

URINARY TRACT INFECTIONS IN RENAL TRANSPLANT RECIPIENTS: A SINGLE CENTER STUDY

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ABSTRACT

Objective: To determine the types and frequency of urinary tract infections among renal transplant recipients.

Methods: A total of 83 renal transplant recipients who attended the Nephrology out patient clinic at King Hussein Medical Center, during the two months of study period (September-November, 2005) were included in the study. Routine urine analysis and urine culture were performed in all patients. The study group had normal kidney function and minimum period of four weeks post renal transplant.

Results: Fifty-six (67%) were males and 27 (33%) were females, their ages ranged between (16-60) years with a mean of 35.9 years. The mean duration of transplantation was 26.4 months, and the mean serum creatinine was 1.14mg/dl. The source of their grafts were living related donors in 71 recipients (85.5%) and living unrelated donors in 12 recipients (14.5%) and none were from deceased donors. Seven recipients (8.4%) were on double immunosuppression therapy (calcineurin inhibitor and steroid) while 76 (91.6%) were on triple immunosuppression therapy. The frequency of urinary tract infections was 28.9%. Asymptomatic urinary tract infections occurred in 9.6%, however, symptomatic urinary tract infections occurred in 19.2%. Females constituted 75% of the asymptomatic group, while males among the symptomatic group were 87.5%. About two-thirds of isolated microorganisms were E.Coli (62.5%). Males with renal transplants had higher frequency of symptomatic urinary tract infections, particularly if the graft was from living unrelated donor. All patients with pre transplant vesicoureteric reflux had symptomatic post transplant urinary tract infections, despite pretransplant unilateral or bilateral nephro-ureterectomy for patients with grade IV vesicoureteric reflux.

Conclusion: Almost one-third of renal transplant recipients will develop urinary tract infections. Vesicoureteric reflux should be treated before renal transplant. Patients should be evaluated for urinary tract infections during routine out patient follow-up, particularly those with post transplant diabetes mellitus

Key words: Asymptomatic bacteriuria, Kidney transplantation, Immunosuppression, Urinary tract infections

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Introduction

The invasion of the urinary tract by uropathogenic bacteria leading to urinary tract infections (UTI's), is a major health problem affecting millions of

people every year with a tremendous economic impact, and might in the worst-case lead to kidney damage and chronic kidney disease.^(1,2)

Urinary tract infection is the most common

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bacterial infection seen in renal transplant recipients, involving as many as 35–79% of those patients.^(3,4,5) While most of infections occurring in the first month post renal transplantation are the same nosocomial infections that occur in surgical patients who are not in a state of immunosuppression,⁽⁶⁾ after the first month of transplantation, the nature of infectious diseases in the transplant recipient changes, as the steady state of immunosuppression will have its effects by that time.⁽⁶⁾

Patients with chronic kidney disease are at risk of infections in general. This risk is maximized when they undergo renal transplantation. UTI's occurring after renal transplantation have been considered to be benign, recent studies suggest that UTI's even if late after renal transplantation have definite risks on the long term graft function.^(7,8)

Urological maneuvers post renal transplantation (indwelling catheters) also carry the risk of increased incidence of UTI's.⁽⁹⁾ It is mentioned that antibiotic prophylaxis as well as early removal of indwelling catheters may lower the incidence of post renal transplantation UTI's.⁽¹⁰⁾

Our patients occasionally report symptoms of UTI's, and as UTI's can be asymptomatic we conducted this study to determine the types and frequency of urinary tract infections among renal transplant recipients.

Methods

This study was conducted at the Nephrology out patient clinic at King Hussein Medical Center (KHMC), Amman-Jordan during the period between September and November 2005. All renal transplant recipients attending the clinic for regular follow up routinely have urine testing beside the usual clinical and laboratory evaluations.

Inclusion criteria were normal kidney functions, where serum creatinine less than 1.4 mg/dl was considered the cutoff point, and time post renal transplantation of more than four weeks (i.e. after removal of the double J catheter). Based on these criteria, 83 patients were included in the study. The original cause of renal failure, the source of the graft and the immunosuppressive regimen, as well as history of pretransplant UTI's and the presence of pretransplant predisposing factors for UTI's were all noted.

Clinical evaluation included history with emphasis on urinary symptoms (frequency, dysuria, graft and supra pubic pain), and complete physical examination. Laboratory evaluation included kidney function test, liver function test, lipid profile, urine analysis (routine and microscopy) and urine culture for all patients. Calcineurine inhibitors (CNI) were also monitored either by trough level or by C2 level, depending on the type of CNI.

Positive urinary cultures were defined as bacteriuria with more than 10^5 colony forming unit (CFU)/ml of mid stream urine, while asymptomatic bacteriuria was defined as two consecutive urinary cultures done two weeks apart with more than 10^5 CFU/ml of midstream urine in asymptomatic patients.

All patients with positive urine cultures whether symptomatic or asymptomatic were treated for two weeks with appropriate antibiotics according to the sensitivity results. Those patients were also followed up until their urine cultures were negative.

Results

Eighty-three renal transplant recipients, attending the nephrology out patient clinic at KHMC during the period between September-November 2005 who fulfilled the inclusion criteria, were specifically asked about symptoms of urinary tract infections and were studied for urinary tract infections.

There were 56 males (67%) and 27 females (33%), their ages ranged between 16 and 60 years with a mean of 35.9 years. The mean post transplant duration was 26.4 months, with a range of 1-160 months. Sixteen patients (19.3%) had pre transplant predisposing factors for UTI's; vesico ureteric reflux (VUR) in six (7.2%) VUR grade IV in four patients and grade II in two patients, diabetes mellitus in eight (9.6%), obstructive uropathy in one (1.2%) and urolithiasis in one (1.2%).

A total of 71 patients (85.5%) had their graft from living related donors, while 12 patients (14.5%) had their grafts from living non-related donors (done out side Jordan) and none had their grafts from deceased donors. The immunosuppressive regimen was triple (CNI, mycophenolate mofetile and prednisolone) in 76 patients (91.6%) and double in seven (8.4%) patients (Table I).

Table I. Demographic data of the study group

Age, range (mean)	16-60 years (35.9y)
Gender: Males n (%)	56 (67.4)
Females n (%)	27 (32.6)
Duration of Transplantation, range (mean)	1-160 months (26.4)
Source of graft: LRD*, n (%)	71 (QAMH, KHMC [^]) 85.5
LNRD**, n (%)	12 (Iraq, Egypt, Pakistan) 14.5
Immunosuppression: Double, n (%)	7 (8.4)
Triple, n (%)	76 (91.6)
Pretransplant risk factors:	
Vesicoureteric reflux, n (%)	6 (7.2)
Obstructive uropathy, n (%)	1 (1.2)
Urolithiasis, n (%)	1 (1.2)
Diabetes, n (%)	8 (9.6)

*LRD: living-related donor; **LNRD: living non-related donor; ^QAMH: Queen Alia Military Hospital, KHMC: King Hussein Medical Center

Symptomatic UTI's were seen in 16 patients (19.2%) (Table II), while asymptomatic UTI's were discovered in 8 patients (9.6%) (Table III).

Table II. Symptomatic group

Age, range (mean)	20-52 year (31.4y)
Gender: Males n (%)	14 (87.5)
Females n (%)	2 (12.5)
Duration of Transplantation, range (mean)	1-33 months (16.5 m)
Source of graft: LRD*, n (%)	12 (QAMH [^] , KHMC ^{^^}) (75)
LNRD**, n (%)	4 (Iraq, Egypt, Pakistan) (25)
Immunosuppression: Double, n (%)	-
Triple, n (%)	16 (100)
Pretransplant risk factors:	
Vesicoureteric reflux, n (%)	6 (37.5)
Obstructive uropathy, n (%)	-
Urolithiasis, n (%)	-
Diabetes, n (%)	-
Post transplant diabetes, n (%)	6 (37.5)

*LRD: living-related donor; ** LNRD: living non-related donor; ^QAMH: Queen Alia Military Hospital, ^^ KHMC: King Hussein Medical Center

Table III. Asymptomatic group

Age, range (mean)	22-52 year (35.7y)
Gender: Males n (%)	2 (25)
Females n (%)	6 (75)
Duration of Transplantation, range (mean)	1-126 months (47.8 m)
Source of graft: LRD*, n (%)	4 (QAMH [^] , KHMC ^{^^}) (50)
LNRD**, n (%)	4 (Iraq, Egypt, Pakistan) (50)
Immunosuppression: Double, n (%)	-
Triple, n (%)	8 (100)
Pretransplant risk factors:	
Vesicoureteric reflux, n (%)	-
Obstructive uropathy, n (%)	-
Urolithiasis, n (%)	-
Diabetes, n (%)	-
Post transplant diabetes, n (%)	2 (25)

*LRD: living-related donor; ** LNRD: living non-related donor; ^QAMH: Queen Alia Military Hospital, ^^KHMC: King Hussein Medical Center

Among the symptomatic group, males were 87.5%, while among the asymptomatic group, females were 75%. In the symptomatic group, 25% patients had their grafts from living non-related donors, while in the asymptomatic group, 50% had their grafts from living non-related donors. All patients with pre transplant VUR had symptomatic post transplant UTI's. Both symptomatic and asymptomatic patients were on triple immunosuppression. The mean time post transplant to report symptomatic UTI's or to uncover asymptomatic UTI's was obviously shorter among the symptomatic group (16.5 months) than among the asymptomatic group (47.8 months).

There were 23 patients with new onset diabetes mellitus post renal transplantation, of them eight patient (34.7%) had post transplantation UTI's, six patients in the symptomatic group, while the other two were in the asymptomatic group.

Results of urine culture showed that *E.coli* was isolated in 62.5%, *Klebsiella species* in 12.5%, *Pseudomonas* in 12.5%, *Proteous* in 4.2%, while other pathogens were isolated in 8.3% (Table IV).

Table IV. Isolated pathogens

Micro organism species	(%)
<i>E. Coli</i>	62.5
<i>Klebsiella</i>	12.5
<i>Pseudomonas</i>	12.5
<i>Proteous</i>	4.2
Others	8.3

Our study shows that asymptomatic UTI's is more common among patients with long duration after successful renal transplantation, and it is more common among females, also it is more likely to be found among patients who had their grafts from living non-related donors. We found both symptomatic and asymptomatic UTI's were among patients on triple immunosuppression, and all patients with pre transplant VUR developed symptomatic UTI's post transplantation despite pretransplant unilateral or bilateral nephro-ureterectomy for patients with grade IV VUR reflux.

Discussion

Urinary tract infections are still very common infection in renal transplant recipients, particularly during the first six months post transplant. UTI's have been reported to occur among renal transplant recipients in as many as 35% to 79% of patients.⁽⁴⁾ The major concern would be that sometimes simple infection in immunosuppressed patients can turn to disastrous outcome in form of bacteremia and even sepsis that may result in loss of the functioning graft or, even worse, loss of life.⁽⁵⁾

Urogenital anomalies and pathologies which predispose to UTI's may also lead to loss of renal function resulting in chronic renal failure. These anomalies and pathologies, if not corrected prior to renal transplantation will lead again to recurrence of UTI's which carries the risk of bacteremia and sepsis in the short term, and in the long term, repeated UTI's may lead to loss of the graft.

Our policy during pre-renal transplantation is to correct any correctable urogenital anomalies, and it is the routine practice to administer prophylactic antibiotics as well as early removal of indwelling catheter and surgical drains.

This study shows that the incidence of UTI's among our renal transplant recipients in total was 28.8%, which is less than what have been reported.^(4,5) We found the incidence of asymptomatic UTI's is 9.6% and that of the symptomatic UTI's was 19.2%, which is quite less than what has been reported;^(3,4,5) this may be explained by the strict and meticulous criteria to select patients at our center as the renal transplantation program is based on live - related donation, and the live – unrelated transplantation is prohibited by law in Jordan (live un-related kidney recipients in this study received their grafts out side

Jordan). These data are consistent with other studies, which showed low incidence of UTI's among live – related renal transplant recipients.⁽³⁾

The association between the type of immunosuppression and significant post transplant bacteraemia was relevant in this study, as all patients with post transplant UTI's, whether symptomatic or asymptomatic were on triple immunosuppression.

Although patients with pre transplant severe VUR (grade IV) underwent nephro-ureterectomy of the affected side, and if it was bilateral VUR, then bilateral nephro-ureterectomy had been done; all patients with pre transplant VUR regardless of the grade had symptomatic post transplant UTI's. This can be explained either due to reflux to the remaining ureteric stump, or reflecting undetected pre-existing urinary bladder dysfunction.

None of the patient with pre transplantation diabetes mellitus had post transplantation UTI's, while significant number of patients with post transplantation diabetes mellitus developed post transplantation UTI's. This is similar to what have been described in previous studies regarding pre transplantation diabetes mellitus,⁽¹²⁾ and post transplantation diabetes mellitus.⁽⁹⁾

E.coli was the most common organism responsible for the UTI's, followed by *Klebsiella* and *Pseudomonas spp.* Although other studies showed that the major cause of UTI's in renal transplant recipients was *Streptococci*,⁽³⁾ this was not the case in our study, but it was similar to what has been reported in other studies involving analysis of more than 11.000 positive urine culture results⁽¹¹⁾ and were also similar to other studies carried out on renal transplant recipients.⁽¹³⁾

Conclusion

UTI's were common complications among renal transplant recipients, should be looked for even if the patient was asymptomatic and should be treated promptly. Predisposing factors to UTI's must be identified and corrected before renal transplantation. Patients with post transplantation diabetes mellitus should be educated about their new onset diabetes and educated about the risks of UTI's.

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