevalence of bacteriuria compared to females in all the age groups. There were only two young patients above 18 and below 20 years age group.

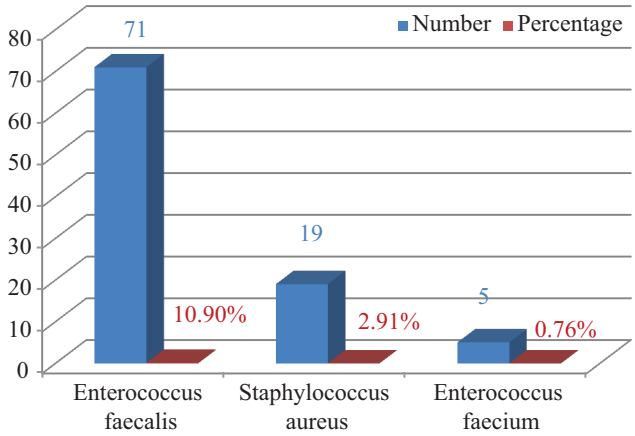

Figure-3: Distribution of Gram-positive bacteria

As shown in table 3 and 4, good susceptibility was seen to amikacin by E.coli (96%) K.pneumoniae (81%), P.aeruginosa (72%) and Proteus spp. (91%). Linezolid and Vancomycin showed 100% activity against Enterococci and Staphylococcus aureus. Amongst fluoroquinolones, ciprofloxacin has low activity (40%) against Pseudomonas while levofloxacin stands good (100%) for Citrobacter and lower (60%) for Proteus. We saw poor response to norfloxacin against most bacteria grown except Proteus spp. which has good (82%). From amongst the cephalosporins, cephalexin, cefixime and ceftazidime are not good options for most bacteria but Cefoperazone-sulbactam stands good (>65%) against E.coli, P.aeruginosa and Proteus spp. Ceftazidime shows 68% and 89% sensitivity against P.aeruginosa and Proteus spp.respectively. ceftriaxone which is very commonly used injectable to start empirically in inpatient setup is not a good choice due to very low sensitivity in E.coli (22%) and

K.pneumoniae (35%). High level Ampicillin resistant is seen in both Gram-positive and negative bacteria.

If we look at E.coli –ESBL (71.42%) and Klebsiella pneumoniae - ESBL(56.90%), best options were carbapenems, colistin, tigecycline, amikacin, piperacillin-tazobactam and nitrofurantoin. There were carbapenemase producers also like in E.coli (4-5%) and Klebsiella (20%). Cotrimoxazole and amoxicillin-clavulanic acid have no good response (<60% sensitivity) to any of these bacteria. Linezolid is good for both the species of Enterococcus (100% susceptible). Nitrofurantoin sensitivity was good in Staph. aureus (96%), E. faecalis (82%) and E.coli (81%). Best response giving carbapenems against K.pneumonaie and P.aeruginosa was by imipenem (83% and 78% respectively) while against Proteus spp.meropenem has good activity (88%). Acinetobacter spp. Which was seen in 6 patients has poor sensitivity to amikacin (20%), imipenem (40%) and colistin (50%) but good sensitivity to cotrimoxazole (80%). We found 3 MRSA out of 19 isolates.

High-grade resistance was seen for many commonly used antibiotics like ampicillin, cotrimoxazole, cefixime, nalidixic acid and amoxicillin/clavulanate (table: 5).

DISCUSSION

In this study, we were supposed to see the prevalence of various bacteria in diabetics with proven UTI and antimicrobial susceptibility patterns. We found that Diabetic males are outnumbering females in terms of prevalence of UTI. This is in contrast to an Indian study[7], a Nigerian study[8] but in favor of study in Sudan[9] and east India.[10]

Most frequently patients were in the affected age group from 51 to 60 years(30.26%).This was Similar to a study by R. Simkhada.[11] but dissimilar to a study in Kuwait by May Sewify et al[12] and in Nepal by PK Jha et al.[13]

Like in almost all the studies from international or national locations[14,15], the most common bacterial isolate was E.coli(59.12%). It was similar to a case-control study done in New Delhi[16] which showed E.coli as most common bacteria in UTI (64.3%). In a study from Nepal[11], it was 52.38%. While in Romanian study[17] it was 70.4%.

In our study, we found Klebsiella pneumoniae (8.60%) and Pseudomonas aeruginosa (2.76%) as next common isolate amongst Gram-negative while Enterococcus faecalis (10.90%) and Staphylococcus aureus (2.91%) are most common Gram-positive isolates. In a study done in Turkey, K.pneumoniae and P.aeruginosa were 9.1% and 3% respectively[18] which was in the same line as ours. Overall in our study second most common isolate is E.faecalis (10.90%) after E.coli (59.12%) which is on the same trend as seen by N.Chatterjee et al.[10] In contrast, second most common isolate in the above mentioned Turkish study was CoNS (24.2%). If we see a retrospective study in Nepal, there was a similar trend of the frequency of Enterococcus spp.(13.84%), K.pneumoniae (8.3%) and S.aureus (7.11%). We also found Citrobacter spp, Proteus spp, and Acinetobacter spp though less frequently.

In this study, seeing antibiotic resistance we found that ampicillin and cefixime are not good options as high-level resistance is seen for commonly grown isolates of E.coli and K.pneumonaie. Citrobacter spp.is 100% resistant to nalidixic acid and cotrimoxazole and equally resistant to amikacin and gentamycin i.e 50%.There is high resistance to gentamycin, ampicillin and amoxicillin-clavulanic acid against Gram-positive organisms especially Enterococcus spp.Fluoroquinolones and cephalosporins are resistant to most of the Gram-negative isolates. Cephalosporin resistance was similarly seen in Nepal[13] and Bangladesh.[19] Good options for them are amikacin, piperacillin/tazobactam, and cefoperazone/sulbactam. Our study has a high prevalence of ESBL in E.coli (71.42%) and K.pneumonaie (56.90%) which needs to be managed with carbapenems as first-line drugs and if not feasible, second-line drugs should be piperacillin/tazobactam or cefoperazone /sulbactam. Though ESBL organisms are in similar frequency as shown in many other studies it was lower compared to a study from Kerala[20] which showed very high-level ESBL growth (approximately 90%) and from Manipal[21] by M.Srinivas et al which showed it 78.6%. Though amikacin is a cost-effective injectable for both non-ESBL and ESBL isolates, its renal toxicity restricts its widespread use.

In our findings, nitrofurantoin had good activity against E.coli and Gram-positive isolates similar to as seen by PK Jha et al[13] and Citrobacter spp. had approximately 50% susceptibility to most of the tested antibiotics but 100% for levofloxacin.

If we see options with antipseudomonal activity in our set up and susceptibility pattern, best antibiotics are Piperacillin / tazobactam and colistin with equal efficacy (82%) followed by imipenem and amikacin (78% and 72% respectively). Here ciprofloxacin has low efficacy (40%) and cotrimoxazole was 100% resistant to P.aeruginosa. Similar findings were seen by M.Srinivas et al[21] with 82% susceptibility to Piperacillin/ tazobactam and 68.2% to cefoperazone/ sulbactam but a very good response to amikacin (93.8%). Meropenem activity against P.aeruginosa in our study was only 50% while M.Srinivas et al[21] found it 87.5%.

In our findings, Gram-positive isolates have shown 100% sensitivity to vancomycin while an article from south India shows 81% and 94% susceptibility respectively by Enterococcus and Staphylococcus.[22] We have less nephrotoxic linezolid with 100% sensitivity against Gram-positive isolates. In an Indian study, Enterococcus faecalis was the most commonly isolated Gram-positive organism with 3.2 percent resistance to vancomycin.[23] We found Acinetobacter spp.in 6 cases showing multidrug-resistant with very low sensitivity even to carbapenems and colistin.

Multi-drug resistant bacteria commonly arise due to the prolonged use of cephalosporins and other antibiotics, particularly their use as prophylaxis treatment, inadequate dosage or inaccurate frequency of administration. This also produces class and cross-resistance. Pseudomonas spp. has become a big challenge to treat. Plasmid-mediated resistance due to the usage of broad-spectrum antibiotics has been considered as one of the factors associated with this

phenomenon.[24]

Amikacin which is easily available and cost-effective remains a good choice for most of the uropathogens if renal status allows and there is a facility to follow renal function test regularly. There is good sensitivity even in current era due to its ability to evade attacks by all antibiotic-inactivating enzymes that are responsible for antibiotic resistance in bacteria, except for aminoacetyltransferase and nucleotidyltransferase.[25] This is accomplished by the L-hydroxyaminobuteroyl amide (L-HABA) moiety attached to N-1 (compare to kanamycin, which simply has a hydrogen), which blocks the access and decreases the affinity of aminoglycoside-inactivating enzymes.[26,27] Amikacin ends up with only one site where these enzymes can attack, while gentamicin and tobramycin have six.

Enterococci are getting commoner in many culture samples especially from urine due to inappropriate and intensive use of broad-spectrum antibiotics.[28] Same are the reasons in cases of other microorganisms. Poultry farms and human foods of animal origin are also contributing significantly to the increasing multidrug resistance amongst isolates.

These are the reasons, why to have knowledge of the pattern of local microbial prevalence and antimicrobial susceptibility to start the most appropriate empirical drug depending on clinical and laboratory profile of patients.

CONCLUSION

Most commonly affected age group with UTI amongst diabetics was from 51 to 60 years where males exceeded females in prevalence. We found E.coli, E.faecalis, and K.pneumoniae as the most commonly grown organisms in descending order. Most of the Gram-negative isolates were susceptible to amikacin, piperacillin/tazobactam, cefoperazone/sulbactam and carbapenems, while Gram-positive cocci were mostly sensitive to nitrofurantoin, linezolid, and vancomycin. Ampicillin, cephalosporins (with the exception of sulbactam combination), cotrimoxazole, and fluoroquinolones are not good choices to start on an empirical basis.

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