Bacterial Profile and Antibiogram of Uropathogens from Diabetic Patients in a Tertiary Care Hospital.

Tanaya Pravin Pawar[1] , Satyajeet K. Pawar*[2] , Satish R. Patil [3] , Prajakta S. Pawar[4]

Tanaya P. Pawar
PG (MSC Med. Microbiology), Krishna Institute of Medical Sciences, Karad.
Krishna Vishwa Vidyapeeth "Deemed To Be University", Karad., Maharashtra, India
Satyajeet K. Pawar* ,
Associate Professor, Department of Microbiology, Krishna Institute of Medical Sciences, Karad, Krishna Vishwa Vidyapeeth "Deemed To Be University", Karad., Maharashtra, India
Satish R. Patil,
Prof. & Head, Department of Microbiology, Krishna Institute of Medical Sciences, Karad.
Krishna Vishwa Vidyapeeth "Deemed To Be University", Karad., Maharashtra, India
Prajakta S. Pawar ,
PG (MSC Med. Microbiology)
Krishna Institute of Medical Sciences, Karad.
Krishna Vishwa Vidyapeeth "Deemed To Be University", Karad., Maharashtra, India

***Corresponding Author's Mailing Address:**
Dr. Satyajeet K. Pawar,
Associate Professor
Dept. of Microbiology,
Krishna Institute of Medical Sciences, Malkapur,
Karad, Maharashtra. India.
Pin. 415539.
Email: drskpawar@gmail.com
Phone Number: 9423034094

ABSTRACT

Background:

Diabetes mellitus is one of the most challenging health problems of the 21st century and is a leading cause of death in developed countries. The treatment of urinary tract infection (UTI) in diabetics is defendant on the identification of the bacteria which is responsible for the cause and

also the effective antibiotics against them. Treatment options for UTI in diabetes may be similar to as in non-diabetics but have to be initiated timely to prevent further complications and may take a longer time for cure. With increasing newer mechanism of resistance to various antimicrobials, prior knowledge of these causative agent in a particular hospital is very important. The study aimed to identify the bacteria responsible for the UTI in diabetic patients and also the antimicrobial susceptibility pattern.

Objective:

To find the prevalence of various Gram negative uropathogens in diabetic patients and antimicrobial resistance pattern among the isolated bacterial strains.

Method:

The urine sample were collected. Identification was done by Gram staining and various biochemical reactions after preparation, cultivation and isolation of urine sample. Antimicrobial susceptibility was done by Kirby Bauer disc diffusion method on Muller-Hinton agar plate.

Result:

The overall prevalence of UTI in diabetic mellitus patient was (54.44%) with the male predominance (62.24%) and in female with (37.75%). The UTI in diabetic patient was common in age 41-60 years (44.89%). *E. coli* (42.86%) was the most predominant bacterial isolate followed by *Kl. pneumoniae* (24.49%), *Ps. aeruginosa* (18.37%), *Aci. baumannii* (7.14%), *Kl. oxytoca* (5.10%) and *Pro. mirabilis* (2.04%). The antimicrobial susceptibility tests revealed that fosfomycin, tigecycline and nitrofurantoin showed maximum susceptibility for all urinary tract infection in diabetic patients. The overall prevalence of multidrug resistance (MDR) uropathogens was 88(88.77%).

Conclusion:

The prevalence of UTI and MDR to commonly used antibiotics among diabetic patients is alarming, and thus, isolation of uropathogenic bacteria and antimicrobial susceptibility testing is crucial for the treatment of UTI in persons with diabetes**.**

KEYWORDS: Urinary tract infection, Diabetes mellitus, Enterobacterales, *Acinetobacter*, *Pseudomonas aeruginosa*, AST, MDR

INTRODUCTION:

Diabetes mellitus is one of the most challenging health problems of the 21st century and is a leading cause of death in developed countries. India has an estimated 77 million people with diabetes, which makes it the second most affected country in the world after China.

Diabetes mellitus is commonly known as just Diabetes, is a group of metabolic disorders characterized by a high blood sugar level for a prolonged period of time. Symptoms often include frequent urination, increased thrust and increased appetite. Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced.

Diabetes mellitus has unfavorable effect on genitourinary system and patients suffering from diabetes mellitus are more susceptible to have urinary tract infections with risk of probably

harmful extension of infection to kidneys. Diabetes mellitus has a number of effects on genitourinary system.[1] Patients either with Type 1 DM or Type 2 DM are at increased risk for urinary tract infections. Diabetes causes several abnormalities of the host immune system that may result in higher risk of infections like UTI.[2] Various impairments in the immune system, in addition to poor metabolic control of diabetes, and incomplete bladder emptying due to autonomic neuropathy also contribute in the pathogenesis of urinary tract infections (UTI) in diabetic patients. Predisposing factors for UTI in diabetics include age, metabolic control and also complications like diabetic nephropathy and cystopathy..[3]

Urinary tract infections are one of the most common infections occurring both in community and hospital patients especially in diabetics. It is a frequent cause of morbidity, mortality and major cause of antibiotic resistance.[4] The most common causative agent is *Ecsherichia coli* and other organisms are *Proteus, Klebsiella, Pseudomonas, Candida albicans*.[5] Chronic diabetes mellitus patients can develop complications like nephropathy, renal papillary necrosis and cystopathy which further makes patients prone to repeated UTI.[6] Urinary tract infections can be symptomatic or asymptomatic.[7] Urinary tract infections occur with increased frequency and severity in patient with diabetes mellitus. Urinary tract infections exist when pathogenic organisms are detected in urine, urethra, bladder, kidney with or without symptoms. Both lower urinary tract along with upper are involved in urinary tract infection.[5] To prevent any complications it is very important to have early diagnosis and treatment of UTI in diabetes patients. To institute a rational use of antibiotics for empirical and decisive treatment of urinary tract infections in this susceptible group, a constant surveillance of antimicrobial susceptibility patterns of uropathogens in diabetic patients should be done. This study focused on various Gram negative uropathogens isolated from diabetes patients and their antimicrobial resistance at this tertiary care centre.

METHODOLOGY:

The present study "Study of Gram Negative Uropathogens in Diabetic Patients and their Antimicrobial Resistance at a Tertiary Care Centre" was carried out in the Department of Microbiology, Krishna Institute of Medical sciences, and Krishna Hospital and Medical Research Centre, Karad, District – Satara.

Sample Size:

In the study by Vishal Sharma *et al*.[8] prevalance of various organism was as follows and accordingly sample size calculated using the formula and is as follows.

Table No. 1: Table for sample size

Table for sample size		
Name of the organisms	Prevalence of Gram negative uropathogens in the study (%)	**Estimated sample size**
E.coli	49(41.5)	**98**
Klebsiella	17(14.4)	**50**
Proteus	12(10.1)	**36**

Formula: - n = 4pq/L

Where, p = Prevalence (41.5)

q = 100 – Prevalence (100 – 41.5 = 58.5)

L = Precision (10)

Therefore, Sample size = $4\times41.5\times58.05/10^{2}$

= 9711/100

= 97.11 i.e. **98**

So, in the present study minimum isolates of Gram-negative pathogens were **98**.

Inclusion Criteria:

Diabetic patients presenting with clinical features of urinary tract infections. Age group – 18 Year onwards. Sex - Both male and female and IPD patients.

Specimen Collection:

The sample was collected in sterile leak proof universal container. After giving proper instructions, midstream urine sample was collected and processed in the laboratory within 2 hours of collection.

Total 180 urine specimens from diabetic mellitus patients were screened for uropathogens. 98 isolates of Gram negative uropathogens were studied further during this period.

Processing of Sample:

Gram Stain:

A loopful of urine was taken on a clean, sterile glass slide, smear prepared and Gram stained. It was air dried and observed under oil immersion lens for the presence of bacteria or candida. Presence of one microorganism per oil immersion field indicates bacterial count of $>10^{5}$ CFU/ml of urine. [11,12]

Microscopy – The stained smear was microscopically examined under oil immersion lens 100X for the presence of Gram-negative bacilli and Gram-negative cocci.

Urine Culture:

The specimens were cultured by semi-quantitative method using MacConkey Agar, Cystine Lactose Electrolyte Deficient (CLED) agar and blood agar as culture medium. The plate was incubated at 37^0C for 24 hrs.

Specimen with more than 10^5 CFU/ml were considered as positive sample.

Biochemical Characterization:

This are still being used for species identification of isolated bacteria from clinical samples. All the biochemical tests were performed according to the standard operating procedure as mentioned in Mackie & McCartney practical medical microbiology 14th edition.[9]

ANTIMICROBIAL SUSCEPTIBILITY TESTING:

Antimicrobial susceptibility testing of isolates was represented by using Kirby-Bauer disc diffusion method on Mueller Hinton agar plate as suggested by Clinical and Laboratory Standard Institute (CLSI 2021)[10] with 0.5 MacFarland standard turbidity of the inoculum. The growth were inoculated into broth medium by selecting 4-5 colonies of same morphology from an agar culture plate and incubated for 3-5 hours to achieve turbid suspension.

Inoculum were done on Mueller Hinton agar plate by using submerged swab of bacterial suspension. By using swab, surface of the plate were lawned in three directions to distribute inoculums and evenly. Antibiotic discs were applied using a sterile forceps within 15 minutes of inoculation.

Then the plates were incubated at 37^0C for 24 hrs after which, by using zone measuring scale inhibition zone were measured and interpreted as per the CLSI standards.

OBSERVATION AND RESULTS:

Over a period of 1 year, 98 isolates of Gram negative uropathogens obtained from patients admitted in various medical, surgical and Intensive care unit were further processed in Department of Microbiology, Krishna Institute of Medical Sciences "Deemed to be University," Karad.

TABLE No. 2 Age, Sex Wise Distribution of Uropathogens

Age	Female (%)	Male (%)	Total (%)
21 – 40	7(7.14)	6(6.12)	13(13.26)
41 – 60	14(14.28)	30(30.61)	44(44.89)
61 – 80	13(13.26)	23(23.46)	36(36.73)

81 – 100	3(3.06)	2(2.04)	5(5.10)
Total	**37(37.75)**	**61(62.25)**	**98(100)**

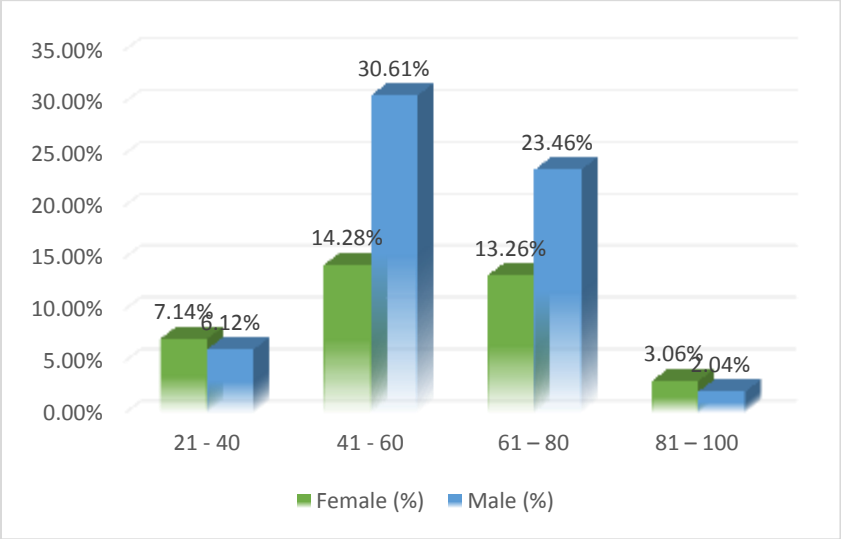

Fig. 1 Age, Sex Wise Distribution of Uropathogens

Maximum isolates were from 41-60 age group 44(44.89%) followed by 61-80 age group 36(36.73%). Least were from 81-100 age group 5(5.10%).

Maximum males were from 41-60 age group 30(30.61%) followed by 61-80 age group 23(23.46%). Least were from 81-100 age group 2(2.04%).

Maximum females were from 41-60 age group 14(14.28%) followed by 61-80 age group 13(13.26%). Least were from 81-100 age group 3(3.06%). (Fig. 1)

TABLE 3 . Distribution of Uropathogens Among Urine Specimen

Bacteria	**Number**	**Percentage (%)**
E. coli	42	42.86
Kl. pneumoniae	24	24.49
Kl. oxytoca	5	5.10
Ps. aeruginosa	18	18.37
Aci. baumannii	7	7.14
Pro. mirabilis	2	2.04
Total	**98**	**100**

Antibiotics	***Escherichia coli***		***Klebsiella spp***		***Pseudomonas aeruginosa***		***Acinetobacter baumannii***		***Proteus mirabilis***	
	S (%)	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**	**S (%)**	**R (%)**
Amikacin	30 (71.42)	12 (28.57)	17 (58.62)	12 (41.37)	6 (33.33)	12 (66.66)	4 (57.14)	3 (42.85)	2 (100)	0 (0)
Gentamicin	23 (54.76)	19 (45.23)	13 (44.82)	16 (55.17)	6 (33.33)	12 (66.66)	2 (28.57)	5 (71.42)	2 (100)	0 (0)
Ciprofloxacin	4 (9.52)	38 (90.47)	4 (13.79)	25 (86.20)	2 (11.11)	16 (88.88)	0 (0)	7 (100)	1 (50)	1 (50)
Cefotaxime	5 (11.90)	37 (88.09)	2 (6.89)	27 (93.1)	5 (27.77)	13 (72.22)	0 (0)	7 (100)	2 (100)	0 (0)
Cefoxitin	17 (40.47)	25 (59.52)	4 (13.79)	25 (86.20)	3 (16.66)	15 (83.33)	1 (14.28)	6 (85.71)	0 (0)	2 (100)
Ceftazidime	8 (19.04)	34 (80.95)	1 (3.44)	28 (96.55)	5 (27.77)	13 (72.22)	0 (0)	7 (100)	1 (50)	1 (50)
Piperacillin-tazobactam	16 (38.09)	26 (61.90)	6 (20.68)	23 (79.31)	5 (27.77)	13 (72.22)	2 (28.57)	5 (71.45)	2 (100)	0 (0)
Cefoperazone sulbactam	18 (42.82)	24 (57.14)	8 (27.58)	21 (72.41)	5 (27.77)	13 (72.22)	4 (57.14)	3 (42.85)	2 (100)	0 (0)
Netilmicin	24 (57.14)	18 (42.85)	13 (44.82)	16 (55.17)	4 (22.22)	14 (77.77)	2 (28.57)	5 (71.42)	1 (50)	1 (50)
Imipenem	17 (40.47)	25 (59.52)	5 (17.24)	24 (82.75)	3 (16.66)	15 (83.33)	1 (14.28)	6 (85.71)	0 (0)	2 (100)
Meropenem	23 (54.76)	19 (45.23)	9 (31.03)	20 (68.96)	4 (22.22)	14 (77.77)	2 (28.57)	5 (71.42)	2 (100)	0 (0)

Tigecycline	38 (90.47)	4 (9.52)	22 (75.86)	7 (21.13)	3 (16.66)	15 (83.33)	6 (85.71)	1 (14.28)	2 (100)	0 (0)
Fosfomycin	41 (97.61)	1 (2.38)	23 (79.31)	6 (20.68)	11 (61.11)	7 (38.88)	2 (28.57)	5 (71.42)	2 (100)	0 (0)
Nitrofurantoin	34 (80.95)	8 (19.04)	17 (58.62)	12 (41.37)	12 (66.66)	6 (33.33)	2 (28.57)	5 (71.42)	1 (50)	1 (50)
Nalidixic acid	1 (2.38)	41 (97.61)	3 (10.34)	26 (89.65)	4 (22.22)	14 (77.77)	1 (14.28)	6 (85.71)	1 (50)	1 (50)
Norfloxacin	6 (14.28%)	36 (85.71)	3 (10.34)	26 (89.65)	2 (11.11)	16 (88.88)	1 (14.28)	6 (85.71)	1 (50)	1 (50)

Of the 98 Gram negative organisms isolated, *Escherichia coli* 42(42.86%) was the most common isolate followed by *Klebsiella pneumoniae* 24(24.49%), *Pseudomonas aeruginosa* 18(18.37%), *Acinetobacter baumannii* 7(7.14%). *Klebsiella oxytoca* 5(5.10%), and *Proteus mirabilis* 2(2.04%) were least isolated (Table. 3).

TABLE No. 4 Antimicrobial Profile of Isolated Uropathogens

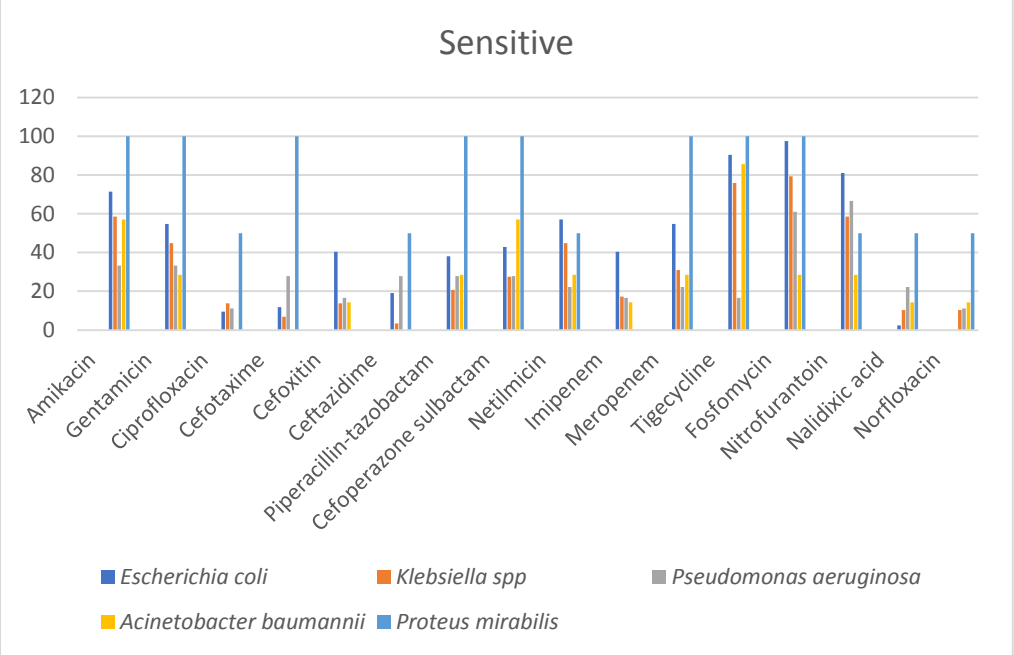

Fig. 2 a] Antibiotics Sensitivity Pattern of Gram-Negative Isolates

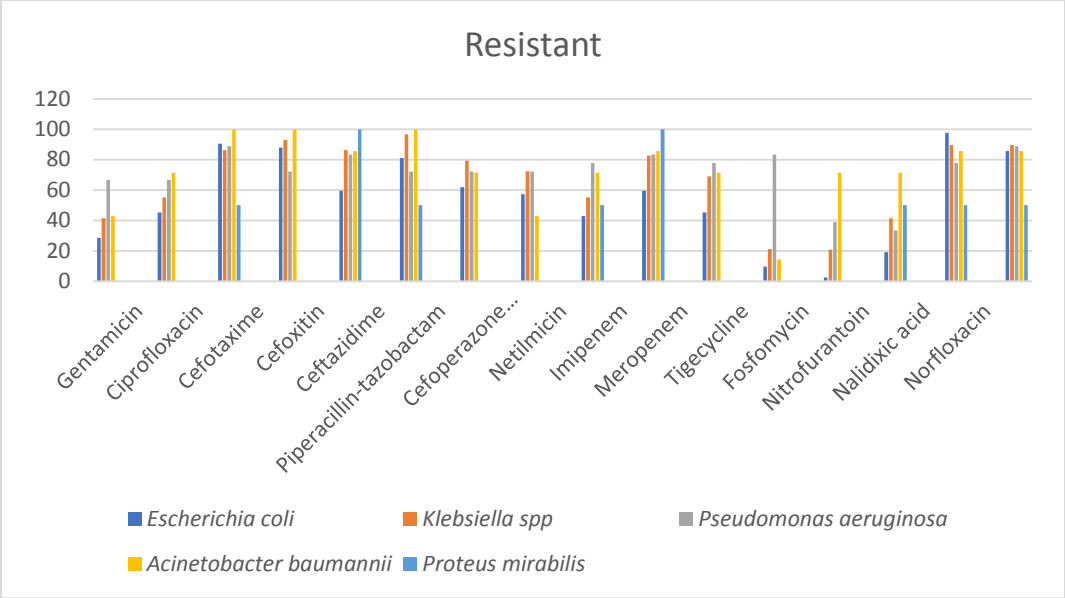

Fig. 2 b] Antibiotics Resistant Pattern of Gram-Negative Isolates

- Among the Uropathogens, *Escherichia coli* was the most common pathogen. *Escherichia coli* showed maximum sensitive to fosfomycin 41(97.61%) followed tigecycline 38(90.47%) and maximum resistance to nalidixic acid 41(97.41%) followed by ciprofloxacin 38(90.47%).
- *Klebsiella species* showed maximum sensitivity to fosfomycin 23(79.31%) followed by tigecycline 22(75.86%) and maximum resistance to ceftazidime 28(96.55%).
- *Pseudomonas aeruginosa* showed maximum sensitivity to nitrofurantoin 12(66.66%) followed by fosfomycin 11(61.11%) and maximum resistance to norfloxacin 16(88.88%) followed by cefoxitin 15(83.33%).
- *Acinetobacter baumannii* showed maximum sensitivity to tigecycline 6(85.71%) followed by amikacin 4(57.14%) and 100% resistance to ceftazidime, cefotaxime and gentamicin.
- *Proteus mirabilis* showed 100% sensitivity to fosfomycin. (Fig. 2 A)

Bacterial isolates	**RG0**	**RG1**	**RG2**	**RG3**	**RG4**	**≥RG5**	**MDR (RG3+RG4+≥RG5) (%)**
E. coli	0	1	7	7	8	19	34(34.69)
Kl. pneumoniae	0	0	2	3	2	17	22(22.44)

Kl. oxytoca	0	0	0	0	1	4	5(5.10)
Ps. aeruginosa	0	0	1	0	1	16	17(17.34)
Aci. Baumannii	0	0	0	0	1	6	7(7.14)
Pro. mirabilis	0	0	0	1	0	1	2(2.04)
Total	0	1	10	11	13	63	**87(88.77)**

Table No. 5 Multidrug Resistance pattern of Gram negative Uropathogens from Diabetic patients

RG0 – Resistant to 0 group of antimicrobials i.e. sensitive to all group of antimicrobials used.
RG1 – Resistant to 1 group of antimicrobials.
RG2 - Resistant to 2 group of antimicrobials.
RG3 - Resistant to 3 group of antimicrobials.
RG4 - Resistant to 4 group of antimicrobials.
≥RG5 - Resistant to greater than or equal to 5 group of antimicrobials.

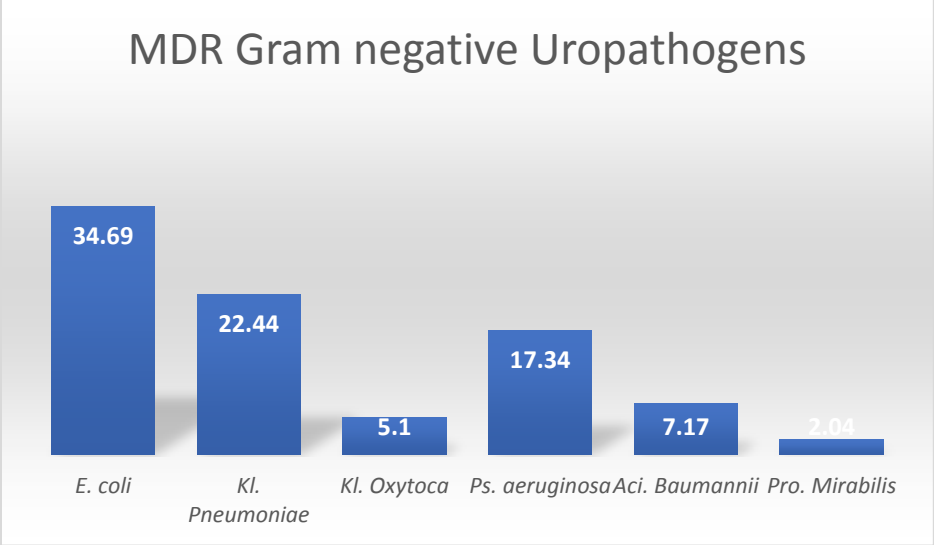

Fig. 3 Multidrug Resistance pattern of Gram negative Uropathogens from Diabetic patients

Of the 98 uropathogens 87(88.77%) isolates were multidrug resistance, among these multidrug resistance isolates *Escherichia coli* contributed 34(34.69%), *Klebsiella pneumoniae* 22(22.44%), *Pseudomonas aeruginosa* 17(17.34%). (Fig. 3)

DISCUSSION:

The present study was done to determine the distribution of various bacteria causing UTI among the diabetics and their antimicrobial susceptibility pattern was studied. A total 180 midstream urine sample from diabetic mellitus patients were screened for uropathogens and were studied further.

The above results represented that the prevalence of UTI among the diabetic patients was 54.44%. In the present study, we observed that the males were in majority 62.24% and

females were 37.75%. Our study was mostly comparable with Sibi *et al.*[13] in which males were affected 68% and females were affected 32%.

The current study delineated that the occurrence of UTI in diabetic patients was observed more frequently in the increasing age group. The significance of UTI in the age group 41-60 years (44.89%) was high as compared to the age group 21-40 years (13.26%), 61-80 years (36.73%) and 81-100 years (5.10%) and this was correlated with the study conducted by N. Bhatiya *et al.*[15] and S. G. Kulkarni *et al.*[16] who also found that the manifestation of UTI was more widespread with increasing age.

The present study revealed that *Escherichia coli* (42.86%) was the commonest organism followed by *Klebsiella pneumoniae* (24.49%), *Pseudomonas aeruginosa* (18.37%), *Acinetobacter baumannii* (7.14%), *Klebsiella oxytoca* (5.10%) and *Proteus mirabilis* (2.04%). This was somewhat similar to the studies conducted by Sabina Fatima *et al*.[17] and B. Natesan *et al.*[7] in which *Escherichia coli* was the predominant organism followed by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa.*

In the present study the bacterial isolates were tested against antimicrobial agents, and their susceptibility pattern was observed.*Escherichia coli* showed maximum sensitivity to fosfomycin (97.41%) followed by tigecycline (90.47%) and nitrofurantoin (80.95%) whereas maximum resistance was to nalidixic acid (97.41%) and ciprofloxacin (90.47%).

Klebsiella species showed maximum sensitive to fosfomycin (79.31%) followed by tigecycline (75.86%) and maximum resistance were to ceftazidime (96.55%) followed by nalidixic acid and norfloxacin (89.65%).*Pseudomonas aeruginosa* showed maximum sensitivity to nitrofurantoin (66.66%) followed by fosfomycin (61.11%) and maximum resistance were to norfloxacin and ciprofloxacin (88.88%) followed by cefoxitin, imipenem and tigecycline (83.33%).

The most effectual antimicrobials against Gram-negative uropathogens in our study were fosfomycin and tigecycline. The sensitivity pattern of fosfomycin was comparable with the study carried out by Shraddha Sharma *et al*.[18] observed 95% sensitivity to fosfomycin whereas Sarita Mohapatra *et al*.[19] showed 100% sensitivity to fosfomycin.

In our study antimicrobial pattern of *Escherichia coli* showed maximum sensitivity to fosfomycin (97.61%) followed by tigecycline (90.47%) and nitrofurantoin (80.95%) which is comparable to Nermin Kamal Saeed *et al*.[20] finding of fosfomycin (99.5%) and Misbahuddin Rafeeq *et al*.[21] findings of tigecycline (95.6%) and nitrofurantoin (82.2%) whereas maximum resistant to nalidixic acid (97.41%) and ciprofloxacin (90.47%) which is nearly matching to Issac Odongo *et al*.[22] 90% resistant to nalidixic acid.

The literature published by Ekadashi Rajni Sabharwal *et al*.[23] observed maximum sensitivity to fosfomycin (84.8%) and nitrofurantoin (83.3%) which is similar to our study were fosfomycin (79.31%) and nitrofurantoin (58.62%). Among cephalosporins group Asmamaw Ameshe *et al*.[24] revealed 100% resistant to ceftazidime which is similar to our study ceftazidime (96.55%) in *Klebsiella species*.

A high level of resistant to various classes of antibiotic was found among uropathogenic isolates. 88.77% of the isolates isolated were multidrug resistant (MDR), which defined as resistance to at least three or more antimicrobial group of agents.[25]

In our study, out of 98 Gram negative Uropathogens from Diabetic patients isolates 88.77% were found to be multidrug resistance (MDR). In a study conducted by Gebremdhin Yenuhun Worku *et al.*[26] 100% isolates were multidrug Resistance (MDR).The other study conducted by Demiss Nigussie *et al.*[27] noted 93.9% MDR, study of Hiwot Ketema Woldemarium *et al*.[28] observed 81.1% MDR, Aley Mohmmed *et al.*[29] reported MDR isolates to be 57.9% respectively.

Study by Seble Worku *et al*.[30] found 56.7% were MDR. In the study of Akua Obeng Forson *et al.*[31] 46% isolates were multidrug resistance (MDR).The findings of our study of 88.77% multidrug resistance is comparable to the study by Sushant Kande *et al.*[32] documenting 87.4% multidrug resistance.

CONCLUSION:

Urinary tract infection (UTI) is one of the most common infections in clinical practice in both healthcare and community settings causing significant morbidity and mortality.

The overall prevalence of Gram negative uropathogens in Diabetic patients was 54.44% and the prevalence of urinary tract infection was higher in males compared to females in diabetic patients. Among the uropathogens *Escherichia coli* was the most common isolate followed by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. In view of our findings, we recommend fosfomycin, tigecycline and nitrofurantoin as a drug of choice for the treatment of UTI in persons with Diabetes based on its demonstrated high sensitivity.

Diabetic patients are at a high risk of development of UTIs, so it is recommended that continued surveillance of resistance rates among uropathogens is needed to ensure rational use of antibiotics for empirical and appropriate recommendations for the treatment of these infections.

ETHICAL APPROVAL:

Ethical and research clearance was approved with protocol number (050/2021-22) by Ethics Committee of Krishna Institute of Medical Sciences, Deemed to be University Karad.

CONSENT:

As per international standard or university standard, patients' written consent has been collected and preserved by the authors.

DATA AVAILABILITY:

The article contains the appropriate and proper data obtained during the experiment which supports the result, discussion and conclusion of the research article.

HUMAN AND ANIMAL RIGHT:

No Animals/Humans were used for studies that are base of this research.

FUNDING:

None.

ACKNOWLEDGEMENT:

The authors are thankful to Department of Microbiology, Krishna Institute of Medical Sciences, "Deemed To Be University", Karad, Malkapur, Karad for providing necessary research facilities to carry out the work.

COMPETING INTEREST:

Authors have declared that no competing interests exist.

REFERENCES:

1. 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(1):1433-5.
2. Kumar JP, Baral R, Khanal B. Prevalence of uropathogens in diabetic patients and their susceptibility pattern at a tertiary care center in Nepal-a retrospective study. Int J Bio Lab Sci. 2014;3(2):29-34.
3. Nitzan O, Elias M, Chazan B, Saliba W. Urinary tract infections in patients with type 2 diabetes mellitus: review of prevalence, diagnosis, and management. Diabetes, metabolic syndrome and obesity: targets and therapy. 2015;8:129-136. doi: 10.2147/DMSO.S51792.
4. Jayadeswari SC, Kunjappan SP. Bacterial Profile of Urinary Tract Infection in Type 2 Diabetes Mellitus. Journal of Evolution of Medical and Dental Sciences. 2020;9(34):2407-13.
5. Chand AE, Goyal SR, Naruka HS *et al*. Prevalence of uropathogens among diabetic patients and their antibiogram at government medical college, Kota. *IP International Journal of Medical Microbiology and Tropical diseases.* 2021;7(1):24-27.
6. Acharya D, Bogati B, Shrestha GT, Gyawali P. Diabetes mellitus and urinary tract infection: spectrum of uropathogens and their antibiotic sensitivity. Journal of Manmohan Memorial Institute of Health Sciences. 2015;1(4):24-8.
7. Natesan B, Thasneem B. A study on bacteriological profile of urinary tract infection in diabetes mellitus patients in a tertiary care hospital. Int. J. Curr. Microbiol. App. Sci. 2017;6(7):2577-83.
8. Sharma V, Gupta V, Mittal M. Prevalence of uropathogens in diabetic patients and their antimicrobial susceptibility pattern. Natl J Lab Med. 2012;1(1):26-8.
9. Collee JG, Miles RS, Watt B. Tests for identification of bacteria. In: Collee JG, Fraser AG, Marmion BP, Simmons A, Mackie, McCartney's, editors. Practical Medical Microbiology. 14th ed. Edinburgh: Churchill Livingstone; 1996. 131–150.
10. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing; CLSI document M100-S31.2021.
11. Betty a forbes, alice s weissfeld, danielf.sahm. *Bailey and scott diagnostic microbiology,13th edition 2013;*919-930.
12. Monica cheeseborough; district laboratory practice in tropical countries- part 2; 2nd edition; camdridge university press, 2006; pgs105-115.

13. Sibi G, Devi AP, Fouzia K, Patil BR. Prevalence, microbiologic profile of urinary tract infection and its treatment with trimethoprim in diabetic patients. Research journal of microbiology. 2011;6(6):543-551.
14. Saleem M, Daniel B. Prevalence of urinary tract infection among patients with diabetes in Bangalore City. International Journal of Emerging Sciences. 2011;1(2):133-142.
15. Bhatia N, Daga MK, Garg S, Prakash SK. Urinary catheterization in medical wards. Journal of global infectious diseases. 2010;2(2):83-90.
16. Kulkarni DS, Talib DS, Naik DM, Kale DA. Profile of urinary tract infection in indwelling catheterized patients. IOSR Journal of Dental and Medical Sciences. 2014;13(4):132-8.
17. Fatima S, Muhammad IN, Usman S, Jamil S, Khan MN, Khan SI. Incidence of multidrug resistance and extended-spectrum beta-lactamase expression in community-acquired urinary tract infection among different age groups of patients. Indian Journal of Pharmacology. 2018; 50(2):69-74.
18. Sharma S, Verma PK, Rawat V, Negi V. Fosfomycin Sensitivity Pattern among Uropathogens Isolated from Patients Visiting Day Care Facility of Sushila Tiwari Hospital in Kumaun Region, Uttarakhand, India. Journal of Clinical & Diagnostic Research. 2021;15(6):30-33.
19. Mohapatra S, Panigrahy R, Tak V, Shwetha JV, Sneha KC, Chaudhuri S. *et al*. Prevalence and resistance pattern of uropathogens from community settings of different regions: an experience from India. Access Microbiology. 2022;4(2):000321.
20. Saeed NK, Al Khawaja S, Al-Biltagi M. Antimicrobial Susceptibilities of Urinary Extended-spectrum β-lactamase *Escherichia coli* to Fosfomycin. Oman Medical Journal. 2021;36(6):e314.
21. Rafeeq M. Isolation and drug susceptibility pattern of uropathogens in Saudi diabetic and non-diabetic patients with urinary tract infection. Bioinformation. 2022;18(8):710-7.
22. Odongo I, Ssemambo R, Kungu JM. Prevalence of *Escherichia Coli* and its antimicrobial susceptibility profiles among patients with UTI at Mulago Hospital, Kampala, Uganda. Interdisciplinary Perspectives on Infectious Diseases. https://doi.org/10.1155/2020/8042540.
23. Sabharwal ER, Sharma R. Fosfomycin: an alternative therapy for the treatment of UTI amidst escalating antimicrobial resistance. Journal of Clinical and Diagnostic Research: JCDR. 2015;9(12):DC06-DC09.
24. Ameshe A, Engda T, Gizachew M. Antimicrobial Resistance Patterns, Extended-Spectrum Beta-Lactamase Production, and Associated Risk Factors of *Klebsiella Species* among UTI-Suspected Patients at Bahir Dar City, Northwest Ethiopia. International Journal of Microbiology. https://doi.org/10.1155/2022/8216545.
25. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG. *et al*. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. Clinical microbiology and infection. 2012;18(3):268-81.

26. Yenehun Worku G, Belete Alamneh Y, Erku Abegaz W. Prevalence of bacterial urinary tract infection and antimicrobial susceptibility patterns among diabetes mellitus patients attending Zewditu memorial hospital, Addis Ababa, Ethiopia. Infection and Drug Resistance. 2021;14:1441-54.
27. Nigussie D, Amsalu A. Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients. Turkish Journal of Urology. 2017;43(1):85-92.
28. Woldemariam HK, Geleta DA, Tulu KD, Aber NA, Legese MH, Fenta GM. *et al*. Common uropathogens and their antibiotic susceptibility pattern among diabetic patients. BMC infectious diseases. 2019;19(1):2-10.
29. Mohammed A, Beyene G, Teshager L. Urinary pathogenic bacterial profile, antibiogram of isolates and associated risk factors among diabetic patients in Hawassa town, southern Ethiopia: a cross-sectional study. Urol Nephrol Open Access J. 2020;8(4):84-91.
30. Worku S, Girum A, Birhan A, Alemu A. Urinary Tract Infection: Antibiotic Resistance Profiles of Bacterial Etiologies and Associated Risk Factors in Diabetic Patients Attending Debre Tabor Hospital, Northwest Ethiopia. https://doi.org/10.21203/rs.3.rs-1316717/v1.
31. Forson AO, Menkah DA, Quarchie MN, Dhikrullahi SB, Olu-Taiwo M, Codjoe FS. Bacterial drug-resistance patterns and genetic diversity of bacteria-associated bacteriuria in diabetic patients in Ghana. IJID Regions. 2021;1:142-9.
32. Kande S, Patro S, Panigrahi A, Khora PK, Pattnaik D. Prevalence of uropathogens and their antimicrobial resistance pattern among adult diabetic patients. Indian Journal of Public Health. 2021;65(3):280-286