Recurrent Urinary Tract Infections in Kidney Transplant Recipients

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ABSTRACT

Urinary tract infection (UTI) constitutes the most frequent infection among kidney transplantation (KT) patients. The epidemiology and specific risk factors for recurrent UTI after KT have not been well studied. The aim of this work was to assess the incidence, pathogenic spectrum, and risk factors for recurrent post-KT UTI. This observational, cross-sectional study included all patients admitted to our transplantation department with a diagnosis of post-KT UTI from January 2010 to December 2011. Recurring post-KT UTI was defined as ≥2 UTIs in 6 months or ≥3 UTIs in 12 months. Factors associated with recurrent post-KT UTI were assessed using logistic regression analysis. The 154 patients were diagnosed with 315 episodes of post-KT UTI (28.6%), with recurrent post-KT UTI among 72% of cases. Most recurrent UTIs (73.6%) occurred during the first year after KT. *Klebsiella* species was the most common isolated pathogen (53.2%), being a serious problem for multidrug-resistance (odds ratio [OR], 13; 95% confidence interval [CI] 5.9–28.6; $P < .001$). The presence of nosocomial infection (OR, 2.8; 95% CI, 1.4–5.4; $P < .003$) and multidrug-resistant bacteria (OR, 3.8; 95% CI, 2–7.2; $P < .001$) emerged as independent predictors of recurrent post-KT UTI. KT recipient demographics and characteristics, factors related to KT and urologic complications, did not differ significantly between patients with versus without recurrent post-KT UTI. In conclusion, in a unit where recurrent post-KT UTI incidence was 72% and *Klebsiella* species was the prevailing uropathogen, nosocomial infection and multidrug-resistant bacteria appeared to be independent predictive factors for recurrent post-KT UTI.

URINARY tract infection (UTI) is the most common infectious complication among kidney transplantation (KT) patients.[1–3] The considerable variation in the reported incidences, ranging from 23%–75%,[4–6] may be due not only to local outbreaks, center-specific antibiotic strategies, and follow-up duration, but also to various definitions and diagnostic criteria for the condition. Many potential risk factors involved in the development of post-KT UTI have been described.[7–11] UTI adversely affects post-KT morbidity[3] and may worsen graft[6,12] and patient survival.[13,14] Recurring post-KT UTI occur in 2.9%–27% of KT recipients.[4,13,15,16] The aim of this work was to assess the incidence, pathogenic spectrum, and risk factors for developing recurrent post-KT UTI.

METHODS

Study Design

We performed an observational cross-sectional study from January 2010 to December 2011 including all patients admitted to the unit with a diagnosis of post-KT UTI, excluding asymptomatic bacteriuria.

All KT patients received perioperative prophylaxis with Cefazolin (1 g single dose) and 1 year of prophylactic treatment with trimethoprim-sulfamethoxazole (80/400 mg daily).

Definitions

The diagnosis of a symptomatic UTI required a quantitative bacterial count $\geq 10^5$/high-power field in an appropriately collected urine specimen in the presence of symptoms or signs of urinary infection. The definition of multidrug-resistant bacteria, resistance to ≥3 antimicrobials of different classes, was based on in vitro antimicrobial susceptibility tests. Recurrent post-KT UTI was defined as ≥2 UTIs in 6 months or ≥3 UTIs in 12 months. Nosocomial infections were defined as those occurring within 48

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hours of hospital admission or directly related to a hospital procedure.

Urinary and Susceptibility Studies

Urinary samples were evaluated with Gram staining for direct examination; cultures were tested using both turbidimetric and colorimetric technique.

Data Collection

KT patients were identified from the department's database of hospital reports. All cases of UTI as either the primary or secondary diagnosis were included in the study. Medical charts were reviewed for demographic and clinical variables, factors related to KT, urologic complications, type of infection, and causative micro-organisms.

Statistical Analysis

Parametric variables expressed as mean values ± standard deviations (SD) were compared using Student *t* test. Nonparametric variables expressed as medians and interquartile ranges (IQR) were compared using the Mann-Whitney test. Categorical variables expressed in percentages were compared using chi-square tests. Binary logistic regression models were used to analyze potential risk factors for developing recurrent post-KT UTI. All *P* values were 2-tailed with values <.05 considered statistically significant. Confidence intervals (CI) included 95% of predicted values. Analyses were performed using SPSS software (version 17; SPSS Inc., Chicago, Ill, United States).

RESULTS

From January 2010 to December 2011, 1101 patients were hospitalized in our unit. During the 24 months, 315 (28.6%) UTIs were idenfied, corresponding to 154 KT patients, including 47.4% males and an overall mean age of 52 ± 15 years. The incidence of nosocomial UTI was 48.2% (n = 152). These were the most severe cases, associated with acute pyelonephritis (odds ratio [OR] 1.9; 95% CI, 1.1–3; $P = .012$), bacteremia (OR, 2.4; 95% CI, 1.3–4.5; $P = .003$) or acute graft dysfunction (OR, 1.9; 95% CI, 1.2–3.3; $P = .007$). There were 5 graft failures and 4 deaths.

Of the 315 UTIs, cases with mixed flora (n = 11) and without isolation of a germ (n = 41) were excluded from further analysis. The uropathogen accounting for the majority of UTIs in the transplantation unit was *Klebsiella* species (46%; *n* = 121). Other germs were *Escherichia coli* (27.4%; n = 72), *Pseudomonas aeruginosa* (14.1%; n = 37), other *Enterobateriaceae* including *Proteus, Morganella, Enterobacter,* and *Serratia* species (8%; n = 21), *Enterococcus* species (3.8%; *n* = 10), and *Acinectobacter* species (0.6%; n = 2). Multidrug-resistant bacteria accounted for 71% (n = 187) of post-KT UTIs in the unit with *Klebsiella* species the most prevailing one (OR, 13; 95% CI, 5.9–28.6; $P < .001$).

Recurrent post-KT UTI was responsible for 72% (n = 227) of all hospitalization for UTI, with median UTIs/KT recipient of 2 (IQR, 1–3) and maximum UTIs/KT recipient of 9. Most recurrent UTIs (73.6%; n = 167) occurred during the first year after KT (OR, 6.6; 95% CI, 3.9–11.4; $P < .001$) and 56.4% (n = 128) took place within the first 6 months post-KT. *Klebsiella* species (55.4%; n = 108) persisted as the most common bacterium among recurrent UTI episodes after KT (OR, 3.9; 95% CI, 2.1–7.3; $P < .001$). The remaining bacteria isolated were *E coli* (18%; *n* = 35), *P aeruginosa* (15.4%; n = 30), other *Enterobacteriaceae* including *Proteus, Morganella, Enterobacter,* and *Serratia* speceis (8.2%; n = 16), *Enterococcus* species (1.5%; n = 3), and *Acinectobacter* species (1%; n = 2). Recurrent UTIs with mixed flora (n = 8) and without isolation of a bacterium (n = 24) were not considered.

KT recipient demographic and clinical characteristics upon hospitalization are shown in Table 1. Patients were divided into 2 groups according to the occurrence or absence of post-KT UTI.

Variables associated with recurrent post-KT UTI upon univariate analysis were the presence of an indwelling urethral catheter, nosocomial infection, and multidrug-resistant bacteria (Table 2). All other variables did not differ significantly between the groups.

Table 1. Demographic and Clinical Characteristics of the KT Patients

Recipient Characteristics	Recurrent Post-KT UTI (n = 227)	Nonrecurrent Post-KT UTI (n = 88)
Age (y; mean ± SD)	50.4 ± 15.3	53.6 ± 14.7
Female (%)	43.8	60.5
Diabetes mellitus (%)	21.9	18.2
HBV/HCV seropositivity (%)	5.6/5.6	0/3.2
Urologic malformations/polycystic kidney disease (%)	8.2/15.1	3.9/16.9
History of vesicoureteral reflux (%)	7.3	5.4
Pretransplantation UTIs (%)	22.4	13.6
Retransplantation (%)	2.7	4.9
Cadaveric donor (%)	94.5	93.8
Induction: thymoglobulin/ basiliximab (%)	23.3/46.7	27.3/45.5
Maintenance immunosuppression (%)		
Cyclosporine/tacrolimus	43.8/45.9	46.7/38.8
Mycophenolate mofetil or mycophenolic acid	85.1	73.8
Sirolimus or everolimus	8.1	13.8
Prednisolone	98.6	91.3
Acute rejection episodes (%)	16.9	13.6
Urinary leak/urinary obstruction (%)	12.2/6.6	15.4/2.3
Surgical wound infection (%)	4.4	3.4
Lymphocele/stones (%)	8.8/8.5	2.3/1.4
Indwelling urethral catheter (%)	18.1	4.5
Ureteric stent (%)	71.4	46.7
Percutaneous nephrostomy (%)	7.5	4.5
Reoperation of the graft (%)	8.9	3.4
Timing posttransplantation (mo; median, IQR)	5 (2–13)	36.5 (9.1–96)
Nosocomial infection (%)	59	20.5
Multidrug-resistant bacteria (%)	81.3	43.7

Abbreviations: HBV, hepatitis B virus; HCV, hepatitis C virus.