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Original Research Article

A study of clinico-microbiological profile and outcome of urinary tract infection in diabetic kidney disease in a tertiary care hospital

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ABSTRACT

Background: this study was done to give insight about the clinical and microbiological profile of UTI in DKD and its therapeutic outcome.
Methods: Patient known case of DKD presenting with signs and symptoms of UTI were included in study. Patients known case of diabetes having diabetic retinopathy and albuminuria with at least UACR of >30 mg/gm of creatinine were considered as having DKD.
Results: We found, most common presenting symptom was fever, present among 35 (47.29%) patients followed by increased frequency of urination among 30 (40.54%) patients. Burning micturition and dysuria/flank pain was present among 20 (27.02%) patients and 10 (13.51%) patients respectively, lower abdominal pain in 08 (10.81%) patients. 52 (70.27%) patients' culture were sterile and 22 (29.73%) patients' culture were non-sterile. Out of 22 patients of non-sterile cultures, 16 (72.72%) patients have lower UTI compared to 06 (27.27%) patients with Upper UTI. E. coli was the most common organism cultured in both types of UTIs. Fungal growth (*Candida tropicalis*) was seen in 03 (50%) patient, all were cases of upper UTI.
Conclusions: The clinical and microbiological profile of UTI in DKD doesn't differ from UTI in diabetics and non-diabetics except for prolonged and severe course of disease. The microbiological susceptibility also doesn't differ much. Lower age is associated with lower UTI. Upper urinary tract involvement is associated significantly with progression of CKD. Involvement of upper urinary tract should be sought in UTI in diabetics and patient with DKD and if found should be aggressively treated.

Keywords: Clinicomicrobiological, DKD, UTI

INTRODUCTION

In 2015, it was predicted that 415 million people worldwide had diabetes; by 2040, it is expected to rise to 642 million, with a disproportionate increase in low- and middle-income nations.[1] Paralleling the sharp global rise in diabetes incidence is the rising prevalence of diabetic kidney disease.[2] About 30% of people with type 1 diabetes mellitus (DM1) and 40% of people with type 2 diabetes mellitus (DM2) acquire this microvascular problem.[3,4] The most common cause of chronic and end-stage renal disease (CKD and ESRD, respectively) worldwide is diabetic kidney disease (DKD).[5]

With 150 million cases worldwide each year, urinary tract infections (UTIs) are among the most prevalent bacterial illnesses.[6] If treated properly and promptly, urinary tract infections (UTIs) can be treated with antibiotics with ease. It comprises pyelonephritis, cystitis, prostatitis, and asymptomatic bacteriuria (ASB). Typically, it involves the bladder (acute cystitis). Clinically speaking, there are two categories of UTI: complicated and non-complicated UTI.

Both Gram-negative and Gram-positive bacteria, as well as some fungi, are responsible for UTIs. Uropathogenic *Escherichia coli* (UPEC) is the most frequent cause of

both complicated and non-complicated UTIs. The altered host response and anatomical and functional abnormalities of the urinary tract are assumed to be the fundamental causes of the increased risk of UTI in people with chronic renal disease. The altered host protection mechanisms are hypothesised to result from: urine's loss of its antibacterial capabilities, mild immunosuppression in uraemia, development of the urothelium's protective mucosa is inhibited.[7-9]

While UTIs in various stages of CKD have similar long-term outcomes, those with GFRs below 30 ml/minute are more likely to experience superimposed AKI during the acute phase of UTI.[10]

In this study we looked on clinical and microbiological profile of UTI in different stages of diabetic kidney disease, therapeutic intervention done such as antibiotics, haemodialysis and outcome of UTI as well as of diabetic kidney disease after single or multiple episodes of UTIs.

METHODS

This open label hospital based observational study was carried out in department of medicine and nephrology of Jawaharlal Nehru Medical College (JNMC) and Hospital, AMU, Aligarh, UP, India. Patients of diabetic kidney disease presenting to medicine outpatient, nephrology clinic and emergency room at JNMC and H, AMU with signs and symptoms of urinary tract infection were recruited. The study was conducted from November 2020 through June 2022 (20 months duration). Following Inclusion criteria was used. Patients having diabetes either type 1 DM or type 2 DM with diabetic kidney disease with at least albuminuria >30 mg/dl or spot UACR >30 mg/gm creatinine with symptoms of UTI either upper UTI (fever/flank pain) lower UTI (dysuria/frequency/hesitancy) with urine automated analysis showing pus cells or nitrite positive or leukocyte esterase positive or culture positive or imaging suggestive of UTI.

Exclusion criteria

Patients with pregnancy, breast feeding, acute coronary syndrome and heart failure., after vigorous exercise, DKA or HHC, hypertensive urgency, stroke, chronic pelvic pain syndrome, immunocompromised status, diagnosed malignancy were excluded.

74 patients were enrolled in this study. The purpose and benefits of the study were explained to patient and written informed consent was taken. The data was collected by preformed structural proforma.

The study was passed by the institutional ethical committee and the study was conducted as per the standards of good clinical practice and the Helsinki declaration.

RESULTS

A total of 74 patients with DKD and UTI were included in study. They were divided into upper and lower UTI based on site of involvement. Their clinical profile and microbiological profile including sensitivity and resistivity pattern is as following.

Clinical profile

Among the study subjects the maximum age was 83 years and minimum was 20 years. The mean age was 55.05±12.13 years.

Table 1: Age distribution of patients.

Age (years)	Frequency	Percentage
<30	05	6.76
30-50	20	27.04
50-70	43	58.10
>70	06	8.10
Total	74	100.00

Mean age: 55.05±12.13, Minimum- 20 years, Maximum- 83 years

Table 1 shows age distribution of patients. It was observed that majority 43 (58.1%) patients were in the age group 50-70 years followed by 20 (27.04%) patients in the age group 30-50 years. About 05 (6.76%) patients were in the age <30 years and 06 (8.1%) patients were >70 years.

Table 2: Gender distribution of patients.

Gender	Frequency	Percentage
Male	22	29.72
Female	52	70.28
Total	74	100.00

Table 2 shows gender distribution of patients. It was observed that majority 52 (70.28%) patients were females and 22 (29.72%) were males.

Table 3: Mode of presentation among patients.

Mode of presentation	Frequency (N=74)	Percentage
Fever	35	47.29
Increased frequency of urination	30	40.54
Burning micturition	20	27.02
Flank pain	10	13.51
Dysuria	10	13.51
Pain in lower abdomen	08	10.81
Generalised weakness	02	2.70

Table 3 shows mode of presentation among patients. The most common presenting symptom was fever which was present among 35 (47.29%) patients followed by

increased frequency of urination among 30 (40.54%) patients. Burning micturition was present among 20 (27.02%) patients and dysuria, flank pain was present among 10 (13.51%) patients each. Pain in lower abdomen was present among 08 (10.81%) patients and generalized weakness among 02 (2.70%) patients.

Table 4: Duration of symptoms (days) among patients.

Duration of symptoms (days)	Frequency	Percentage
≤3	51	68.91
4-6	17	22.97
7-10	02	2.71
>10	04	5.41
Total	74	100.00

Table 4 shows duration of symptoms (days) among patients. Most of the patients 51(68.91%) were symptomatic since ≤3 days followed by 17 (22.97%) patients for 4-6 days. About 02 (2.71%) patients were symptomatic for 7-10 days and 04 (5.41%) patients were chronically symptomatic since >10 days.

Microbiology of UTI in DKD

Table 5 shows urine culture among patients. About 52 (70.27%) patients urine culture was sterile and 22 (29.73%) patients urine culture was non-sterile.

Table 5: Urine culture among patients.

Urine culture	Frequency	Percentage
Sterile	52	70.27
Non-sterile	22	29.73
Total	74	100.00

Organisms cultured

Table 6 shows organisms cultured and type of UTI among patients. Out of 22 patients whose urine culture was non-sterile, 16 (72.72%) patients were diagnosed with lower UTI compared to 06 (27.27%) patients with Upper UTI. *E. coli* was the most common organism cultured in both types of UTI. Fungal growth (*Candida tropicalis*) was seen in 03 (50%) patient with upper UTI and none among lower UTI patients. The organisms like *Klebsiella pneumonia* among 03 (18.75%) patients and *Pseudomonas aeruginosa*, *Staphylococcus albus*, other staphylococcus species was present among 01 (6.25%) patient each with lower UTI.

Table 6: Organisms cultured and type of UTI among patients.

Organisms cultured	Upper UTI (N=06) n (%)	Lower UTI (N=16) n (%)
E. coli	05 (83.3)	10 (62.5)
Candida tropicalis	03 (50.0)	00 (0.00)
Klebsiella pneumonia	00 (0.00)	03 (18.75)
Pseudomonas aeruginosa	00 (0.00)	01 (6.25)
Staphylococcus albus	00 (0.00)	01 (6.25)
Other *staphylococcus* species	00 (0.00)	01 (6.25)

Sensitivity pattern of organism cultured

Table 7 shows susceptibility pattern of antibiotics to organisms cultured among patients. It was observed that *E. coli* was susceptible to meropenem, *Klebsiella pneumoniae* was susceptible to nitrofurantoin and meropenem. *Pseudomonas aeruginosa* was susceptible to colistin and polymyxin. *Staphylococcus albus* and *Candida tropicalis* was susceptible to antifungal.

Table 7: Susceptibility pattern of antibiotics to organisms cultured among patients.

Organisms cultured	Antibiotics				
	Nitrofurantoin	**Meropenem**	**Piperacillin**	**Colistin**	**Polymyxin**
***E. coli* (n=15)**	13	15	12	-	-
***Klebsiella pneumonia* (n=03)**	03	03	02	-	-
***Pseudomonas aeruginosa* (n=01)**	-	-	-	01	01
***Staphylococcus albus* (n=01)**	-	01	01	-	-
Other *staphylococcus* species (n=01)	01	-	-	-	-

Table 8: Susceptibility pattern of antibiotics to organisms cultured among patients.

Organisms cultured	Antibiotics				
	Fosfomycin	**Cefoperazone**	**Levofloxacin**	**Linezolid**	**Amikacin**
***E. coli* (n=15)**	15	01	10	-	06
***Klebsiella pneumonia* (n=03)**	03	-	02	-	01
***Pseudomonas aeruginosa* (n=01)**	-	-	-	-	-
***Staphylococcus albus* (n=01)**	-	-	01	01	01
Other staph. species (n=01)	-	-	01	-	-

Table 9: Resistivity pattern of antibiotics among patients.

Antibiotics	*E. coli* (n=15)	*Klebsiella pneumonia* (n=03)	*Pseudomonas aeruginosa* (n=01)	*Staphylococcus albus* (n=01)	Other staph. species (n=01)
Amoxicillin	15	03	01	01	01
Ampicillin	15	03	01	01	01
Linezolid	05	02	01	-	01
Cefuroxime/cefotaxime	15	03	01	01	01

Table 8 shows susceptibility pattern of antibiotics to organisms cultured among patients. *E. coli* and *Klebsiella pneumoniae* was susceptible to Fosfomycin. About 10 patients with *E. coli* culture and 02 patients with *Klebsiella pneumoniae* culture was sensitive to levofloxacin. All the cultures of *Staphylococcus albus* was sensitive to levofloxacin, linezolid and amikacin.

Resistance pattern of organism cultured

Table 9 shows resistivity pattern of antibiotics among patients. All the organisms cultured among patients in this study were resistant to amoxicillin, ampicillin, cefuroxime/cefatoxime. About 05 patients with *E. coli* culture and 02 patients with *Klebsiella pneumoniae* culture were also resistant to linezolid.

Response of UTI in DKD

After treatment, 74 (98.65%) patients were cured and 01 (1.35%) patient with lower UTI expired.

Effect of UTI on DKD

Table 10 shows effect of UTI on diabetic kidney disease (DKD) among patients. There was no effect of UTI on DKD among majority 60 (81.08%) patients followed by decrease in GFR was observed among 08 (10.81%) patients. Progression was observed among 03 (4.05%) patients each. One patient progressed from non-dialysis to dialysis and another patient from CKD 3B to ESRD. About 02 (2.70%) patients showed increased proteinuria and 01 (1.35%) patient was expired.

Table 10: Response on diabetic kidney disease (DKD) among patients.

Response on DKD	Frequency	Percentage
No effect	60	81.08
Decrease in GFR	08	10.81
Progression	03	4.05
Increase in proteinuria	02	2.70
Death	01	1.35
Total	74	100.00

DISCUSSION

In our study it was observed that majority 43 (58.1%) patients were in the age group 50-70 years followed by 20 (27.04%) patients in the age group 30-50 years. About 05 (6.76%) patients were in the age <30 years and 06 (8.1%) patients were >70 years. Our finding is similar to a study done in Bengaluru in 2021 by Shankar et al who studied UTI among 129 CKD patients, UTI was most common between 61 to 70 years of age (25.58%), followed by 51-60 years (19.3%).[11] This age distribution of UTI in DKD patients is similar to UTI in diabetics not having CKD. 12. Jagadeeswaran et al showed 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.[12] In our study it was observed that majority 52 (70.28%) patients were females and 22 (29.72%) were males. Our finding is confirmed by many studies among both DKD and diabetics not having CKD. Hsiao et al showed that females (36.1%, 60/166) were more prone to have upper UTIs than males (11.8%, 13/110).[13] Arjumand et al also found UTIs are more in female.[14] The shorter urethra, close closeness of the female urethral meatus to the anus, and sexual activity have all been identified as variables that contribute to the increased occurrence in women. But different researchers from different part of country reported different sex distributions also. Shankar et al studied UTIs in CKD patients and showed out of the total number of patients studied (n=129), 76.2% were males and 23.8% were females.[11] Comparing symptoms as we found in our study to different researchers we observed that our finding is similar to another study done by Shankar et al who found the most common presenting symptoms were urinary complaints (63%) such as burning micturition (dysuria), increased frequency of micturition followed by fever (23%), pain abdomen(11%), and other nonspecific complaints (3%).[11] However Pughalendi et al showed that commonest presenting symptoms were fever and abdominal pain, while vomiting and burning micturition were less common.[15]

Most of the urine culture is sterile in our patient is may be due to irrationale prescription of antibiotics by local quacks or self-prescription before presenting to a hospital. Similar finding as our study was also seen in study done by Shankar et al on UTIs in CKD.[11] It showed 1 patient (9%) had a growth of two microorganisms and other 118 (91%) had a growth of a single organism. The total number of microorganisms grown was 131. 123 (94%) were gram positive, four (3%) were gram negative, four (3%) were *Candid*a species. *E. coli* (61.8%) was the most common culture grown organism, followed by

Klebsiella (13.74%) and *Pseudomonas* (7.6%). The most common gram-positive organism isolated was *Enterococcus* (2.29%), followed by *Staphylococcus aureus* (0.76%). However, in this study *Staphylococcus albus* and other staph species were common among gram positive bacteria. Result of our study is further strengthen by similar finding in a study done by Pughalendi et al in Southern India on UTIs in CKD patient which also showed 47.7% had *E. coli* growth, the next common organism found was *K. pneumoniae* at 15.4%.[15] However in this study 12.3% the inference was sterile with no bacterial growth which is different from our study which showed 70% of no bacterial growth. *Citrobacter diversus* was seen in 6.2% patients and 4.6% showed growth of *Enterococcus* and non-albicans *Candida* each. The microbiological profile doesn't differ in UTIs in diabetics as compared to DKD. Kumar et al compared UTI in diabetics and non-diabetics and showed diabetic group had an overall twice risk of UTI (p=0.01; OR: 2.04; CI: 1.12, 3.71) and female gender in diabetic group had a risk of almost five times (p=0.01; OR: 4.93; CI: 1.12, 20.16) that of the non-diabetic group of developing urinary tract infection.[16] Almost 30% patients in the diabetic group with culture-proven UTI were asymptomatic as compared to only 5% in the non-diabetic group (p=0.03; OR: 7.79; CI: 0.92, 66.18). There was no other significant difference between the presentations of UTI in the two groups. *E. coli* (60%), *Klebsiella* species (17%), *Pseudomonas* (14%) and *Enterobacter* species (9%) were common cause among Gram negative and Coagulase negative *Staphylococcus* species (34%) (*S. albus*) were common among Gram positive organism in both diabetic and non-diabetic group. Antibiotic susceptibility pattern of micro-organism: It shows that most of the common bacteria causing UTI are still sensitive to most of the current first line antibiotics. So currently recommended empirical treatment for UTI in diabetes can be safely given to patient of DKD also. But as DKD patient need prolonged treatment as shown by our study same empirical treatment should be given but for a prolonged period.

Most of the Gram negative bacteria which are the most common cause are sensitive to urinary antiseptics such as Fosfomycin, nitrofurantoin, most of the fluroquinolones as well as carbapenems such as meropenem and ureidopenicillin such as piperacillin. So, depending on site of involvement whether upper UTI or lower UTI, specific antibiotic can be used. *Pseudomonas* was positive in culture from one of the patients with upper UTI which is sensitive to colistin and polymyxin B only and resistant to most of the anti-pseudomonal antibiotics, ultimately the patient expired even with lower UTI with urosepsis. 3 cases grow *Candida tropicalis*, all 3 were cases of upper UTI, one of them also grow *E. coli*. responded well to inj fluconazole and injection meropenam but needed for prolonged period of time. Gram positive bacteria were also sensitive to almost all first line antibiotics used as empirical treatment of UTI.

In our study we found that after treatment, 74 (98.65%) patients were cured and 01 (1.35%) patient with lower UTI expired. Most of the patient were treated successfully shows that UTI in DKD can be treated with the same rate as in non-diabetics and diabetics without CKD but only require prolonged period of treatment and degree of renal insufficiency should be kept in mind for dose and choice of antibiotics. One patient that expired was infected with multi drug resistant strain *Pseudomonas*. Many antibiotics can't get concentrated in urine in renal insufficiency and in presence of renal insufficiency dosage of some antibiotics need to be reduced to prevent inadvertent toxicity of antibiotics. There is a chance that the urine medication concentration in patients with chronic insufficiency and cystitis won't be high enough to completely destroy the causative organism.[17]

Outcome of diabetic kidney disease

There was no effect of UTI on DKD among majority 60 (81.08%) patients followed by decrease in GFR was observed among 08 (10.81%) patients. Progression was observed among 03 (4.05%) patients each. One patient progressed from non-dialysis to dialysis stage of CKD and another patient progressed from CKD 3B to ESRD. About 02 (2.70%) patients showed increased proteinuria and 01 (1.35%) patient was expired. It was found that effect of UTI on DKD was better among patients with lower UTI compared to upper UTI. Decrease in GFR was observed among 08 patients and 01 patient among upper UTI and lower UTI group respectively and this difference is statistically significant. Increase in proteinuria was observed among 02 patients with upper UTI and none among patients with lower UTI and this difference is also statistically significant. This finding suggests that patients of DKD with upper UTI can have sequalae in form of worsening of baseline renal function, increase in proteinuria and overall progression of CKD while lower UTI have little impact on progression of CKD.

Because of the pandemic, limited number of patients can be included in the study. Many patients presented late with history of antibiotics intake so their culture came out to be sterile and causative organism couldn't be correctly identified. It was a single centre prospective descriptive study. Future studies needed with comparison with other causes of CKD to correctly attribute factors related to diabetic kidney disease.

CONCLUSION

The clinical and microbiological profile of UTI in DKD doesn't differ from UTI in diabetics and non-diabetics except for prolonged and severe course of disease. The microbiological susceptibility of organism in UTI in DKD is similar to diabetics and non-diabetics. Upper urinary tract involvement is associated significantly with progression of CKD. Involvement of upper urinary tract

should be sought in UTI in diabetics and in patient with DKD and if found should be aggressively treated.

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