Prevalence and Antibiogram of Urinary Tract Infections in Renal Transplant Recipients at a Tertiary Care Hospital in North India

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Abstract

Introduction: Although, urinary tract infections (UTI) remain the most common cause of mortality and morbidity in renal allograft recipients, there is scarce data from India on the etiology and antibiogram of UTI post kidney transplantation. Therefore, the current study was undertaken to evaluate the prevalence, etiology and the antibiogram of pathogens causing UTI in this cohort.

Methods: Renal allograft recipients enrolled during the study period were screened for UTI by standard microscopy and routine culture on the day of admission and subsequently every 3rd day post-surgery till discharge. If UTI was present, the etiological agent and its antibiogram were recorded along with the demographic details of the patients.

Results: The prevalence of UTI post-transplantation at our centre was 30%. E.coli and Klebsiella pneumoniae were the most common organisms isolated in 42% and 39% cases, respectively. Majority of patients developed UTI on Day 6 (36.6%) and Day 9 (36.6%) post-transplant. Our study revealed a high percentage of resistance to commonly used 1st and 2nd line antibiotics like third generation cephalosporins (96.6%), fluoroquinolones (96.6%), and aminoglycosides (56.7%) and carbapenems (55.2%).

Conclusion: Considering the high prevalence of UTI and antibiotic resistance rates in kidney transplant patients in our study, there is an urgent need for developing hospital based local antibiogram for appropriate management of UTI. Fosfomycin as an empirical therapy might be a useful choice for adequate coverage of potential pathogens at our centre. Further multi-centric studies on a larger sample size are recommended from India for formulating antibiotic policy.

Introduction

Urinary tract infections (UTI) remain a common cause of mortality and morbidity post renal transplant. It is well-documented that renal transplant recipients are more likely to develop an episode of UTI as opposed to the general population. The reported prevalence of UTI in renal recipients in the past decade ranges between 13 to 80% across various studies. The Spanish Network for the study of Infection in Transplantation (RESITRA) described an incidence of UTI of 0.45 episodes per 1000 transplantation days among 2052 renal transplant patients followed for 3 years. Urinary tract infection in renal transplant patients constitute of approximately 40-50% of all infectious complications in the post-transplant period.

The established risk factors for acquiring a UTI in kidney transplant patients are urinary bladder catheterization, cadaveric kidney transplant, abnormalities of the native kidney or the allograft (such as vesicoureteral reflux), rejection episodes, and use of immunosuppressive drugs, gender, age, invasive urological maneuvers, as well as hospitalization itself.

With the emergence of Multi drug resistant organisms (MDROs), especially in gram negative bacteria, management of patients with UTI...
post transplantation is becoming exceedingly difficult. Therefore, knowledge of etiology of UTI and local antibiogram of the pathogens in kidney transplant patients is imperative for early diagnosis of UTI and its management to minimize rejection episodes.

Data from India on UTI prevalence, etiology and antibiogram in post renal transplant patients is scarce. In recent years, a few studies from North and South India on UTI in kidney transplant patients have reported a considerably high prevalence of UTI in renal transplant patients. This study aims to assess the prevalence of UTI, its etiology and antibiogram in renal transplant patients.

**Materials and Methods**

This was a hospital based retrospective as well as prospective observational study conducted at Sir Ganga Ram Hospital, a 675 bedded tertiary care hospital. The study involved the department of Clinical Microbiology & Immunology and Department of Nephrology. The study included 100 consecutive pediatric and adult patients, who had undergone renal transplantation during the 6 month study period. Chronic kidney disease (CKD) patients admitted for renal transplant surgery but failing to undergo transplant surgery due to medical/surgical complications were excluded from the study.

**Methods**

Baseline demographics of all patients including age, sex, type of donor—whether cadaveric or live were recorded. The patients were screened for UTI on the day of admission (Day 0) and subsequently every 3rd day till discharge by performing routine microscopy and urine culture. A positive urine culture (bacterial growth of ≥ 10⁶cfu/ml) in the presence of significant pyuria (pus cells ≥ 10/ ul) was defined as UTI. Phenotypic identification of organisms till species level was done using MALDI-TOF MS (Biomerieux Marcy l Étoile, France). Antibiotic susceptibility testing (AST) was performed using automated systems VITEK 2 systems (Biomerieux Marcy l Étoile, France) and interpreted according to Clinical and Laboratory Standards Institute (CLSI) interpretative guidelines. The day of the UTI was recorded to assess the time of development of UTI post-transplantation.

**Statistical analysis**

Data collected in a predesigned performa was entered in MS EXCEL Software. Data including demographic details of study cases and variables pertaining to the details of UTI episodes if any, viz. the time of infection from the day of transplant, the etiology of UTI and the antibiotic susceptibility results of the organisms were documented. Descriptive statistics were analyzed using SPSS software version 17.0. Continuous variables were presented as mean ± SD. Categorical variables were expressed as frequencies and percentages. The Pearson’s chi-square test was used to determine if there is a relationship between two categorical variables. P<0.05 was considered statistically significant.

**Ethical clearance**

The study was approved by the Institutional ethics Committee (Reference letter number: EC/10/18/1417) prior to the start of the study.

**Results**

**Demographic data**

A total of 100 patients (males: n=87, females: n=13) undergoing renal allograft transplant were included in the study. The overall prevalence of UTI among the study population was observed to be 30%. The mean age of the study population was 39.4 years, ranging between 12 to 67 years. The prevalence of UTI was maximum in the age group between 26 years to 50 years (56%), while it was 19 % and 25 % in the age groups between 0 to 25 years and 50 to 75 years, respectively, and was not significantly associated with UTI (p= 0.305). The percentage of males and females developing UTI post kidney transplant was observed as 29.9% (26/87) and 30.8% (4/13), respectively (p =1.00). The overall length of stay (LOS) of patients ranged from 10 days to 50 days with an average of 16.8 days. In patients developing UTI, the LOS was 18.3 ± 4.4 days against 16.2 ± 6.3 days in patients who did not develop UTI post transplantation (p=0.007). The average duration of catheterization post-transplant was 7.4 days ranging between 6 to 21 days. Patients developed UTI between 3 to 18 days post renal transplant (Mean= 6.7 days). The majority of UTIs occurred on Day 6 (36.6%) and Day 9 (36.6%) post-transplant.

A total of 31 microorganisms were isolated from the 30 patients, as 1 patient had poly microbial infection due to Enterococci spp. and Candida spp. Out of these 31 organisms, 28 (90.3%) were by gram negative bacteria (GNB),
and 2nd line antibiotics were observed in enterobacteriaceae in our study as: Ceftriaxone (96.6%), Ciprofloxacin (96.6%), Amikacin (58.7%), Piperacillin-tazobactam (62.1%) and Meropenem (55.2%). We also observed 10% resistance to colistin in enterobacteriaceae (Figure 2).

Discussion

UTI has been observed as the most common bacterial infection post renal transplantation. Once thought of as a benign pathologic process, UTI has emerged as a potential threat to the function and survival of the graft kidney in renal allograft recipients.

In the present study, we report a prevalence of 31% UTI among renal allograft recipients. A comparable prevalence of 33% and 33.3% have been reported in previous studies by Shirazi et al., and Gondos et al., respectively. Studies from across the world, including Mexico, Brazil, Libya and those conducted in the African-American belt also report such high prevalence of UTI in this susceptible cohort.

In India, previous studies from New Delhi and Telangana reported a prevalence of 32.86% and 41.9% UTI post transplantation. The high prevalence of UTI in kidney transplant patients in various studies could be explained due to the use of high dose immunosuppressive agents, surgical trauma and the presence of post-operative indwelling catheters and ureteric stents.

The mean age of our study population was 39 years. Mohan et al., reported a similar age of transplant patients in their study (32.4 years ± 10.2 years). In contrast, data from the West particularly America and Europe shows higher mean age of population in kidney transplant patients (Mean= 54 years). The younger mean age group of kidney transplant patients in our study could be due to higher prevalence of uncontrolled diabetes mellitus and hypertension in the Indian population as compared to Western countries.

In our study we did not observe a significant association between gender and UTI post kidney transplantation which is in concordance with other studies.

The etiology of UTI is varied in different hospital settings but the current data suggest UTI due to GNB remains the leading cause of UTI, similar to the results of our study (Fig1). In our study, E.coli (39%) and Klebsiella pneumoniae (42%) were the leading causes of UTI. Comparable results were reported in a study by Menegueti et al., conducted on 1,847 urine cultures from kidney transplant patients. Klebsiella pneumoniae (36%) and E.coli (20%) were most frequent pathogens causing UTI in their study. In contrast, a recent study from New Delhi reported higher rates of UTI due to E.coli (72.46%) post renal transplantation surgery. E.coli and Klebsiella being a major component of fecal flora are most likely introduced into the urinary tract through catheterization, thereby resulting in frequent UTIs due to these organisms.

UTI in renal allograft recipients are usually hospital acquired infections as they are acquired after 48 hours of hospital admission. Our study showed high rates of UTI due to Multidrug resistant organisms (MDROs). ESBL producing Enterobacteriaceae and carbapenem resistant Enterobacteriaceae (CRE) rates were observed as 96.6% and 55.2%, respectively, in our study. Another Indian study conducted on renal allograft recipients in 2014 reported rates of 46.6% and 33.3% ESBL and CRE producing pathogens, respectively. Similarly, Origuen et al., compared patients between 2002 and 2004 with another cohort between 2011 and 2013 and observed the progressive increase in MDR pathogens and ESBL producers from 43.9% to 67.8% and 6.6% to 26.1%, respectively. The rate of CRE (1-3%) reported in Western data is low compared to that reported from India. The possible reason for high rates of MDROs in our study may be attributed to high prescription of antibiotics at our centre (189 Daily Defined Doses/100 bed days). Our hospital being a referral tertiary care centre with a dedicated kidney, liver and bone marrow transplant units has admissions of critical patients often with high case mix index (CMI) who require higher prescription of antibiotics which may contribute to the emergence of MDROs. In our study population, the patients received an average of 7.4 days of empirical antibiotics before developing UTI. In a large study of over 1500 kidney transplant recipients by Yuan et al, use of broad-spectrum antibiotics for 5 days or more within 1 month before UTIs was associated with more frequent UTIs due to MDROs.

UTI in kidney transplant patients due to MDROs like ESBL and CRE have shown to result in impaired graft function or graft loss and increased length of stay. UTI by CRE may warrant escalation of antibiotic therapy by polymyxins as the last resort antibiotics. However, colistin administration is fraught with complications due to its nephrotoxicity. Nephrotoxicity associated with colistin (43-60%) in kidney transplant patients is potentiated by the use of concomitant nephrotoxic agents, like calcineurin inhibitors. CRE are often susceptible to fosfomycin and thus fosfomycin may be an attractive antibiotic therapy in UTI due to CRE, while it poses challenges for its sensitivity testing. At our centre cefuroxime is often used as an empirical treatment of UTI before urine culture and sensitivity results are available. The antibiotic of our study suggests that this may be inappropriate in the current situation due to high prevalence of MDROs and requires urgent revision of antibiotic policy. We recommend the use of fosfomycin as an empirical therapy for UTI for adequate coverage of potential pathogens and escalate or de-escalate as quickly as possible based on susceptibility results. Similarly, Bader et al also suggest the use of higher antibiotics like aminoglycosides and colistin as alternatives in MDR Gram-negative UTIs in their study population based on their local antibiotic.

Although our study results provides an important insight to the prevalence and antimicrobial of UTI in kidney transplant patients at our centre but interpretation and extrapolation of our study results is limited by the small sample size of our study. Therefore, multi centric studies on a large population cohort may be required to formulate antibiotic guidelines for the early and appropriate treatment of UTI.
in the renal allograft recipient.

References


