

## The Study of Clinical, Microbiological Profile and Risk Factors of Urinary Tract Infection in Renal Transplant Recipients



### Nephrology

**KEYWORDS:** Graft Outcome, Renal transplant, Urinary Infection.

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### ABSTRACT

Renal transplantation has a better quality of life and better survival when compared to dialysis as a modality of management of end stage renal disease patients. Urinary tract infection (UTI) is a common complication after kidney transplantation. A retrospective case-control study was conducted in Department of Nephrology, Madras Medical College for 1 year from May 2012 to April 2013, to identify the microbiological profile and risk factors of UTI. *Klebsiella oxytoca* was the organism commonly isolated followed by *E.coli*. Recurrent UTI occurred in 6 patients commonly due to *klebsiella oxytoca*. There was no correlation with diabetes ( $p=1.0$ ), cytomegalovirus disease ( $p=0.78$ ) and anti rejection therapy ( $p=0.46$ ) with incidence of UTI in renal transplant recipients. There was increased incidence of UTI in patients with hepatitis C virus (HCV) co-infection ( $p=0.0091$ ). The graft outcome ( $p=0.037$ ) was poor in those with UTI. Structural and functional abnormalities of urinary tract increase the risk of UTI, except vesico ureteric reflux (VUR), and Horse Shoe kidney. Graft pyelonephritis is associated with poor outcome.

### Introduction

Renal transplantation has a better quality of life and better survival when compared to dialysis as a modality of management of end stage renal disease patients. Renal transplant outcome has improved over the past few decades, as a result of development of new immunosuppressive drugs such as mycophenolate mofetil and tacrolimus, with decreased incidence of acute rejection episodes. In spite of advances in prophylaxis and treatment, infection remains the major cause of morbidity and mortality in patients with renal transplant. UTI is a common bacterial infection in renal transplant recipient<sup>1</sup>. The majority of infections occur in the first year following transplantation. UTI can worsen the graft and patient survival<sup>2</sup>. A significant percent of patients may develop acute pyelonephritis, which is a risk factor for graft deterioration<sup>3</sup>.

The aim of the study was to find the microbiological profile and identify the risk factors for UTI in renal transplant recipients, and to study the effect of UTI on graft function and long term graft survival.

### Materials and methods

The study design was retrospective case-control study. The patients who underwent renal transplant in Department of Nephrology, Madras Medical College Chennai and presenting with fever or urinary symptoms in the form of dysuria, frequency, urgency suprapubic pain or pain over graft, or fever of unknown origin, during the period of May 2012 - April 2013, were included in the study.

All patients underwent urine analysis, complete haemogram, blood urea, serum creatinine, serum electrolytes, serum bilirubin, serum albumin, globulin and alkaline phosphatase, urine gram stain and culture including fungal, blood culture and sensitivity for enteric and non enteric organism, hepatitis C virus screening. Ultra sonogram abdomen including kidney, ureter and bladder. When complication was suspected, selected patient underwent CT abdomen.

### Observation and Results

The total number of patients included in the study was 141. The number of male patients was 110. The mean age in male cohort was  $33.70 \pm 8.77$ . The number of female patients was 31. The mean age in the female cohort was  $30.18 \pm 10.54$ . The number of patients who received live related transplant was 100.

The patients who had at least one episode of urinary tract infection were 58. The incidence of UTI was 41%. UTI occurred in 17 (54%)

female patients and 41 (37%) male patients which was not significant ( $p=0.099$ ).

Incidence of urinary infection in live donor was 43% (43) and in deceased donor was 37% (15). The organism most commonly isolated was *Klebsiella* (43%), followed by *E. coli* (31%). According to time of post transplant, in the 1<sup>st</sup> month *klebsiella* UTI was more common in both males and females. In males, in the 1 to 6 months period post transplant and more than 6 months post transplant also *klebsiella* urinary infection was more common. In females the common organism in more than 6 months post transplant was *E. coli*. No organism could be identified in 3 patients with clinical features of UTI like pyuria, fever and tenderness over graft, which subsided with antibiotic treatment. Fungal UTI occurred in 5 patients, with 4 episodes occurring in less than 1 month post transplant. All the episodes of fungal urinary infections were due to *candida albicans*.

Out of 58 patients with UTI, six patients had recurrent episodes of infection. The organism most commonly isolated in those with recurrent UTI was *klebsiella oxytoca*. One patient had *E.coli* UTI. New onset diabetes after transplant (NODAT) was noted in 4 patients with recurrent urinary tract infection. HCV infection occurred in 3 patients with recurrent urinary tract infection. Recurrence of disease with proteinuria (FSGS/ImmunoglobulinA nephropathy) occurred in 2 patients.

Renal abscess occurred in two patients, in the late post transplant period (more than 18 months). The serum creatinine at the time of abscess formation was 1.8mg and 1.6mg respectively in the two patients.

Four patients presented with low grade fever and graft dysfunction. All of them underwent allograft biopsy for graft dysfunction which showed graft pyelonephritis. All patients had no urinary symptoms in the form of dysuria, frequency and pain or tenderness over the graft. Diabetes was present in two of those patients. Stenting was done in 3 out of four patients. All of those with stenting developed urinary tract infection immediately after stent removal. Two patients had recovery of renal function following treatment of urinary tract infection. One patient had partial recovery of renal function. One patient gradually progressed to end stage renal disease over a period of 5 months.

**Table 1. Urinary Infection and Graft Outcome**

Serum creatinine in mg/dl	Urinary tract infection	Without UTI
Mean	1.718	1.484
Standard deviation	0.87	0.55

P-value 0.037

There was a correlation between UTI and poor allograft outcome which was manifested as raised serum creatinine in those with UTI (table1).

UTI occurred in 48 of 123 patients with early graft function. UTI occurred in 10 of 18 patients with delayed graft function. Even though a trend towards more UTI in those with delayed graft function, than in those with early graft function, there was no significance ( $p=0.20$ ). UTI occurred in 18 out of 43 patients with diabetes mellitus. Urinary tract infection occurred in 40 out of 98 patients in those without diabetes. There was no correlation with diabetes and the incidence UTI in renal transplant recipient.

UTI occurred in 7 out of 15 patients with cytomegalovirus (CMV) disease. UTI occurred in 51 out of 126 patients without CMV disease. There was no correlation with CMV disease and the incidence UTI in renal transplant recipient.

UTI occurred in 16 out of 45 patients, who received Anti-rejection therapy (ART). UTI occurred in 42 out of 96 patients, who never received ART. There was no correlation with anti rejection therapy and the occurrence of UTI in renal transplant recipient.

**Table-3. Structural Abnormalities and UTI**

Structural lesions	Age/ Sex	Organism	Time of occurrence	Number of episodes	Co-morbidities
Ureteric stricture	26 M	Klebsiella oxytoca	11 month	1	HCV infection/ ART
Ureteric stricture with VUR	21 M	Klebsiella oxytoca	4 <sup>th</sup> day, 10 <sup>th</sup> month, 12 <sup>th</sup> month	3	ART
Meatal Stenosis	20 M	Culture negative	3 <sup>rd</sup> month	1	HCV infection
PUJ Obstruction	45 M	E. coli	1 year 5 month	1	NODAT
Scar in the kidney	34 F	E. coli	6 year	1	HCV infection
Neurogenic bladder	35 M	Klebsiella oxytoca	2 month onwards	6	CMV infection
Horse Shoe kidney	22 M	No		0	
VUR	30 M	No		0	

Patient with Horse shoe kidney and VUR had no episode of UTI. Others had at least one episode of UTI. Klebsiella oxytoca is the organism commonly isolated. Three patients had UTI in the 1 to 6 month period. Three patients had UTI in the late post transplant period. Four patients had immunomodulatory viral co-infection. Two patients with stricture urethra developed late rejection after UTI (table3).

**Table 2. Hepatitis C Virus Infection and UTI**

Hepatitis C virus	UTI	No UTI
HCV infection	18	10
No HCV infection	40	73

P-value 0.0091

UTI occurred in 40 out of 114 patients without hepatitis C infection. UTI occurred in 18 out of 28 patients with hepatitis C co-infection.

There was a strong correlation with hepatitis C co-infection and UTI in the post transplant period (table2).

## Discussion

Infection is a common complication in the renal transplant recipient. In the initial months of post transplant period bacterial infection is more common, with UTI occurring as a common infection among bacterial infections.

According to Hussain, et al, the incidence of UTI was 46%<sup>4</sup>. The incidence of UTI in our cohort was 41%. The reported frequency varies in various studies ranging from 18% to 79%. According to Roberto Rivera-Sanchez et al et al, E. coli was the most common organism in 31%, followed by candida albicans 21% and enterococcus species in 10%<sup>5</sup>. In our study Klebsiella species in 43% is the most common organism isolated followed by E.coli in 31%.

According to Magali Gril, et al, there was more incidence of graft pyelonephritis in female recipient<sup>3</sup>. In our study also there was increased incidence of UTI in female recipient, which did not reach statistical significance. The increased incidence of urinary infection in female may be due to anatomic factors like shorter female urethra and proximity of the vagina and urethra to the anal canal favouring colonization<sup>6</sup>.

There is no correlation between diabetes, cytomegalovirus infection and rejection episodes with the incidence of urinary tract infection as shown in various study<sup>7</sup>.

According to David Roth, et al, the risk of infection is considered as a function of time line, initial 6 months and more than 6 months. In the initial 6 months, the morbidity and mortality due to all infections in the post transplant patient with HCV infection is increased by a factor of 2.51<sup>8</sup>. When the mortality due to infection alone is considered, it is increased by a factor of 26.6 fold<sup>8</sup>, in post transplant when compared to pre transplant. In our study, in univariate analysis there was significantly increased risk of UTI in the post transplant, with HCV co-infection. Three patients with HCV co-infection post transplant presented with recurrent urinary infection. Two patients developed jaundice with active hepatitis after repeated urinary tract infection and succumbed to the illness<sup>9</sup>.

According to Kamath, et al, there was a correlation with pre transplant glomerular disease and urinary infection<sup>10</sup>. According to the author the pre transplant immunosuppression, by increasing the net immunosuppression post transplant, predisposes to urinary infection. In our cohort there was increased incidence of urinary infection in those with proteinuria due to recurrent glomerular disease with two patients presenting as recurrent UTI, even though they received no immunosuppression during the pre transplant period.

Renal abscess occurred in two patients in our study. The late occurrence of renal abscess complicating UTI was due to both of them having immunomodulatory viral infection, hepatitis C virus in one and recurrent cytomegalovirus in the other patient. Both patient underwent image guided percutaneous aspiration, but had progressive worsening of the disease and succumbed to the illness.

In our study, two patients with stricture urethra developed late rejection after UTI. One patient with Horse shoe kidney and the other with VUR had no episode of UTI. Since the bladder function is normal, there was no increased risk of UTI in isolated vesicoureteric reflux disease and Horse Shoe kidney in renal transplant recipient.

According to Pelle, et al, there was a poor long term outcome in those with acute graft pyelonephritis. When compared to those without UTI there was a lower creatinine clearance of 50% in those with post transplant UTI, over 4 years follow up<sup>11</sup>. In our study, there was a worse graft outcome in the form of raised creatinine in those with urinary infection.

## Conclusion

Urinary tract infection is a common infection in renal transplant recipient. Klebsiella species was the organism frequently isolated in the culture. There was no correlation with cytomegalovirus disease, diabetes and rejection episodes on the occurrence of UTI. The incidence of UTI was increased in those with hepatitis C virus co infection. Structural and functional abnormalities were a risk factor for UTI except VUR. UTI in the renal transplant recipient was associated with poor long term graft function.

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