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Original Article

A Retrospective Study on Antibiotic Microbial Sensitivity in Type II Diabetes Mellitus Patients with Urinary Tract Infections

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ABSTRACT

Objectives: The present study was aimed to observe the antibiotic microbial sensitivity patterns in type II Diabetes Mellitus patients with Urinary tract infections. **Methods :** A retrospective study was conducted in the Department of Endocrinology and Metabolism at Sri Venkateswara Institute of Medical Sciences, Tirupati during a period of 6 months (July to December 2019). 120 culture urine samples were taken for the study as per inclusion and exclusion criteria. All the data were collected, recorded, tabulated and analysed using Microsoft Excel worksheet (Microsoft Corp, Redmond, WA). Continuous and categorical data were expressed in terms of mean ± Standard deviation (SD) and percentage respectively. Antibiotic microbial sensitivity was expressed in terms of percentage. **Results:** Out of the total of 120 subjects, the most commonly affected age group was 51-60 years (33.33%). Here females (55%) dominated males (45%) in number. Most commonly isolated Gram-negative organisms were *Escherichia coli* (35%) and *Klebsiella pneumoniae* (15.8%) whereas Gram-positive organisms were *Enterococcus faecalis* (17.6%) and *Staphylococcus aureus* (9.16%). Most of the gram-negative bacteria were having a good sensitivity to amikacin (56.75%) and gram-positive bacteria were mostly sensitive to nitrofurantoin (46%). **Conclusion:** *Escherichia coli* was the major isolated micro-organism followed by *Enterococcus* and *Klebsiella*. Amikacin showed more sensitivity towards gram-negative organisms, whereas Nitrofurantoin showed more sensitivity towards gram-positive organisms. Most uropathogens isolated in Type II Diabetes mellitus were sensitive to Amikacin. This study enlists certain antibiotics which can be used as first-line agents by the physician while awaiting for urine microscopic culture sensitivity results.

Key words: Diabetes Mellitus, Retrospective Study, Urinary Tract Infection, Antibiotic Sensitivity, Gram-Positive Organisms, Gram-Negative Organisms.

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INTRODUCTION

Diabetes mellitus (DM) is a worldwide health problem with dramatically raised prevalence over the past two decades and expected prevalence of 593 million by 2035.[1] Over 425 million people are currently living with DM. Based on the report of the International Diabetes Federation (IDF), China has the largest number of diabetic cases (11.43cr.), followed by India (7.29cr.) in 2017. The prevalence of type II diabetes mellitus in number of adults has increased almost four times in less than four decades from 108 million in 1980 to 422 million. Diabetes mellitus is a group of metabolic diseases characterised by hyperglycaemia resulting from defects in insulin secretion, insulin action or both. The chronic hyperglycaemia of diabetes is associated with long term damage, dysfunction and failure of different organs especially the eyes, kidneys, nerves, heart and blood vessels. Diabetes mellitus is a major predisposing factor for the development of Urinary Tract Infection (UTI) as it modifies the host defence mechanism, Immunologic impairments, such as defective in migration and phagocytic properties of polymorph nuclear leucocytes were occurred in diabetes mellitus patients. Urinary tract infection (UTI) is the most common infection among patients with DM and is responsible for considerable morbidity particularly if it is unrecognised or untreated. Patients with type II DM are at increased risk of urinary tract infection being the most common frequent site.[2,3] Bacteriuria is more common in diabetics than in non-diabetics due to a combination of host and local risk factors.

The patients with urinary tract infections varies from asymptomatic Bacteriuria to lower UTI (cystitis), pyelonephritis and severe urosepsis. The complications of Urinary tract infections such as emphysematous cystitis and pyelonephritis, renal abscesses and renal papillary necrosis were all encountered more frequently in type II diabetes mellitus patients than in the general population. Type II DM is not only the risk factor for community-acquired UTI but also for health-care associated UTI, catheter associated UTI, post renal transplant-recurrent UTI. Type II DM is also a risk factor for fungal UTI, mostly caused by Candida. The increased risk of UTI among diabetic patients, coupled with the increase in the incidence of type II DM worldwide.[4]

The diagnosis of urinary tract infections should be suspected in any diabetic patient with symptoms consistent with urinary tract infections. These symptoms are frequency, urgency, dysuria and supra-pubic pain for lower urinary tract infections and costo-vertebral angle pain/tenderness, fever and chills, with or without lower urinary tract symptoms for upper urinary tract infections.[5] Diabetic patients are prone to have a more severe presentation of urinary tract infections though some patients with diabetic neuropathy may have altered clinical signs. Once the diagnosis of urinary tract infections is suspected, a midstream urine specimen should be examined for the presence of leukocytes, as pyuria is present in almost all cases of urinary tract infections.[6]

Escherichia coli, *Klebsiella pneumoniae*, *Enterobacter aerogenes*, *Proteus mirabilis*, *Enterococcus faecalis*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* were the most common etiological agents causing UTI.[7,8] The current study aims to assess the causative organisms and the antibiotic sensitivity patterns in type II diabetes mellitus with UTI.

MATERIALS AND METHODS

Study design and Ethical consideration

A Retrospective Study conducted on Antibiotic Microbial Sensitivity in Type II Diabetes Mellitus Patients with Urinary Tract Infections in the Department of Endocrinology and Metabolism at Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India in 2019. The ethical clearance was obtained from the Institutional Ethics Committee with approved IEC NO. 920 from Sri Venkateswara Institute of Medical Sciences. The study was performed as per ICH GCP Guidelines.

Selection criteria

Patients who were diagnosed as type II Diabetes Mellitus with Urinary Tract Infections and whose pus cells count >8 hpf (high power field) were taken as inclusion criteria. Urinary tract infections in non-diabetic patients, Pregnant and Lactation women were excluded.

Sample size

One hundred and twenty patients who were diagnosed as type II Diabetes mellitus with UTI were taken as sample size and examined as per study guidelines.

Method of Collection of Data

The patient case reports were taken from the medical records department based on inclusion and exclusion criteria. Data regarding isolated organisms were collected. All the necessary parameters like baseline characteristics (age, gender, duration of DM, systolic Blood pressure, Diastolic blood pressure, HbA_{1c}, duration of fever, duration of hospital stay) and clinical manifestations (fever, vomiting, dysuria, abdominal pain, lower backache, frequent urination) were recorded .we also collected all the necessary information to evaluate the microbial sensitivity with respect to the antibiotics.

Statistical analysis

Data was recorded on a predesigned proforma and managed using Microsoft Excel worksheet (Microsoft Corp, Redmond, WA). Data entered were double-checked for any possible errors. Continuous data were expressed in terms of mean ± Standard deviation (SD). Categorical data were expressed in terms of percentage. Antibiotic microbial sensitivity was expressed in terms of percentage. Data were analysed according to the objectives of the study.

RESULTS

This study was attempted to evaluate the isolated organisms, antibiotic microbial sensitivity pattern in type II diabetes mellitus patients with urinary tract infections. The study included 120 patients who came to the endocrinology department.

Distribution of data based on age group

As per study among the 120 subjects, majority of affected patients were in the age group of range 51-60 years (33.3%) followed by the age group of 61-70(26.66%) and next 41-50 (25%) (Table 1).

Table 1: Distribution of study population based on age group and gender.

Age Group (years)	Males	Females	Total no of patients N=120	Percentage (%)
21-30	1	1	2	1.6
31-40	1	5	6	5
41-50	20	10	30	25
51-60	14	26	40	33.3
61-70	12	20	32	26.66
71-80	6	4	10	8.33
Total	**54**	**66**	**120**	**100**

Distribution of data based on gender

Among the 120 patients involved in the study 54 (45%) were males and 66 (55%) were females (Figure 1).

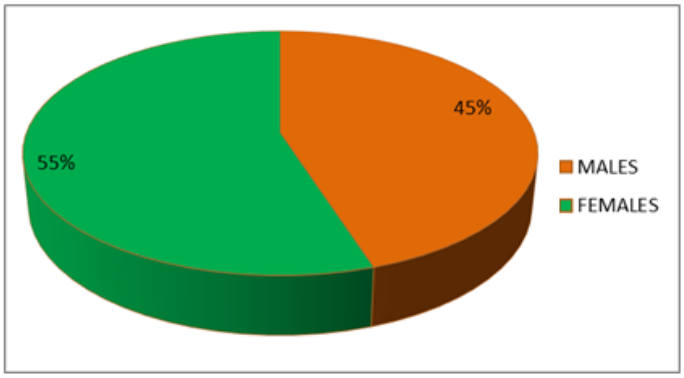

Figure 1: Sex distribution of the study population.

Baseline Characteristics of Enrolled Subjects

Among the 120 patients involved, the affected mean age group of the study population was 55.60±4.7 years. Majority of the study subjects were females. Mean HbA_{1c} was 10.42±2.12 %. Duration of DM among these patients was 10.49±4.7 years. Mean systolic BP was 121.19±22.8 mm of Hg and diastolic BP was 80.78±10.45 mm of Hg, Duration of fever was 2.1±1.67 days and mean duration of hospital stay among these patients was 9.41±4.9 days after starting antibiotic therapy (Table 2).

Table 2: Baseline characteristics of enrolled subjects.

Parameters	Values
Age (Mean±SD)	55.60±11.46 years
Sex (Male/Female)	54/66
Duration of DM (Mean±SD)	10.49±4.7 years
Systolic BP (Mean±sd)	121.19±22.8 mmHg
Diastolic BP (Mean±sd)	80.78±10.45 mmHg
Hba_{1c} (%) (Mean±SD)	10.40±2.12 %
Duration of fever (Mean±SD)	2.1±1.67 days
Duration of hospital stay (Mean±SD)	9.41±4.9 days

Clinical Manifestations

Fever (60.83%) was the most commonly observed symptom in the diabetes mellitus patients with urinary tract infections followed by vomiting (44.16%), Dysuria (42%), lower backache (19%) and abdominal pain (29%) (Figure 2).

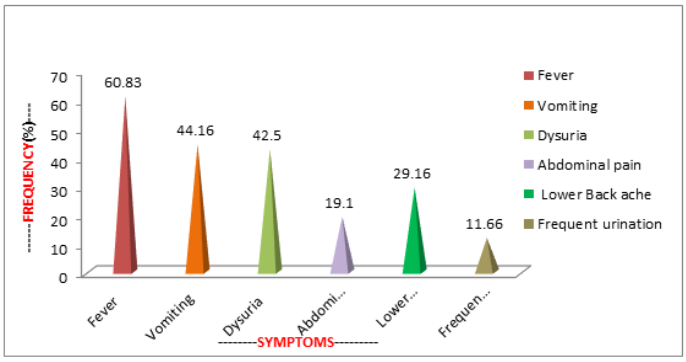

Figure 2: Frequency of Clinical Manifestations in type II DM patients with UTI.

ISOLATED ORGANISMS FROM THE SAMPLE SIZE

Among the organisms isolated, *Escherichia coli* (35%) was the most common organism isolated followed by *Enterococcus faecalis* (17.6%), *Klebsiella pneumoniae* (15.8%), *Proteus mirabilis* (10.85%), *Staphylococcus aureus* (9.16%), Citrobacter (5.84%) and 5.84% of the study population did not show any bacterial growth. Among Gram-negative organisms isolated, *Escherichia coli* was the most commonly isolated organism followed by *Klebsiella pneumoniae*, *Proteus mirabilis*, Citrobacter. While Gram-positive organisms isolated include *Enterococcus faecalis* followed by *Staphylococcus aureus* (Figure 3).

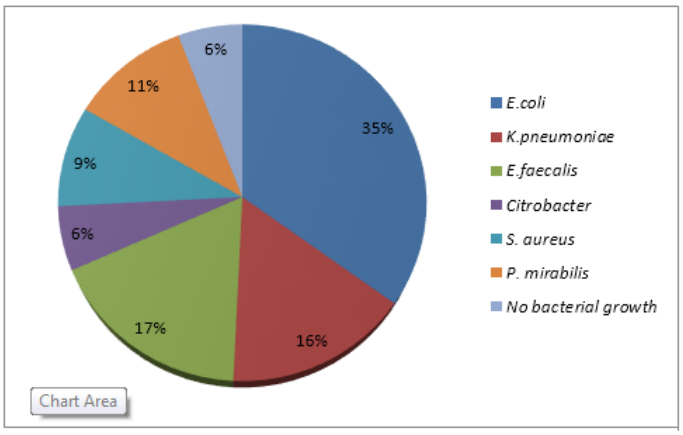

Figure 3: Isolated Organisms in type II DM with UTI patients.

Data Evaluation of Antibiotic Sensitivity towards Micro-Organisms

Data analysis showed that gram-negative organisms like *Escherichia coli* were highly sensitive to amikacin (90%) followed by cefoperazone/sulbactam (79%). *Klebsiella pneumoniae* was sensitive to amoxicillin/clavulanic acid (68%) followed by cotrimoxazole (63%). Citrobacter was sensitive to amikacin (71%) followed by piperacillin/tazobactam (57%), imipenem (57%), gentamicin (57%) and ciprofloxacin (57%). *Proteus mirabilis* was sensitive to gentamicin (53%) followed by cefoperazone/sulbactam (46%). Whereas gram-positive organisms like *Enterococcus faecalis* were sensitive to amoxicillin/clavulanic acid (76%) followed by nitrofurantoin (52%) and *Staphylococcus aureus* was sensitive to cotrimoxazole (45%) followed by nitrofurantoin (40%). (Table 3). Gram-negative organisms were sensitive to Amikacin (56.75%), Cefoperazone/sulbactam (53.5%) and Piperacillin/tazobactam (46%) (Figure 4) .While Gram-positive isolates were sensitive to Nitrofurantoin (46%) followed by Amoxicillin/clavulanic acid (42.5%) and Piperacillin/tazobactam (39.5%) (Figure 5). Most uropathogens isolated in this study were sensitive to Amikacin (47.1%) followed by Cefoperazone/sulbactam (46.5%), Nitrofurantoin (44%) and Piperacillin/tazobactam (43.8%) (Figure 6).

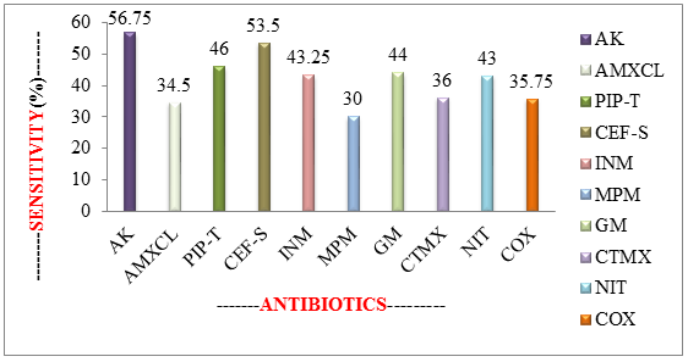

Figure 4: Overall Antibiotic sensitivity for Gram-negative Bacteria.
Note:AK-Amikacin, AMXCL-Amoxycillin/clavulanicacid, PIP-T—Piperacillin/tazobactam, CEFS-Cefoperazone/sulbactam, INM-Imepenem, MPM-Meropenem, GM-Gentamicin, CTMX-Co-trimoxazole, NIT- Nitrofurantoin, COX-Ciprofloxacin.

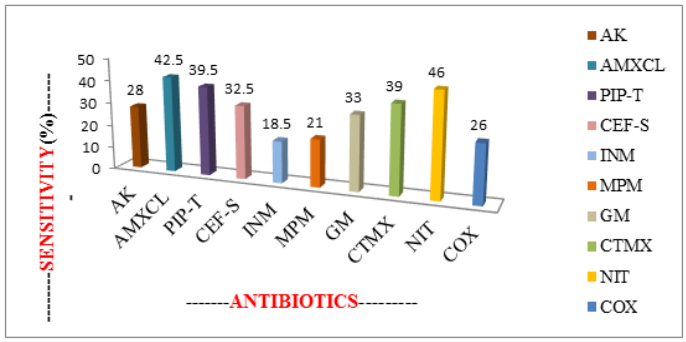

Figure 5: Overall Antibiotic sensitivity for Gram-positive Bacteria.
Note: AK-Amikacin, AMXCL-Amoxycillin/clavulanicacid, PIP-T—Piperacillin/tazobactam, CEFS-Cefoperazone/sulbactam, INM-Imepenem, MPM-Meropenem, GM-Gentamicin, CTMX-Co-trimoxazole, NIT- Nitrofurantoin, COX-Ciprofloxacin.

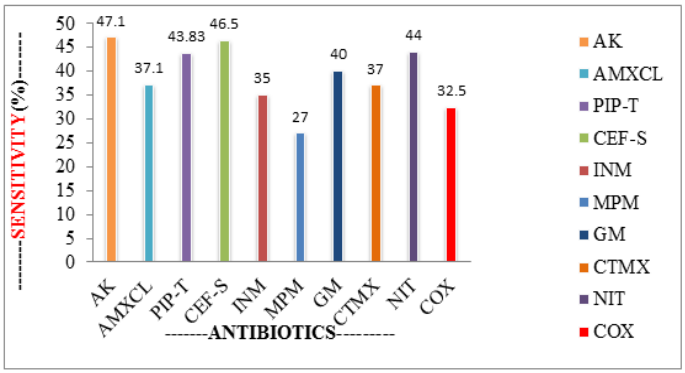

Figure 6: Overall sensitivity of commonly used Antibiotics.
Note: AK-Amikacin, AMXCL-Amoxycillin/clavulanicacid, PIP-T—Piperacillin/tazobactam, CEFS-Cefoperazone/sulbactam, INM-Imepenem, MPM-Meropenem, GM-Gentamicin, CTMX-Co-trimoxazole, NIT- Nitrofurantoin, COX-Ciprofloxacin.

Table 3: Antibiotic Sensitivity towards Gram negative and Gram positive Bacteria.

Antibiotics	Sensitivity (%)					
	Gram-negative bacteria				Gram-positive bacteria	
	E. coli	*K. pneumoniae*	Citrobacter	*P. mirabilis*	*E. faecalis*	*S. aureus*
AK	90	36	71	30	38	18
AMXCL	19	68	28	23	76	9
PIP-T	74	53	57	0	43	36
CEF-S	79	47	42	46	38	27
INM	43	42	57	31	10	27
MPM	43	11	43	23	24	18
GM	45	21	57	53	48	18
CTMX	29	63	29	23	33	45
NIT	67	50	40	15	52	40
COX	29	42	57	15	43	9

Note: AK-Amikacin, AMXCL-Amoxycillin/clavulanicacid, PIP-T—Piperacillin/tazobactam, CEFS-Cefoperazone/sulbactam, INM-Imepenem, MPM-Meropenem, GM-Gentamicin, CTMX-Co-trimoxazole, NIT- Nitrofurantoin, COX-Ciprofloxacin.

DISCUSSION

In this current study, we studied 120 diabetic patients to know the prevalence of various bacteria in diabetics with proven UTI and antibiotic sensitivity pattern. We found that females outnumbered males in terms of the prevalence of UTI. 51-60 years age group were most commonly affected with UTI among Type II diabetes mellitus patients. This was similar to an Indian study,[9] a Nigerian study[10] but it was different from a study in Sudan[11] and East India.[12]

Most frequently affected patients belong to the age group 51 – 60 years (33.3%). This was similar to a study by R Simkhada[13] but the study was different in Kuwait by May Sewify *et al.*[14] and in Nepal by PK Jha *et al.*[15] Like in almost all the studies from International or National locations[16,17] the most common isolate was *E. coli* (35%). It was similar to a case-controlled study done in New Delhi[18] which showed *E. coli* was the most common bacteria in UTI (64.3%) whereas in a study from Nepal,[13] it was 52.38% while in a Romania study[19] it was 70.4%.

In our study, we found *K. pneumoniae* (15.8%), *Proteus mirabilis* (10.85%) and Citrobacter (5.84%) were the next common isolates amongst Gram-negative after *E. coli*. While *E. faecalis* (17.6%) and *S. aureus* (9.16%) were the most common Gram-positive isolates. *E. coli* was the most common isolate followed by *E. faecalis* which is same as seen in the study by Chatterjee *et al.*[14] If we observe the retrospective study in Nepal, there was a similar trend of the frequency of *Enterococcus* species (13.84%), *K. pneumoniae* (8.3%) and *S. aureus* (7.11%). We also found Citrobacter species, Proteus species less frequently.

Most Gram-negative organisms were sensitive to Amikacin (56.75%) followed by Cefoperazone-sulbactam (53.5%) and Piperacillin-tazobactam (46%).

Most Gram-positive organisms were sensitive to Nitrofurantoin (46%) followed by Amoxicillin/clavulanic acid (42.5%) and Piperacillin/tazobactam (39.5%). In our study, Nitrofurantoin had good activity against E.coli and Gram-positive isolates similar to as seen by PK Jha *et al.*[12]Most uropathogens isolated in Type II DM were sensitive to Amikacin (47.1%) followed by Cefoperazone/sulbactam (46.5%), Nitrofurantoin (44%) and Piperacillin/tazobactam (43.83%).

CONCLUSION

In the current study it was concluded that *E. coli*, *E. faecalis* and *K. pneumoniae* were the most commonly isolated organisms in descending order and Citrobacter, *Proteus mirabilis* were less frequently isolated organisms. Most of the Gram-negative isolates were sensitive to Amikacin, Cefoperazone/sulbactam, Piperacillin/tazobactam and Nitrofurantoin, while Gram-positive isolates were sensitive to Nitrofurantoin followed by Amoxicillin/clavulanic acid and Piperacillin/tazobactam. Most uropathogens isolated in this study were sensitive to Amikacin followed by Cefoperazone/sulbactam, Nitrofurantoin and Piperacillin/tazobactam were the good choices of antibiotics to start on empirical basis whereas Amikacin is a cost-effective injectable drug but its renal toxicity restricts its wide spread use.

This study recommended that these drugs should be the first-line drugs prescribed by clinicians while awaiting urine Microscopic culture sensitivity (M/C/S) results in patients with UTI. Antibiotic sensitivity pattern of UTI pathogens should be periodically assessed to reduce the unnecessary use of antibiotics.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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