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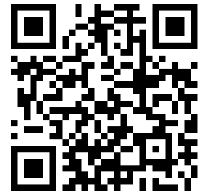
PJMLS
Print ISSN: 2707-4471. Online ISSN: 2707-448X

Research Article	Pak-Euro Journal of Medical and Life Sciences
DOI: 10.31580/pjmls.v5i2.2552	Copyright © All rights are reserved by Corresponding Author
Vol. 5 No. 2, 2022: pp. 223-228	
www.readersinsight.net/pjmls	
Submission: June 21, 2022	**Revised:** June 28, 2022 **Accepted:** June 30, 2022

FREQUENCY OF URINARY TRACT INFECTIONS IN RENAL TRANSPLANT RECIPIENTS WITH COMMON BACTERIA AND ITS SENSITIVITY



Hazratullah[1*], Nasir Khan[2], Asif Malik[2], Atta U Rahman[2]

[1]**Department of Urology,** Khyber Teaching Hospotal, Peshwar, Pakistan

[2]**Department of Urology and Transplant,** Institute of Kidney Diseases (IKD), Peshawar, Pakistan

***Corresponding Author:** Dr. Hazratullah. E. mail: hazratullah72@yahoo.com

Abstract

Objectives: *Primary Objective of this study was to determine the frequency of urinary tract infections among renal transplant recipients. Secondary Objective was to determine common pathogens with their antibiotic sensitivity among renal transplant recipients.*

Materials and methods: *This Cross sectional descriptive study was conducted at Institute of Kidney Diseases (IKD) Hayatabad, Peshawar from January 2008 to December 2012. We included 74 live related renal transplant recipients. Each renal transplant recipient was followed up to 3months for developing urinary tract infection.*

Results: *A total of 74 patients were followed after renal transplant. Among them 12 (16.22%) were females and 62 (83.78%) were males respectively. They were all live related renal transplants. A total of 27(36.48%) patients had Urinary Tract Infection during first 3 months of transplantation (60 ± 15 days). Female patients were more susceptible to UTI than male patients (5 female 41.66%; 22 male 35.48%). On univariate analysis, older age ($p = 0.015$), female gender ($p < 0.001$), hyperglycemia ($p = 0.037$) and acute rejection episodes ($p = 0.046$) were all risk factors for developing urinary tract infection. Isolated bacteria were Escherichia coli (59.25%), Candida albicans (18.51%), Klebsiella (11.11%), Enterococcus spp. (7.40%), followed by Pseudomonas aeruginosa 3.70%. Antibiotic resistance was 26% for ciprofloxacin and 33% for ampicillin.*

Conclusion: *Urinary tract infection is a major problem in renal transplant recipients. The female gender, increasing age and uncontrolled hyperglycemia are the risk factors for UTI in renal transplant recipients. There is high resistance to ampicillin and quinolones in renal transplant recipients.*

Keywords: *Antibiotic sensitivity, Common bacteria, Renal transplant recipients, Urinary tract infection*

INTRODUCTION

Urinary Tract Infection (UTI) is the single most important postoperative complication in renal transplant recipients and it remains a major problem despite advances in organ transplantation (1, 2). Urinary tract infection in post-transplant patient has been associated with increased morbidity, mortality, and hospitalization rate and graft failure (3). The acute pyelonephritis especially in early post-transplant period is a risk factor for renal graft dysfunction in long term (4). The estimated incidence of urinary tract infection in post renal transplant recipients is between 10 to 90% (5, 6). There are multiple risk factors for the development of UTI in post renal transplant recipients which can be divided into pre-operative, intra-operative and post-operative risk factors. Pre-operative factors are related to host and include female gender, diabetes mellitus and the presence of urological abnormalities. Intra-operative factors of note include the use of deceased donor renal graft, the use of ureteric stents and prolonged indwelling bladder catheterization. Post-operative factors of note include acute renal graft dysfunction and rejection and excessive immunosuppression to treat rejection episodes (4, 7, 8). Mycophenolic acid may also be a predisposing factor for UTI and pyelonephritis (7). Anatomical abnormality of the native or transplanted kidneys, neurogenic bladder and renal insuffiency may also be some of the reasons for the high incidence of UTI in renal transplant recipient (9).

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E. coli is the one of the most common uropathogen causing UTI in renal transplant patients (10-13). Other typical microorganisms causing post renal transplant UTI are Klebsiella pneumoniae, Pseudomonas aeruginosa and Enterococci species (14, 15). In addition Corynebacterium, uroplasma urealyticum of group D2 has been identified as a potential pathogen (11-16). The number of pathogenic multi-drug resistant (MDR) gram negative bacteria is increasing globally.

MATERIALS AND METHODS

This Cross sectional descriptive study was conducted at Institute of Kidney Diseases (IKD) Hayatabad, Peshawar .We included 74 live related renal transplant recipients irrespective of age and gender. Patients having indwelling catheter, an alternative site of infection detected through clinical examination, history of diabetes (Fasting blood glucose of >126mg.dl), immunosuppressive states like HIV and other structural abnormality like vesico-ureteral reflux were excluded from the study. The above mentioned conditions act as confounders and if included will introduce bias in the study results. All renal transplant recipients were worked up with detailed history and clinical examination and followed by routine (urine, blood tests and imaging) and specific (HLA typing, viral screen) pre-operative investigations.

We defined UTI in post renal transplant patients as the presence of bacteriuria on urine culture reports and receiving one or more courses of antibiotics. This definition of UTI therefore included all cases of acute simple cystitis, transplant pyelonephritis and asymptomatic bacteriuria treated with antibiotics. If there was an unexplained rise in serum creatinine in patients with asymptomatic bacteriuria, only then it was treated with antibiotics. All episodes of UTI were included from first month of post renal transplant up to 3 months. Patients with systemic symptoms like fever, chills, decrease urine output and laboratory reports showing rising creatinine, raised total leucocyte count and C - reactive protein were presumed as having acute pyelonephritis.

All patients were prepared for renal transplantation as decided by the concerned urologist and transplant surgeon. The kidney grafts were placed in left iliac fossa extraperitoneally and renal artery to external iliac artery and renal vein to external iliac vein anastomosed respectively. The ureter was anastomosed to the urinary bladder through extra vesicle Lisch-Gregoire technique. Preoperative antibiotic prophylaxis was routine for all patients. Induction therapy consisted of either intravenous basiliximab or thymoglobulin and methylprednisolone, together with cyclosporine and mycophenolate. Maintenance therapy included a combination of tacrolimus, mycophenolate and prednisolone throughout the post-transplant duration. Prednisolone was tapered to 5 –7 mg/day wherever possible. Mycophenolate mofetil remained at 1 g twice daily unless there was leucopenia, intolerable gastrointestinal side-effects. In such cases the dose was reduced. Prophylactic agents included trimethoprim sulfamethoxazole, valgancyclovir and omeprazole. All patients had an indwelling catheter to measure urine output and this was routinely removed 3–5 days after transplantation. All patients had a ureteric stent inserted and this was routinely removed at 4 weeks after transplantation. The renal transplant patients were kept under observation in ward for 7days and discharged on 8th postoperative day if indicated. Follow up of the post-transplant patients was scheduled weekly for 3 months and fortnightly for another 2 months and then monthly for year through outpatient department. In case of rejection pulse therapy with methyl prednisolone and thymoglobulin were used. All patients were carefully followed to detect UTI. A clean mid-stream urine specimen were collected from all patients with significant WBC count in urine in a sterilized container and sent to hospital laboratory for culture to detect common bacteria like E. coli, Pseudomonas, Enterococcus and Klebsiella. After detecting the bacteria, it was tested for sensitivity against commonly used antibiotics like vancomysin, oxacillin, amikacin, ceftriaxone, ceftazidime, ampicillin, piperacillin, ciprofloxacin, nalidixic acid, imipenem, and clavulanic acid. All the laboratory investigations were done under supervision of an expert pathologist having minimum of five years of experience.

Data were collected on Performa and analyzed using SPSS version 20. Mean and standard deviation were calculated for quantitative variables like age. Percentage and frequencies were computed for categorical variables like gender, UTI and common pathogens.

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RESULTS

The cross section included 74 patients who were followed after renal transplant. Among them 12 (16.22%) were females and 62 (83.78%) were males respectively. They were all live related renal transplant. Urinary tract infection was recorded in 27 (36.48%) patients at first 3 months after transplantation. Female patients were more prone force UTI than male patients (5/12 female 41.66%; 22/62 male 35.48%). On univariate analysis, older age ($p = 0.015$), female gender ($p < 0.001$), hyperglycemia ($p = 0.037$) and acute rejection episodes ($p = 0.046$) were the risk factors for developing urinary tract infection. Furthermore, greater number of HLA mismatches and a pre-existing history of UTIs were not identified as risk factors. Gram negative bacteria were commonly isolated including *Escherichia coli* (59.25%), Klebsiella (11.11%), Enterococcus spp. (7.40%), followed by Pseudomonas aeruginosa 3.70%. Candida albicans (18.5%) was the commonest fungus isolated. Antibiotic resistance was 26% for ciprofloxacin and 33% for ampicillin. Therapeutic alternatives in such cases were cephalosporins, carbapenems, aminoglycosides and vancomycin.

Table I. Demographic details of transplant recipients

Variables	UTI n = 27 (36.4 %)	No UTI n = 47 (63.5%)	P value
Age ±SD	51.2 ± 10.5	40 ± 12.3	0.01
Day of UTI presentation ± SD	60 ± 15	--	--
Gender			
Male	22 (81.4)	40 (85.1)	< 0.001
Female	5 (18.5)	7 (14.8)	
Preexisting history of UTI			
Yes	7 (26)	10 (21.2)	0.08
No	20 (74)	37 (78.7)	
Preexisting urinary tract abnormality			
Yes	8 (29.6)	15 (31.9)	0.07
No	19 (70.3)	32 (68)	
Hyperglycemia			
No	13 (48)	30 (63.8)	
Pre and post-transplant	5 (18.5)	7 (14.8)	0.04
Post-transplant	9 (33.3)	10 (21.2)	
Acute rejection episode			
Yes	3 (11.1)	12 (25.5)	0.04
No	24 (88.8)	35 (74.4)	

Table II. Common organisms isolated, number of antibiotics received per dose and class of antibiotics used in renal transplant recipients

Organism	Number (% age)
E. coli	16 (59.25%)
Candida	5 (18.51%)
Klebsiella	3 (11.11%)
Enterococcus	2 (7.40%)
Pseudomonas	1 (3.70%)
Number of antibiotics received per episode	
One	19 (70%)
Two	5 (20%)
Three	3 (8%)
Class of antibiotics used	
Penicillin	8 (30%)
Cephalosporin	7 (26%)
Carbapenem	5 (18.5%)
Fluoroquinolones	2 (7.4%)
Other	5 (18.5%)
Resistance	
Ampicillin	9 (33%)
Quinolones	7 (26%)

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DISCUSSION

UTI is the most common infection seen after kidney transplantation with variable incidence rates (17, 18). This is due to the variable definitions, different diagnostic criteria and variable use of prophylactic antibiotics in literature. In our study, 27 (36%) patients developed UTI out of 74 patients which are similar to the result of Kanisauskaite *et al.* However results of this study are lower than those reported by Poumard *et al.* (5). In this study we found that female patients are more susceptible to urinary tract infection (41.66%) as compared to male (35.48%) which is similar to the result reported by Memikoglu *et al.*

Both early and late onset UTIs may or may not have negative effect over graft function. Some studies show adverse effect of UTI on graft and other show no effect at all [19]. It has been proposed that surveillance of UTI should continue for a longer period in post renal transplant recipients. Kumar *et al*. have proposed surveillance of urinary tract infection over the first 100 days. DuPont *et al*. has observed that urinary tract infection can cause graft dysfunction even at one year after a kidney transplant surgery. Rizvi *et al.* reported UTI in (65%) kidney transplant recipients in the first three months of post transplantations. Renoult *et al.* reported UTI in 74% of patients within one month of post renal transplant. We found the urinary tract infection in first 3 months after a renal transplant; therefore we suggest that surveillance should be carried out for the first 3 months after surgery. Risk factors for UTI in renal transplant recipient included female gender, structural abnormality, reflux kidney, history of diabetes mellitus, chronic pyelonephritis, long term urethral catheterization, longer hospital stay and different immunosuppression drugs (20). The incidence of early UTI was 17% in both genders (21), 60% in female recipient and 47% in male recipient after 3 years.

The reason of high incidence of UTI in female is due to short urethra and proximity of urethral opening to vagina and anus (22). We found the urinary tract infection in female (41.66%) compared to male recipients (35.48%). Chuang *et al.* reported 68% of female renal transplant recipients in comparison to 30% male transplant recipients. Prevention of both asymptomatic bacteriuria and UTI in renal transplant recipients improved with the introduction of routine preoperative antibiotic prophylaxis, minimization of indwelling urethral catheter and long term antibiotic prophylaxis (23). Trimethoprim sulphamethaxazol reduced the risk of UTI threefold. It is used as a prophylactic antibiotic for 6 months to one year (24). Baituk TD *et al*. demonstrated that antibiotic prophylaxis is the standard of care in most renal transplant programs. Kasiske BL *et al.* advocates that no recent guidelines address the optimal drug, dose or duration of antibiotic prophylaxis or antibiotic susceptibility of UTI isolates in post-transplant patients.

In our study we were using Trimethoprime-sulphamethaxazole as prophylaxis for six months after kidney transplant surgery. Urinary culture and sensitivity are carried out due to high level of antibiotic resistant of urinary pathogens of renal transplant recipients (25). Most of the UTI episodes occur in the first three months of post-transplant (26). The most frequent organism's isolates from the renal transplant recipient were *E. Coli*, Klebsiella, Enterococcus, pseudomonas (26). Sharma *et al*. demonstrated *E. coli* as a common isolate followed by staphylococcus, Enterococcus and pseudomonas. We also found E coli in 16 patients (59.25%) as the leading cause of UTI in renal transplant recipients. The second most common organisms detected in our study were Candida albicans in 5 patients (18.5%) which followed by Enterococcus in 3 patients (11.11%), Klebsiella in 2 patients (7.4%) and pseudomonas in one patients(3.7%) . Roberto Rivera Sanchez *et al.* (16) demonstrated ciprofloxacin resistance was observed in 22% and ampicillin in 33% against isolated gram negative organisms. In our study we observed ampicillin resistance in 26 % and ciprofloxacin resistance in 33 % against an isolated gram negative organism.

CONCLUSION

This study confirmed that UTIs remain a major problem in renal transplant recipients. The female gender, increasing age and uncontrolled hyperglycemia are the risk factors for UTI in renal transplant recipients. There is high resistance to ampicillin and quinolones in renal transplant recipients.

Conflict of Interest:

Authors declare no conflict of interest.

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