



Urinary tract infection leading to hospital admission during the first year after kidney transplantation: A retrospective cohort study



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ABSTRACT

Introduction: Urinary tract infection (UTI) is the most common infectious problem in kidney transplant recipients (KTR). It has been associated with risk factors inherent to the transplant and it could negatively affect clinical outcomes. The aim of this study was to describe demographic, clinical and microbiological characteristics of patients with UTI.

Methods: We underwent a retrospective study reviewing the database of kidney transplants patients in a national reference center in Colombia. We included patients admitted for inpatient treatment related to urinary tract infection in the first year after transplantation.

Results: We describe clinical information from 65 patients, the mean age was 46 years, the most common comorbidity was hypertension (n=48/62, 77.4%) followed by diabetes mellitus (n=11/62, 17.7%); 77% (n=50/65) of the infections were diagnosed in the first 6 months after transplant and 70% (n=45/65) had pyelonephritis. Acute dysfunction of the graft was the most common complication in 59% (n=33/56) of cases. The most common etiological agent described was *E. coli* in 67% (n=37/55) of patients followed by *Klebsiella pneumoniae* (n=13/55). Bacteremia was present in 25% of cases. Infection with extended-spectrum betalactamases producing bacteria was present in 42% (n=18/42) of our isolations and multidrug resistance was documented in 39% (n=21/54) of isolates.

Conclusion: Most UTI leading to hospitalization in KTR occur in the first six months. Pyelonephritis explains the majority of clinical diagnosis. The rate of blood stream infections and multidrug resistance bacteria is high, justifying an empiric broad-spectrum antibiotic treatment.

1. Introduction

Chronic kidney disease (CKD) is a general term that embraces a group of diverse disorders affecting function and structure of the kidney. Chronic kidney failure (CKF) is the end stage of this spectrum and it is considered an important health problem worldwide [1]. Patients who progress to end stage renal disease (ESRD) require treatment with renal replacement therapy (RRT) either with hemodialysis (HD), peritoneal dialysis (PD) or kidney transplantation (KT). Those who undergo KT have less than half of the risk of death than those on dialysis; therefore, it is considered currently as the treatment

of choice for the most part of CKF patients [2]. The kidney is the most common transplanted organ and for 2013 it represented the 60% of all solid organ transplants in United States [3]. However, kidney transplant recipients (KTR) are exposed to important risks such as toxicity to medications, graft rejection immunosuppression, surgical complications, neoplasms and infections [4].

Urinary tract infection (UTI) is the most common cause of infection in KTR, its incidence is variable due specially to differences in surveillance methods, use of prophylactic antibiotics and definitions [5]. Nevertheless, it has been estimated that up to 85% of KTR will develop at least one episode of UTI [6]. It is the most common cause of

Abbreviations: CKD, Chronic kidney disease; CKF, Chronic kidney failure;; ESRD, end stage renal disease;; HD, hemodialysis;; KTR, kidney transplant recipients;; MDR, Multidrug resistant; MMF, mycophenolate mofetil; mTOR, mammalian target of rapamycin; PD, peritoneal dialysis; RRT, renal replacement therapy;; UTI, Urinary tract infection; TMP/SMX, Trimethoprim-sulfamethoxazole; XDR, Extensively drug-resistant

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sepsis in KTR and it is responsible for the 30% of all bacteremia in this subset of patients. Furthermore, it affects importantly survival, being the cause of the death in 11% of patients during the first month after transplantation [7]. Different risk factors have been related to the development of UTI in KTR, including female sex, time on hemodialysis before transplantation, previous history of recurrent UTI, time of bladder catheterization after transplant surgery, vesico-urethral reflux, polycystic kidney disease, diabetes mellitus and more than 2 episodes of asymptomatic bacteriuria [8]. The etiology of UTI among KTR resembles those in general population: *Escherichia coli* is the most common bacterial agent and along with *Klebsiella pneumoniae* and *Enterococcus spp* claim for more than 90% of all infections. KTR are at increased risk of contracting infection from resistant bacteria and atypical microorganisms as well [9].

New immunosuppressive drugs have considerably reduced the rates of acute graft rejection but may have raised the rate of post-transplant infections. Consequently, epidemiological profile of admissions for KTR has changed in the last decade. While in the late eighties the most common cause for admission within 24 months after transplantation were related to rejection in 44% of patients; currently infection is the main reason for inpatient treatment, being present up to 40% of patients [10,11]. The aim of this study is to describe the demographic, microbiological and clinical data from KTR developing UTI requiring admission and inpatient treatment during the first year after transplantation in a teaching hospital, which is considered a reference center for kidney transplantation in Colombia.

2. Materials and methods

2.1. Study design, setting and patients

We performed a retrospective cohort study, reviewing the database register for kidney transplant patients in Hospital Universitario de San Vicente Fundación (Medellín – Colombia) from January first 2006 to September 31st, 2014. Data was collected in predesigned forms containing demographic and transplant related information, clinical features, microbiological isolation and antibiograms. Transplants were undergone at our center, a tertiary care teaching center which has made more than 3800 kidney transplants in the last 20 years.

We included patients older than 18 years old, admitted for inpatient care associated with UTI during the first year after transplantation. Patients with missing information, ambulatory treatment, asymptomatic bacteriuria and those transferred to other institution in the first 24 h were excluded. The ethical committees of Hospital Universitario San Vicente Fundación and the Instituto de Investigaciones Médicas (IIM) from the Universidad de Antioquia approved the investigation. No personal information from the patients was provided in the form and confidentiality was protected.

Depending on the risk, patients transplanted during this period were induced with thymoglobulin (high immunological risk) or basiliximab (low risk patients), they also received perioperative prophylaxis with a first generation cephalosporin and maintenance immunosuppression was based on calcineurin inhibitors, mycophenolate mofetil (MMF), mammalian target of rapamycin (mTOR) inhibitors and low dose of corticosteroids. Prophylactic antibiotics were provided during first three to six months after transplant with trimethoprim/sulfamethoxazole for preventing *Pneumocystis jirovecii* infection. In the protocol of our hospital all of indwelling bladder catheters were removed in the first 4 days post-transplant.

2.2. Definitions and variables

- Asymptomatic bacteriuria: More than 10^5 colony-forming units (CFU)/mL in a patient without fever or urinary tract symptoms.
- Urinary tract infection: More than 10^5 CFU/mL in a well processed urinary sample, associated with lower urinary tract symptoms such

as dysuria, intermittent urinary stream, straining, hesitancy, terminal dribbling, incomplete emptying, urgency, frequency, incontinence and nocturia; or evidence of systemic compromise with fever, general symptoms, urinary symptoms and lab tests suggesting urinary origin of the infectious process despite negative urine culture.

- Pyelonephritis was defined as the presence of UTI with fever ($> 38^\circ\text{C}$) and/or graft pain.
- Acute kidney injury (AKI) was defined as an increase in serum creatinine by >0.3 mg/dl within 48 h; or increase in serum creatinine to >1.5 times baseline, which is known or presumed to have occurred within the prior 7 days [1].
- Multi-drug resistant bacteria (MDR) were defined as those isolates with antibiogram proven resistance to 3 or more different families of antibiotics. Extensively drug-resistant bacteria (XDR) were defined, as bacterial isolates remain susceptible to only one or two families of antimicrobials [12].
- Early post-transplant UTI: Those UTI presenting in the first 6 months after kidney transplant [5,13].

2.3. Variables

- General data: We recorded age, gender, ethnicity, past medical history, cause and date of transplantation, immunosuppressive therapy and antibiotic prophylaxis.
- Clinical data: Chief complain symptoms were registered as well as fever, vital signs, headache, nausea, vomiting, dysuria, intermittent urinary stream, straining, hesitancy, terminal dribbling, incomplete emptying, urgency, frequency, incontinence, nocturia, right flank pain, length of stay, requirement of intensive care support; complications such as shock, acute kidney injury, requirement of hemodialysis during the admission, pyelonephritis, abscess formation, multiple organic dysfunction syndrome and death of all causes.
- Microbiological isolations: Urine cultures coming from patients included in the study were reviewed, the susceptibility profile of the isolations to the most common used antimicrobials (based on minimal inhibitory concentration) was analyzed and subcategorized as sensible, intermediate or resistant to a determined antibiotic. We also determined the presence of bacteremia based on blood cultures taken at admission and registered the antibiotics received during the infectious episode.

2.4. Data analysis

Data were collected in a predefined format and filled in a database in Microsoft Access 2010 (Microsoft, Redmond, Washington). Results are expressed as mean \pm SD, and as the median with the interquartile range. The goodness of fit to the normal distribution was statistically assessed by using the Kolmogorov–Smirnov test or Shapiro Wilk depending on the number of registries. Statistical analysis was done using SPSS (version 22.0, SPSS, Chicago, Illinois).

3. Results

We reviewed 198 clinical charts and included in the final analysis 65 patients (Fig. 1). Thirty-six (55,4%) were female and the mean age was 46 years (range 18–80). The most common reported comorbidity was hypertension present in 77.4% (n=48/62), followed by diabetes mellitus in 18% (n=11/62) and heart failure in 9.8% (n=6/61). Fourteen percent (n=8/58) of our patients had previously known history of recurrent UTI. Renal replacement therapy previous to transplantation was provided with hemodialysis to 67% (n=39/58) of patients, 19% (n=11/58) were on peritoneal dialysis and 14% (n=8/58) had both therapies in some point of their disease. The main causes of renal failure that led to transplantation were unknown (38%, n=25/65), diabetic nephropathy (12%, n=8/65) and lupus nephropathy

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