ORIGINAL ARTICLE

Urinary tract infections in kidney transplant recipients 1st year after transplantation

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Background: One of the main causes of adverse complications following kidney transplantation is urinary tract infection (UTI). This study was done to define the incidence rate, clinical profiles, causative microorganisms, and UTI risk factors among kidney transplant recipients in Mashhad city. **Materials and Methods:** In this retrospective study, we perused medical files of 247 kidney recipients who underwent transplant surgery at Mashhad University Montaserie Hospital, during 2012–2014. All patients were followed for UTI during the 1st year after surgery. **Results:** 75 episodes of UTI developed by 152 pathogens in 56 (22.7%) of patients during 1-year follow-up. 26.6% of total UTIs were diagnosed within the 1st month after transplantation. The most frequently isolated uropathogens were *Escherichia coli* (55.3%, *n* = 84). The high rate of candiduria (8.5%) was observed, too. **Conclusion:** UTI is known as one of the hospitalization reasons in kidney transplantation recipients. Defining appropriate antibiotic prophylaxis against bacterial and fungal agents and early removal of urethral catheter are suggested to decrease posttransplantation complications.

Key words: Candiduria, *Escherichia coli*, follow-up, kidney transplantation, urinary tract infection

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INTRODUCTION

Kidney transplantation is the best choice for patient treatment with advanced chronic renal disease. Transplantation enhanced life expectancy and quality in these patients.[1-4]

Successful renal transplantation is depended on a good compromise between sufficient immunosuppression and adequate level of immune competence which avoid acute rejection and maintaining immunity to prevent infection occurrence, respectively.[5,6] Kidney transplant recipients are more sensitive to infections caused by many risk factors. They include immunosuppression, concomitant states such as urinary reflux disease, diabetes, and renal calculi.[7] Despite noticeable progress in surgical procedure and immunosuppression after kidney transplantation, urinary tract infection (UTI) remains as an important problem in these patients.[8] UTI is the most frequency infectious complications, which is reported in up to 86% of transplanted cases.[9] It is considered as the most important risk factor for weak graft function, mortality, and morbidity.[2] Although infection mortality rate has declined from 50% to 5% within last 20 years; it remains as a severe complication posttransplantation, in particular since infections have altered epidemiology.[8] It is crucial to use the best microbiological diagnostic causal factors, which ascertain targeted therapy and reduce much use of antimicrobial drugs.[10]

Management of infectious complications is a big problem in kidney recipients.[11] The infection rate

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is different, regarding to environmental, social, and financial properties between countries all over the world; and different studies report various frequency, bacteria, and risk factors.[8] According to the importance of renal transplantation in Iranian patients and few studies about infections in kidney transplant recipients in Iran, this study was done to determine epidemiological, clinical, and subclinical characteristics and causative agents and patient-specific risk factors for UTIs in transplant recipients 1-year posttransplantation in Mashhad city.

MATERIALS AND METHODS

This single-center retrospective study was performed based on medical findings of kidney transplant recipients in Montaserie Hospital Transplant Center of Mashhad University of Medical Sciences(MUMS) city during 2012–2014.

Patients who underwent kidney transplantation during at least one year before the study, with complete medical records were entered in the present research. We omitted individuals who did not live in Mashhad city. Following variables were gathered for each patient: Transplantation date, gender, recipient age, donor type (cadaveric or live), medical comorbidities, chronic renal failure etiology, infection, the date of infection, and mean serum creatinine levels during infection. Transplantation techniques were accomplished using standard procedures by the same surgery team. Ureteral stent routinely used intraoperative for patients. Native patient's kidneys were not removed usually, and the graft kidney was set in the right or left side of iliac fossa.

Recipients who did not live in Mashhad and patients with incomplete clinical data or acute rejection after transplantation were excluded from the study. Patients received immunosuppressive therapy and antimicrobial prophylactics including prednisolone, cyclosporine, and mycophenolate moftile, statin drug, co-trimoxazole, and ceftriaxone after surgery. Isoniazid was prescribed for skin positive test recipients or donors. Recipients did not receive any drugs against cytomegalovirus (CMV). Methyl prednisolone/rabbit antithymocyte globulin was applied for antirejection treatment.

MacConkey and blood agar culture medium (Germany, Co Merck) were used. Urine culture and analysis were done according to Pourmand *et al.*'s study in 2013.[12]

UTI was defined based on clinical signs such as fever, urgency, dysuria, frequency, and pyuria. The signs were confirmed by positive urine culture (>10^5 cfu/mL), microscopic examination, leukocyte esterase stick, and/or nitrate. Causative pathogens were isolated from urinary cultures. It is necessary to collect bacterial culture specimen before antibiotic therapy.

All data were accurately recorded and analyzed with SPSS version 18 software (SPSS Inc., Chicago, IL, USA). Descriptive statistics including frequency, mean, and standard deviation were considered for all variables. Logistic regression models were used to distinguish independent risk factors for infection. All the analyses were two-sided. $P < 0.05$ was considered significant statistically. The study was approved by the Ethics Committee of Mashhad University of Medical Sciences (Code: 940940, Date: May 2016).

RESULTS

Two hundred and forty-seven renal transplant recipients including 146 males and 101 females were entered in this study. Their mean age was 34.94 ± 13.89 years (the youngest one was 6, and the oldest one was 66). All patients were followed-up for 1 year after transplantation. Medical comorbidities of kidney recipients were hypertension (n = 133; 53.8%), diabetes mellitus (n = 105; 42.5%), chronic obstructive pulmonary disease (n = 2; 0.8%), hepatitis (n = 12; 4.8%), dyslipidemia (n = 12; 4.8%), and other disease (n = 7; 2.8%).

Common causes of renal failure were hypertension (58 cases), diabetes mellitus (20 cases), polycystic kidney (34 cases), reflux nephropathy (24 cases), pyelonephritis (2 cases), lupus (2 cases). Renal failure occurred in 41 cases due to other chronic disease; the cause was indeterminate in 66 cases.

UTI incidence was 22.7% among kidney transplant recipients of this research. Seventy-five UTI episodes occurred by 152 pathogens in 56 patients. Forty-one patients had one UTI, 11 individuals had two UTIs, and four cases had three UTIs.

Demographic features of UTI and non-UTI subjects are summarized in Table 1. Univariate analysis demonstrated that solely female gender was an independent risk factor among different assessed parameters; it was associated with UTI risk (odds ratio=0.689; P = 0.001). The utmost frequent isolated microorganisms were *Escherichia coli*, coagulase-negative *Staphylococcus*, and *Klebsiella* spp. 26.6% of infection episodes occurred during the 1st month after transplantation. Meantime between transplantation and UTI occurrence was 79.5 ± 83.4 days. Causative organisms are presented in Table 2 based on infection time after transplantation. 12.5% of recipients who were 60 years or older developed posttransplant UTIs.

Bacteremia was developed in 13 patients, which it was originated from urinary tract in four cases. *Enterococcus*,

Table 1: Demographic features of 247 cases, who underwent kidney transplantation

	Female gender, *n* (%)	Age, mean±SD (range)	Cadaveric donor, *n* (%)
UTI$^+$ (*n*=56)	35 (62/5)	34.88±12.83 (8–66)	47 (83/9)
UTI$^-$ (*n*=191)	125 (34/5)	34.95±14.22 (6–65)	132 (69/1)
P	0.001	0.901	0.092

SD=Standard deviation; UTI=Urinary tract infection

Table 2: Pathogens diagnosed in infectious subject's in different times after transplantation

Microorganisms causes UTI	Months, *n* (%)				Total, *n* (%)
	0-3	3-6	6-9	9-12	
Bacterial					
Klebsiella	13	2	4	-	19 (12.5)
Escherichia coli	38	15	16	15	84 (55.3)
Enterococcus	1	-	-	-	1 (0.7)
Coagulase negative *Staphylococcus*	14	1	3	2	20 (13.2)
Streptococcus	6	-	-	-	6 (3.9)
Other	6	1	1	1	9 (5.9)
Fungal					
Candida albicans	9	-	1	3	13 (8.5)
Total	87 (57.2)	19 (12.5)	25 (16.5)	21 (13.8)	152 (100)

UTI=Urinary tract infection

E. coli, and *Klebsiella* were detected microorganisms in blood cultures. Nearly, 61.5% of bacteremia occurred during 3 months after transplantation; however, patients were taking Potent antibiotics during the first 3 months, they were taking strong immunosuppressive drugs too.

13.3% of UTIs happened during hospitalization period. The mean level of serum creatinine was 1.93 ± 1.26 at the detection time of UTI. 53 patients (15 in UTI cases and 38 in non-UTI cases) developed CMV infection. No deaths were reported due to UTI during 1-year follow-up.

DISCUSSION

Kidney transplantation is the best treatment for patients at the end-stage of renal disease (ESRD).[13,14] Number of kidney recipients is estimated more than 1.4 million worldwide, with 8% rising incident rate, annually.[15]

Indeed, abundant documents reflect general increment of infections in kidney transplant patients over the last decade. This trend is shift from cardiovascular disorders to infectious diseases as the main cause of death; many reports indicated admission rates enhancement for infections complications during the 1st year posttransplant.[16]

It seems that patients who receive allograft transplant are more susceptible to infections compared to general population.[17] There are accumulating evidence which express direct association between posttransplantation extent immunosuppression therapy and infection occurrence risk. It is not due to specific type of drugs while high dosage intake is related to fewer acute rejections and more infections occurrence, such as UTI.[16]

UTI is one of the causes of pyelonephritis, bacteremia, CMV infections, graft loss, and patient survivals rate reduction.[18] It is the frequent kind of infection in kidney allograft recipients with a varied range 6%–86%.[9] The significant variation in UTI reported rates may be due to local outbreaks, varying resistance incidences, postoperative medical care, center-specific immunosuppressive therapy, hygienic states, and different diagnostic criteria.[9,19] 22.7% of renal transplant recipients who were entered in this retrospective research developed at least 1 UTI episode during the 1st year after transplantation. Pourmand's study in Tehran in 2007 reported *Klebsiella* as the most found pathogen. UTI rate was 41.5% in their study.[20] UTI prevalence was lower in our center; the predominant causative agent was *E. coli* in this search; it is compatible with various others studies from worldwide.[6,21-26] Over half of infection episodes occurred during 3 months posttransplantation when an immunosuppression strategy was intensive in cited period.

Fungal UTI may cause serious complications that influence graft success and patient survival.[9] Valera *et al.* expressed that fungus microorganisms are cause of 3% of whole UTIs.[21] Candiduria incidence was 8.5% based on our results. 30% of septicemia originated from urinary tract which most isolated pathogen was *E. coli*. Dantas *et al*. declared that 60% of bacteremias are from this site.[27]

Most of ESRD occurred due to hypertension and unknown reasons in our studied population. The last one constitutes 26.7% of all ESRD causes, while it estimated to be 14.4% in other Iranians studies, 19.9% in Saudi Arabia and 14% in Qatar.[15] John *et al*. in Germany expressed that main primary ESRD causes were due to urinary tract malformation, glomerular disorders, and renal dysplasia and to a less scale due to metabolic disorders, polycystic kidney disease, and neurogenic bladder.[28] Iqbal *et al*. cited calculi disease, hypertensive nephropathy, glomerulonephritis, polycystic kidney disease, and diabetic nephropathy as kidney failure reasons, too.[29] Actually, hypertension could be related to kidney dysfunction and is not primary cause of renal failure.[30]

While infectious complications are described as important cause of death in kidney transplant patients, UTIs have not been associated with high mortality rate in any reports; our results indicated that there were no relations between UTIs and graft failure. Age, female gender, cadaveric donor, and diabetes mellitus are considered as some potential risk

factors for UTI occurrence in kidney recipients.[9] Adamska *et al*. expressed that age and length of hospital stay are statistically affect bacterial infections occurrence.[7]

Female kidney transplant patients have a statistically significant higher occurrence of UTIs versus male allograft recipients in this center ($P < 0.005$) which was similar to other studies.[1,8,31-33] It seems that shorter urethra and nearness of urethral opening to anus and vagina are causes of this high prevalence in female gender.[23]

Taminato *et al*. indicated that deceased kidney recipients are 20% more susceptible to develop infections, while our study results showed no differences between deceased and live donor recipients.[11] It seems that it is due to cold ischemia time reduction and proper organ preservation. Bacterial infections are more prevalent among older ones; it thought that impaired cellular immunity and immunosuppression tolerance are causes of old patients susceptibility to infection;[30,34] However, no evidence were not found in this study to approve this matter.

CONCLUSIONS

This study revealed that many recipients did not know their renal failure cause. UTI is responsible for hospitalization after renal transplantation, early creatinine clearance reduction, reoperation risk increment, and early poor renal function. Invasive catheters and prophylactic antibiotics intake should be managed to reduce bacterial and fungal infection incidence after transplantation. Our results confirmed the previous researches, but a cohort study is suggested to investigate bacterial and fungal infections effects on long-term survival. This study was done on kidney transplant recipients, and we did not work on antimicrobial resistance, we suggest doing similar study on liver and bone marrow recipients in association with antimicrobial resistance evaluation.

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Conflicts of interest

There are no conflicts of interest.

AUTHORS' CONTRIBUTION

AB, SFSh, ZL, AKh , MKh , SSh and ESE contributed in the conception and design of the work, analysis, drafting and revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work.

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