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CLINICAL STUDY

A single-centre report of acute pyelonephritis in a patient after kidney transplantation – analyses of risk factors

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ABSTRACT

BACKGROUND: Urinary tract infections (UTI) are the most common infectious complications after kidney transplantation (KTx) with highest incidence in the first three months of transplantation. UTI in transplant recipients increase morbidity and mortality, risk of graft failure and incidence of acute rejection episodes. According to published data, urinary tract infections significantly affect graft survival. The aim of our study was to identify possible risk factors for the development of UTI.

MATERIAL AND METHODS: We retrospectively analyzed a cohort of patients who received kidney transplantation between January 2014 and December 2016 in the Transplant Center of Louis Pasteur University Hospital in Košice. One hundred and fifty-three patients after kidney transplantation were included in the study.

RESULTS: A total of 47 Caucasian patients (30%) developed UTI, namely – acute pyelonephritis after KTx. We identified independent risk factors associated with UTI such as female gender OR (7.98, 95% CI 2.88–22.12, $p < 0.001$), diabetes mellitus (OR 5.26, 95% CI 2.01–13.74, $p = 0.001$; 95% CI 4.57–53.82, $p < 0.001$) urologic complication (OR 15.68, 95% CI 4.57–53.82; $p < 0.001$) and acute rejection episode (OR 3.15, 95% CI 1.13–8.76, $p = 0.027$). The most common microbiological agent was Escherichia coli.

CONCLUSION: We identified the aforementioned risk factors of urinary tract infections in the files of our patients. Statistically, the most significant risk factors are the female gender, and presence of urological complications. The urological complications and BMI of the patients are considered modifiable factors. Based on our analysis, we confirmed a significantly higher number of ACR patients who overcame infection which is in accordance with the published data on association of UTI with the development of acute cellular rejection (ACR) *(Tab. 2, Fig. 1, Ref. 15)*. Text in PDF *www.elis.sk*

KEY WORDS: acute pyelonephritis, kidney transplantation, risk factors, urinary tract infections.

Introduction

Kidney transplantation is the treatment of choice in cases of chronic renal failure. It dramatically improves quality of life and life expectancy as compared to conventional hemodialysis in end-stage renal disease (ESRD). More data suggest that urinary tract infection (UTI) is the most common infection after kidney transplantation. The risk of first-time hospitalization for pyelonephritis among renal transplant recipients is high. Analyses of several studies indicate that recurrent post-transplant pyelonephritis was associated with an excessive risk of graft loss and death (1). UTI typically occurs during the first three months after kidney transplantation. The prevalence of UTI in these patients is diverse. Different studies have reported prevalence rates of UTI ranging from as low as 6 % to as high as 86 % (2, 3, 4, 5). This wide range is likely due to varying definitions of the disease, and diverse strategies for prophylaxis, screening, and treatment of UTI (6). Risk factors for UTI include female gender, advanced age, pre-transplant UTIs, prolonged period of haemodialysis before transplantation, immunosuppression, acute rejection episodes, impaired graft function, bladder catheter applied postoperatively, technical complications associated with ureteral anastomosis, intraoperative ureteral stents, surgical manipulation of the graft (allograft trauma), contaminated graft perfusion solution, diabetes mellitus, history of vesicoureteral reflux, history of polycystic kidney disease, cadaveric donor, schistosomiasis (7).

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Methods

Study design

Between January 2014 and December 2016, 162 recipients of Caucasian origin underwent kidney transplantation (KT) in the Transplant Centre of Louis Pasteur University Hospital in Košice. All participating patients signed a written consent to be included

Tab. 1. Clinical and laboratory characteristics of study participans.

Kidney transplant recipient			
	No UTI	UTI	p
Female (%)	26	47	0.013
Age (years)	46.6±13.4	50.2±14.5	0.14
Age > 60 y (%)	17	27.7	0.13
BMI (kg/m2)	25.0±3.8	26.1±3.9	0.091
KREAT 1 (μmol/l)	143.4±48.7	141.7±73.2	0.87
KREAT 2 (μmol/l)	126.7±50.9	140.4±70.4	0.238
Diabetes mellitus (%)	18	44.6	0.001
Induction ATG (%)	28.3	25.5	0.723
Urologic complication (%)	6.6	34	<0.001
Any complication	22.6	53.2	<0.001
Nephrostomy (%)	2	15	0.004
Rejection (%)	12	30	0.009
ReTx (%)	9.5	13	0.572
LD-DBD	15.1	14.9	0.974

Data are shown as mean ± standard error of mean (SEM), BMI – body mass index, KREAT 1 – is the creatinine value at the time of KT, KREAT 2 – is the creatinine value one year after UTI, ATG – antithzmocyteglobulin, ReTx – retransplantation, LD-DBD – type of donor : living donor and donor after brain death

in the study. The aim of the thesis was retrospectively analyse the risk factors of acute pyelonephritis in patients who underwent KT. In our study we retrospectively analysed the data of 153 kidney transplant recipients who met the inclusion criteria. Paediatric KT recipients were excluded from the study, as well as patients who died in the study period and who had primary non-function (PNF) of the graft and had to undergo graftectomy. We evaluated the incidence of acute pyelonephritis in the first twelve months after KT. We have chosen the first 12-month time span due to various UTI incidences in patients after kidney transplantation. Additionally, we aimed to identify risk factors that were related to the development of the acute pyelonephritis in the kidney transplant recipient. We analysed the following baseline data such as age, age > 60 year, gender, body mass index, renal function at the time of kidney transplant (kreat1) and 1 year after acute pyelonephritis, diabetes mellitus, induction by thymoglobulin (ATG), urologic complication, any complication, percutaneous nephrostomy, acute rejection, re-transplantation and type of donor (DBD – donor after brain death and LD – living donor).

Urinary tract infection

Diagnosis of acute pyelonephritis met the criteria for diagnosing the disease according to the European association of Urology. Symptoms in acute pyelonephritis were fever > 38 °C, urinary urgency or frequency, dysuria, chills, suprapubic tenderness, transplant tenderness, nausea and vomiting. The antibiotic treatment was started when the patient had one of the latter symptoms. Urinary culture was examined prior to the first dose of antibiotic therapy. We then examined urinary culture three times. All patients received short-term antibiotic prophylaxis with aminopenicillin three days intravenously at a dose of 1.5 g every 12 hours. In the next step they used prophylaxis by trimethoprim/sulfamethoxazole to prevent the *Pneumocystis carinii* pneumonia. This drug was given *per o*s once a day for 3 months after KT.

Immunosuppressive treatment

All patients used an immunosuppressive agents such as corticosteroids, mycophenolate mofetil and calcineurin inhibitors, especially tacrolimus. At the beginning, the patients received pulses of methylprednisolone (3x500 mg – per day 0, 1 and 2) and continued to use of prednisone at a dose of 20 mg. The starting dose of tacrolimus was 0.2 mg/kg and titrated serum at level of 10–15

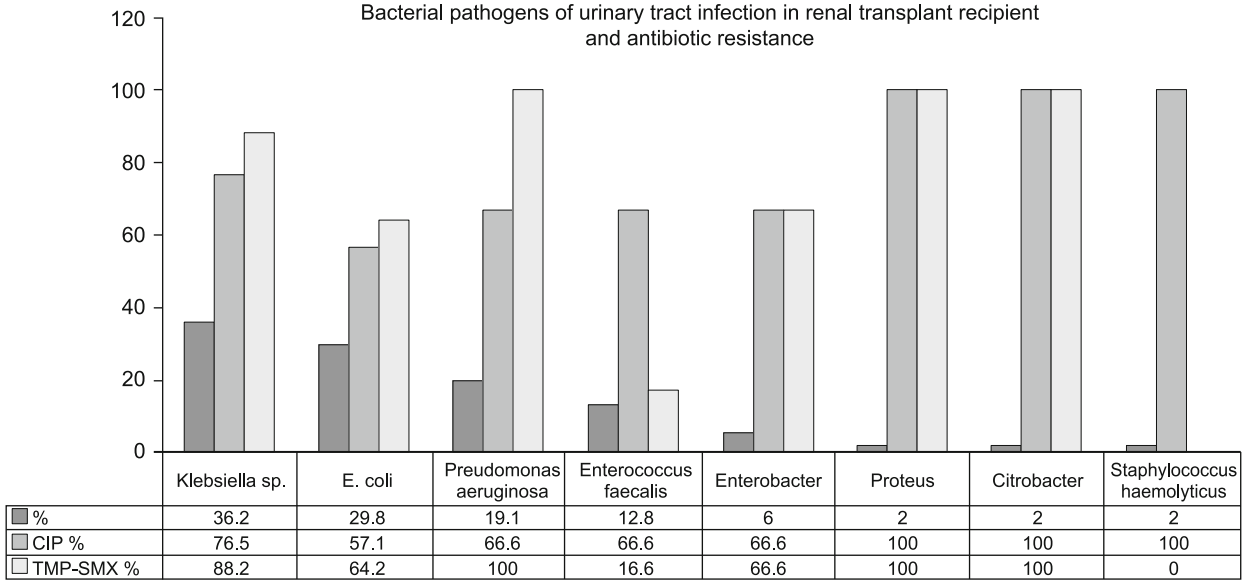

Fig. 1. Bacterial pathogens of Urinary tract infection in renal transplant recipient and antibiotic resistance.

Tab. 2. Independently risk factors for acute pyelonephritis.

Logistic regression model				
	OR	95% CI		p
Female	7.98	2.88	22.18	<0.001
Age	0.98	0.95	1.02	0.45
BMI	1.17	1.04	1.32	0.009
Diabetes mellitus	5.26	2.01	13.74	0.001
Rejection	3.15	1.13	8.76	0.027
Urologic complication	15.68	4.57	53.8	<0.001

ng/ml. The induction by thymoglobulin was used in patients at high immunological risk.

Statistical analysis

Statistical analyses were performed using SPSS statistics 17.0 software (SPSS Inc. Chicago, IL, USA). Continuous variables are presented as mean ± standard error of mean (s.e.m). p values were considered significant at level < 0.05. The risk factors were detected by multivariate analysis.

Results

During the three-year period, we included a total of 153 adult patients, who underwent kidney transplantation. Our patients (100 %) were of Caucasian ethnicity. Table 1 displays clinical and laboratory characteristics of our study populations. The median age of our study subjects was 49.04 ± 20.12 years. Cadaveric donors represented a predominant source of kidney transplantations. Acute pyelonephritis developed in 47 (30 %) kidney recipients. In Table 1, we analysed continuous variables in two groups of patients, namely those with UTI and those without UTI. In this table we present the univariate analysis. This analysis showed that female gender, diabetes mellitus, urologic complication, any complications, nephrostomy and acute rejection were significantly higher in the group with UTI. The differences between the two groups relative to other variables such as age, age over 60 years, BMI, graft function, ATG induction, retransplantation and living donor were not significant. From urinary cultures, we identified bacterial microorganisms responsible for the development of UTI. The most commonly identified bacterial pathogen was *Klebsiella* species (36.2 %), followed by *Escherichia coli* (29.8 %), *Pseudomonas aeruginosa* (19.1 %) and *Enterococcus faecalis* (12.8 %). Other microorganisms such as (*Enterobacter*, *Proteus mirabilis*, *Citrobacter* and *Staphylococcus haemolyticus*) were represented in minimal numbers (Fig. 1). These data were consistent with those in the published literature.

Discussion

According to the available literature, the risk factors responsible for the development of UTI are diverse. Our aim was to identify the risk factors of the development of acute pyelonephritis in patients of Caucasian ethnicity after kidney transplantation in our Transplant Centre of University hospital of L. Pasteur, Košice, and to compare them with the results of other centres, whose data were introduced in the recently available literature. In this analysis, we identified 30 % patients who developed UTI after KTx. By means of the multivariate statistics models we identified independent risk factors such as female gender, BMI, history of diabetes mellitus, acute rejection and urologic complication. The results of the analysis are shown in Table 2. Many previous studies identified female gender as a risk factor for the development of UTI. Female gender is a risk for the development of UTI in terms of female topographic anatomy of the urethra. Female gender is also a risk factor in the development of UTI in the general population of patients who have not undergone kidney transplantation, as confirmed in our recent subset analysis.

Another modifiable risk factor for the development UTI was body mass index. We observed a more frequent occurrence of urinary tract infection in a group with higher BMI. Also, ERBP (European Renal Best Practice) guidelines recommended to contraindicate kidney transplantation in patients with BMI greater than 30 kg/m^2 (8).

In our study, we found an association between the history of diabetes mellitus and increased risk of UTI in kidney transplant recipient (OR 5.26, 95% CI 2.01–13.74; p = 0.001). Impaired cellular immunity and possibly a lower tolerance to immunosuppression along with immunocompromising comorbidities such as diabetes mellitus may also contribute to the significantly higher percentage of urinary tract infection (7). Some studies indicate that the history of diabetes mellitus increases the susceptibility to UTI (9, 10, 11) but other studies have not confirmed the impact of DM on the development of UTI in patients after kidney transplantation (12, 13, 14). Diabetes mellitus is strongly associated with mycotic-mediated UTI, typically by infection of *Candida albicans*. Such patients in some centres use fluconazole for1 months after kidney transplantation. By means of the multivariable Cox regression analysis, Lee et al. identified a significantly higher incidence of acute cellular rejection in patients after kidney transplantation with untreated urinary tract infection (HR 2.8, 95% CI, 1.3–6.2, p = 0.01). The analysis was performed on 247 patients in total, while 147 patients received antibiotic therapy and 100 patients did not (15). We have seen a similar trend in our patient set. The UTI group of patients had a significantly higher incidence of acute cellular rejection episodes. Limitation of our study is the relatively small number of patients and retrospective character of the study.

Conclusion

In our patient population, we identified the most statistically significant UTI risk factors to be female gender and the presence of urological complications. Modifiable risk factors are BMI and urological complications. In line with the literature on association of UTI with the development of acute cellular rejection (ACR), we also confirmed in our analysis a significantly higher incidence of ACR in patients overdosed with UTI medication. The recommended prophylaxis of *Pneumocystis pneumoniae* with trimethoprim-sulfamethoxazole does not represent a sufficient prophylaxis of UTI in our patients.

References

1. Graverse ME et al. Risk and outcome of pyelonephritis among renal transplant recipients. BMC Infect Dis 2016; 16: 264.

2. Rubin RH. Infectious disease complications of renal transplantation. Kidney Int 1993; 44: 221–236.

3. Karakayali H, Emiroglu R, Arslan G, Bilgin N, Haberal M. Major infectious complications after kidney transplantation. Transplant Proc 2001; 33: 1816–1817.

4. Giral M, Pascuariello G, Karam G, Hourmant M, Cantarovich D, Dantal J et al. Acute graft pyelonephritis and long-term kidney allograft outcome. Kidney Int 2002; 61: 1880–1886.

5. Chuang P, Parikh CR, Langone A. Urinary tract infections after renal transplantation: a retrospective review at two US transplant centers. Clin Transplant 2005; 19: 230–235.

6. Ariza-Heredia EJ, Beam EN, Lesnick TG et al. Urinary tract infections in kidney transplant recipients: Role of gender, urologic abnormalities and antimicrobial prophylaxis. Ann Translant 2013; 18: 195–204.

7. Säemann M, Hörl WH. Urinary tract infection in renal transplant recipients. Eur J clin Invest 2008; 38: 58–65.

8. Abramowicz D et al. European renal best practice guideline on kidney donor and recipient evaluation and perioperative care. Nephrol Dial Transplant 2015; 30: 1790–1797.

9. Glazier DB.et al. Urinary tract infection associated with uretheral stents in renal transplantation. Can J Urol 1998; 5: 462–466.

10. Almond PS et al. Risk factor for chronic rejection in renal allograft recipients. Transplantation 1993; 55: 752–756.

11. Goya N et al. Prevalence of urinary tract infection during outpatient follow-up after renal transplantation. Infection 1997; 25: 101–105.

12. Takai K et al. Urinary tract infections following renal transplantation. Clin Transplant 1998; 12: 19–23.

13. Chuang P et al. Urinary tract infection fter renal transplantation: a retrospective review at two US transplant centers. Clin Transplant 2005; 19: 230–235.

14. Rabkin DG et al. Early catheter removal decreases incidence of urinary tract infections in renal transplant recipients. Transplant Proc 1998; 30: 4314–4316.

15. Lee JR et al. Independent risk factors for urinary tract infection and for subsequent bacteremia or acute cellular rejection: A single center report of 1166 kidney allograft recipients. Transplantation 2013; 96: 732–738.

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