

Full Length Research Paper

## Urinary tract infections in Saudi renal transplant recipients

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Urinary tract infections (UTIs) are common post-renal transplant complications. During the first month post-transplantation, bacterial septicemia due to UTIs is an important cause of morbidity and mortality. The incidence, risk factors and causative bacteria of UTIs were assessed in 27 renal transplant recipients (RTRs). Bacterial UTI was diagnosed based on urine culture that was positive for bacterial growth greater than  $10^5$  colony-forming unit (CFU)/ml. The average age of the participants was  $41.3 \pm 16.2$  years, ranging from 16 to 73 years. Male RTRs were 51.9% (N = 14) and females were 48.1% (N = 13). Patients who received kidneys from living-related donors were 63.0% (N = 17) and those who received cadaveric kidneys were 27.0% (N = 10). Incidence of urinary tract infections post-renal transplant was 55.5% (N = 15). Gender (69.2% of the female RTRs developed UTI versus 30.8% of the males) and age (66.7% of the RTRs  $\geq 50$  years developed UTI) seemed to be risk factors for post-renal transplant UTIs. *Escherichia coli* was the most common pathogen (53.3%, N = 8) followed by *Pseudomonas aeruginosa* (20%, N = 3). Most of the UTIs (73.3%) were detected within one month post-renal transplant. Recurrent infection was observed in 40.1% of the patients. The implication of this study is the need to implement a new prophylaxis regimen that takes into consideration the causative bacteria and its antibiotic sensitivity.

**Key words:** Urinary tract infection, kidney, transplant, incidence, *Escherichia coli*.

### INTRODUCTION

Renal transplantation is the treatment of choice for patients with chronic renal failure resulting from most causes (Djamali et al., 2006). Urinary tract infections (UTIs) are common post-renal transplant complications (Al-Hasan et al., 2011) and it is the most frequent infection in renal transplant recipients (RTRs) (Fiorante et al., 2011; Mitra and Alangaden, 2011). More than 80% of RTRs experience at least one episode of infection during the first year post-transplantation (Rubin and Tolkoff-Rubin, 1991). Furthermore, bacterial septicemia due to

UTIs in the first month post-transplantation is an important cause of morbidity and mortality (Nielsen and Korsager, 1977; Peterson et al., 1982; de Souza and Olsburgh, 2008).

Renal transplant recipients are usually immunosuppressed and as a result they are at higher risk of developing infections (Ahmed et al., 2008; Giullian et al., 2010). In addition, during the post-operative period, they are exposed to urethral and intra-vascular catheterization and to invasive instruments (Rubin et al., 1981; Rubin and

**Table 1.** Incidence of UTI among transplant patients according to gender, sources of the transplanted kidney and age.

Sample		Developed UTI	Did not develop UTI	Total
Gender	Male	6	8	14
	Female	9	4	13
	Total	15	12	27
Source of Kidney	Living-related	10	7	17
	Cadaveric	5	5	10
	Total	15	12	27
Age	< 30	4	3	7
	≥ 30 and < 40	3	3	6
	≥ 40 and < 50	2	3	5
	≥ 50	6	3	9
	Total	15	12	27

Tolkoff-Rubin, 1991; First, 1993; Alangaden et al., 2006; Guillian et al., 2010). It has been shown that early catheter removal resulted in a reduced incidence of UTI (Rabkin et al., 1998; Crouzet et al., 2007). Other reported risk factors are gender, age and the source of the transplanted kidney. A retrospective cohort study including 213 patients found that the significant risk factors for post-transplant UTI were advanced age, female gender, reflux kidney disease, use of azathioprine and cadaveric donors (Chuang et al., 2005).

Due to the impact of infectious diseases on the survival of the graft and the patient (Dupont et al., 2010), prevention and treatment of the infection play an important role in the overall success of the transplant (Ahmed et al., 2008). Accordingly, this current work is a pilot retrospective study that reports the incidence of UTIs, time of infection and causative organisms of UTIs among Saudi post-renal transplant recipients. This study is considered essential for the proper prevention and treatment of post-renal transplantation UTI's.

## METHODOLOGY

In this retrospective study, 27 adult renal transplant patients' charts at the renal transplant unit, at King Abdulaziz Medical City at the National Guard Health Affairs, were reviewed. The patients' age, gender and whether they received a living-related or a cadaveric kidney were recorded. Bacterial UTI was diagnosed based on urine culture that was positive for bacterial growth greater than  $10^5$  CFU/ml and white blood cells (WBCs) count was also obtained. The Infectious Diseases Society of America did not put restriction on the screening or treatment protocols in asymptomatic bacteriuria in renal transplant recipients (Nicolle et al., 2005). All the RTRs received cefazolin 1 g pre-op and norfloxacin 400 mg q.d for four weeks post-op as a prophylaxis. In addition to antibacterial agents, the patients received the following immunosuppressant combina-

tion; cyclosporine or tacrolimus, mycophenolic acid and prednisone. Finally, it must be mentioned that the results of the study are presented as descriptive statistics.

## Urine culture

A 0.001 ml (small) calibrated inoculating loop was dipped into the urine sample and then was allowed to drain. A loop full was delivered to the middle of one side of a blood agar/MacConkey biplate making one vertical streak, then a cross streak at 90°. This streaking was repeated for the second side. Then, the plate was promptly incubated at 35 to 37°C aerobically overnight. After 24 h, the number of colonies on the media in each plate was recorded. The species with > 50 colonies in the plates showing potentially significant growth were identified and then were subjected to antimicrobial susceptibility testing. If the species are mixed, the predominant species (>100 colonies) were identified and then were subjected for antimicrobial susceptibility testing. All cultures exhibiting significant growth were identified using VitekII-XL system (BioMerieux, France®).

## RESULTS

The results are summarized in Tables 1, 2 and 3. The mean age of the 27 participants was  $41.3 \pm 16.2$  years, with a range of 16 to 73 years. As seen in Table 1, the gender distribution of the RTRs was 51.9% males and 48.1% females. Of all the RTRs, 63.0% received their kidneys from living-related donors and 27.0% received cadaveric kidneys. More than half of the participants developed post-transplantation UTIs (55.5%) (Table 1). In these RTRs, bacterial counts were  $> 10^5$  CFU/ml and WBC counts ranged from "0 to 2" to "> 30" WBC/mm<sup>3</sup>. Female RTRs had a higher incidence of UTI (69.2%) compared to male RTRs (30.8%). Of the 15 RTRs who developed UTIs, 66.6% received their kidneys from living-

**Table 2.** Distribution of UTI in female and male transplant patients according to the source of the transplanted kidney.

Gender	Source of the transplanted kidney		Total
	Living-related	Cadaveric	
Male	5	1	6
Female	5	4	9
Total	10	5	15

**Table 3.** The causative bacteria in transplant patients who developed UTI and the time of infection.

Causative bacteria	Time of infection		Number of patients
	< 1 month	> 1 month	
<i>E. coli</i>	5	3	8
<i>P. aeruginosa</i>	3	0	3
<i>E. coccus</i>	1	0	1
<i>E. bacter</i>	1	0	1
Acinetobacter	1	0	1
Citrobacter	0	1	1
Total	11	4	15

related donors and the rest received their kidneys from cadaveric donors (Table 1). It is worth mentioning that of the 17 patients who received kidneys from living-related donors, 58.8% developed UTI, while of the 10 patients who received cadaveric kidneys, 50.0% developed UTI, Table 1. With regard to age, 40% of RTRs who developed UTIs were  $\geq 50$  years of age. Alternatively, it can be seen that 66.7% of patients who are  $\geq 50$  years of age developed UTIs while the incidence was 40 to 57.2% for other age groups. The average age of the patients who developed UTI was  $42.5 \pm 18.5$  years and those who did not develop UTI was  $39.9 \pm 13.4$  years.

As seen in Table 2, 55.6% female RTRs who developed UTI received kidneys from living-related donors and 44.4% received cadaveric kidneys. On the other hand, 83.3% of the males who developed UTI received kidneys from living-related donors and 16.7% received cadaveric kidneys.

With regard to the causative bacteria, Table 3, *E. coli* was the most common pathogen that caused UTIs among RTRs (53.3%) followed by *P. aeruginosa* (20%) then by *E. coccus*, *E. bacter*, *Acinetobacter* and *Citrobacter* (6.7% for each of them). In general, most of the UTIs (73.3%) were detected within the first month post-transplantation as the majority of infections caused by *E. coli* (62.5%), and all the infections caused by *P. aeruginosa* were detected during the first month post-transplantation. Recurrent infection was observed in 40.1% of the RTRs (39% for females and 40.6% for males) and they occurred  $23 \pm 13$  days after the transplant.

## DISCUSSION

The incidence of post-renal transplantation UTIs is highly variable with reported ranges of 6 to 86% (Säemann and Hörl, 2008; Dupont et al., 2010) to 10 to 98% (de Souza and Olsburgh, 2008). The variability in the incidence rates of post-transplantation UTIs was attributed to variations in study design, local outbreaks, definition and diagnostic criteria. The incidence in the current study is 55.5%, which is well within the previously reported values (Rubin, 1993). This rate is considered substantial and requires attention.

The facts that almost 70% of the females who received renal transplants developed UTIs (compared to 31% of the males) and that 70% of the all RTRs who developed UTIs were females, implies that female RTRs are more prone to UTIs. In general, female recipients are at higher risk than male recipients (Rabkin et al., 1998; Memikoğlu et al., 2007; Csete, 2008; Lorenz and Cosio, 2010). A recent study conducted in Tunisia has found that female gender was the only risk factor for developing UTI in RTRs (Barbouch et al., 2012). Abbott et al. (2004) found that the risk for UTI was the same for either sex during the first 6 months after transplantation; however, females tend to be at higher risk than men beyond that period. The anatomical differences in the urinary tract of males and females has been blamed for the higher incidence of UTIs in females (Foxman, 2010; Barbouch et al., 2012).

The incidence of UTIs was slightly higher in RTRs who received kidneys from living-related donors (58.8%) than in RTRs who received cadaveric kidneys (50%). These

differences might not be statistically significant, especially when the uneven distribution of the source of kidneys in this study sample is taken into consideration. Nevertheless, these results show high incidence of UTI regardless of the source of the transplanted kidney. Within female RTRs, a similar trend was noticed as 55.6% transplanted with living-related kidneys and 44.4% transplanted with cadaveric kidneys developed UTIs. While among male RTRs, 88.3% of the recipients who developed UTIs received kidneys from living-related donors. Although the results in this study were not conclusive, there is sufficient evidence from literature to support the fact that the source of the transplanted kidney is a risk factor for post-transplantation UTI.

Some researchers have concluded that transplanting a kidney from living-related donors is a risk factor for developing UTI (Charfeddine et al., 2005; Tabatabaei et al., 2006), while others concluded that a cadaveric kidney is a risk factor (Midtvedt et al., 1998; Dantas et al., 2006; Säemann and Hörl, 2008; Rivera-Sanchez et al., 2010). Rigorous investigation into the medical history and extensive laboratory testing of living-related donors would help in reducing the incidence of UTIs in recipients of kidneys from these donors. It is worth mentioning that it has been proposed that the delayed graft function after renal transplantation may contribute to the observed incidence of UTI in recipients of cadaveric kidneys (Lorenz and Cosio, 2010).

With respect to age, the current results imply that advanced age of RTRs is associated with a higher incidence of UTIs. It has been shown that advanced age is a risk factor for developing UTIs in RTRs (Dharnidharka et al., 2006; Säemann and Hörl, 2008; Snyder et al., 2009). The current investigation found that 66.7% of the RTRs who are  $\geq 50$  years of age developed UTI which is in agreement with Trouillhet et al. (2005) finding that RTRs who are 65 years or older have 70% chance of developing UTI. There was not a large difference between the average age of RTRs who developed UTIs and that of those who did not develop UTIs. These current results are similar to results of a study that was performed on a much larger sample size (500 patients) which found that the average ages of RTRs who develop UTIs and of those who did not were  $45 \pm 12.7$  and  $43 \pm 12.5$ , respectively (Chuang et al., 2005).

Several pathogens can cause UTIs in RTRs which are similar to those implicated in UTIs in non-immuno-compromised patients. In the current investigation, *E. coli* was found to be the most common causative agent of UTIs, followed by *P. aeruginosa*. Other pathogens were *E. coccus*, *E. bacter*, *Acinobacter*, and *Citrobacter*. These results are in-line with previous reports. Several reports have found that *E. coli* is the most frequent causative pathogen of post-renal transplantation UTI (Rice et al., 2006) and its implication in UTI can be as high as 58%

(Fiorante et al., 2010) or 71% (Valera et al., 2006; Khawcharoenporn et al., 2012) followed by *P. aeruginosa* (Hsueh et al., 2011). It has been suggested that the uropathogenic serotypes and adherence factors of *E. coli* contribute to allograft injury in RTRs (Rice et al., 2006). Furthermore, a multi-drug resistant strain, *E. coli ST131*, has been reported as a possible threat to renal transplant recipients (Johnson et al., 2010).

The majority of UTIs reported in this study were detected within one month of renal transplant. Usually, UTI during the first three months after transplantation is frequently associated with pyelonephritis, bacteremia, and a high rate of relapse with conventional antibiotics (Rubin et al., 1981). A recent review of the literature has concluded that in the first 3 months post-transplantation, pyelonephritis is the most common presentation and it is associated with a relatively high incidence of bacteremia while in the following periods, most episodes are subclinical and asymptomatic (Dupont et al., 2010). The results in the current study are in agreement with previously reported data.

Examination of the available literature reveals that 35 to 74% of UTIs were detected one month after transplantation (Renoult et al., 1994; Gołębiowska et al., 2011; Valdez-Ortiz et al., 2011). On the other hand, the incidence of UTI one-year post transplantation is less than 14% while the incidence of UTI secondary to bacteremia is less than 7% (Green et al., 2011). Although there is general agreement that UTI occurring six months or later after transplantation is relatively benign and can be treated with short term antibiotics, there are reports that such late UTIs might be associated with increased risk of mortality and graft loss (Abbot et al., 2004). The latter finding was a result of a retrospective cohort study on 28,942 Medicare primary renal transplant recipients in the United States Renal Data System (USRDS) database.

The recurrent UTI rate found in the current study is similar to previous reports which put the recurrent rates at 44.4 to 55% (Laboudi et al., 2008; Pinheiro et al., 2010). Chuang et al. (2005) have found that post-transplantation UTIs significantly increase mortality but not graft survival. Therefore, prevention of UTI in high-risk renal transplant recipients or those with recurrent UTI may possibly decrease post-transplant mortality.

## CONCLUSION

The results of this study have confirmed that the problem of UTIs in RTR's is significant, and gender and advanced age are possible risk factors. The recurrence rate was also considered to be alarming. The most important implication of this work is the need for the implementation of a new prophylaxis regimen at the renal transplant unit at King Abdulaziz Medical City at the National Guard Health

Affairs that takes into consideration the epidemiology of the current results.

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