Urinary Tract Infections in a Cohort of Kidney Transplant Recipients

Infeções do Trato Urinário numa Coorte de Transplantados Renais

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Acta Med Port 2014 May-Jun;27(3):364-371

ABSTRACT

Introduction: Urinary tract infection is the most common infectious complication following renal transplantation and its frequency is insufficiently studied in Portugal. The aim of this study was to characterize the incidence of urinary tract infections and recurrent urinary tract infections in renal transplant recipients.

Material and Methods: This was a retrospective cohort observational study, obtained from clinical files of all patients who received a renal transplant at the Hospital of Santa Cruz, from January 2004 to December 2005, with a mean follow-up period of five years or until date of graft loss, death or loss of follow-up. After a descriptive analysis of the population, we used bivariate tests to identify risk factors for urinary tract infections.

Results: A total of 127 patients were included, with a 593 patients.year follow-up. We detected 53 patients (41.7%) presenting with at least one episode of urinary tract infection; 21 patients (16.5%) had recurrent urinary tract infection. Female gender was the only risk factor associated with the occurrence of urinary tract infections ($p < 0.001$, OR = 7.08, RR = 2.95) and recurrent urinary tract infections ($p < 0.001$, OR = 4.66, RR = 2.83). *Escherichia coli* (51.6%), *Klebsiella pneumoniae* (15.5%) and *Enterobacter* spp (9.9%) were the most frequently identified pathogens. Patients did not reveal an increased mortality or allograft loss. However, urinary tract infections were the most important cause of hospital admissions.

Discussion: Female gender was the only risk factor for urinary tract infections in this population. *Escherichia coli* was the most frequent agent isolated.

Conclusion: Despite preventive measures, urinary tract infections remain an important cause of morbidity and hospital admissions.

Keywords: Urinary Tract Infections; Postoperative Complications; Risk Factors; Kidney Transplantation; Portugal.

RESUMO

Introdução: A infeção do trato urinário é a complicação infeciosa mais comum no período pós transplante renal, estando a sua frequência pouco caracterizada na população portuguesa. Este trabalho teve como objetivo determinar a incidência de infeções do trato urinário e infeções do trato urinário recorrentes em transplantados renais.

Material e Métodos: Tratou-se de um estudo observacional de coorte retrospetiva, com consulta dos processos clínicos de doentes transplantados entre Janeiro de 2004 e Dezembro de 2005, no Hospital de Santa Cruz, com seguimento durante cinco anos ou até à data de perda de enxerto, morte ou perda de *follow-up*. Após uma análise descritiva da população, utilizámos testes bivariados para identificação de fatores associados a infeções do trato urinário.

Resultados: Em 127 doentes incluídos com seguimento de 593 doentes/ ano, 53 (41,7%) tiveram pelo menos um episódio de infeção do trato urinário e 21 (16,5%) tiveram infeções do trato urinário recorrentes. O género feminino foi o único fator associado com ocorrência de infeções do trato urinário ($p < 0,001$, OR = 7,08, RR = 2,95) e infeções do trato urinário recorrentes ($p < 0,001$, OR = 4,66, RR = 2,83). Os agentes etiológicos mais frequentes foram *Escherichia coli* (51,6%), *Klebsiella pneumoniae* (15,5%) e *Enterobacter* spp (9,9%). As infeções do trato urinário não causaram aumento de mortalidade ou perda de enxerto, mas foram a principal causa de internamentos hospitalares.

Discussão: Na nossa população, apenas o género feminino foi identificado como fator de risco para o desenvolvimento de infeções do trato urinário, recorrentes ou não. *Escherichia coli* foi o agente etiológico mais frequente.

Conclusão: Apesar das medidas preventivas adotadas, as infeções do trato urinário continuam a ser uma importante causa de morbilidade e de internamentos hospitalares.

Palavras-chave: Infeção do Tracto Urinário; Complicações Pós-operatórias; Factores de Risco; Transplantação Renal; Portugal.

INTRODUCTION

Renal transplantation is for many patients the elective form of renal replacement therapy (RRT).[1,2] Over the last years, with the reduction of the risk associated to immune-mediated acute renal graft rejection, the importance of other mechanisms of graft lesion as Urinary Tract Infection (UTI) has increased.[2,3] UTI is the most common infection in the post-transplantation period, with an incidence varying between 23 and 75%, higher to the observed frequency in general population.[1-6] Most cases of UTI seem to occur during the first year post-transplant and some studies have shown that an ITU within the first six months upon transplant is associated to a higher risk of kidney allograft loss and higher mortality.[1-6] Recurrent UTIs are an additional complication increasing the risk of graft fibrosis and functional deteriora-

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Recebido: 02 de Novembro de 2013 - Aceite: 02 de Fevereiro de 2014

tion.[1,3,7] Due to recurrence, causative micro-organisms may develop multi-resistances making the use of different antibiotic regimens necessary, namely second-line antibiotics and intravenous antibiotic administration.

Several risk factors for recurrent or non-recurrent UTI have been described in patients with a kidney transplant.[1-3,5] Pre-transplant factors include female gender, diabetes mellitus and urinary tract abnormalities (including prostatic hyperplasia in men).[1-3,5] Surgical procedures involved in transplantation, mainly those related to the instrumentation of the urinary tract, are also related to peri-transplant UTIs.[1-3,5] After transplantation, immune suppression is the major determinant of UTIs.[1-3]

Despite existing data regarding the incidence of infections in the Portuguese population of patients who underwent renal transplantation, the percentage of UTIs has not been determined.[8] Establishing this frequency is therefore relevant, as well as the identification of the factors involved and which are potentially modifiable within the National context. From a preventive perspective, it is also important to characterise which micro-organisms are responsible for most post-transplant UTIs, as these may vary amongst different Portuguese clinical centres.[2]

Our study aimed to principally determine the incidence of UTIs and recurrent UTIs in patients who underwent renal transplantation at the Renal Transplantation Unit of the Hospital of Santa Cruz Lisbon Western Hospital Centre (*Unidade de Transplantação Renal do Hospital de Santa Cruz - Centro Hospitalar de Lisboa Ocidental - CHLO)*. We also aimed (i) to assess the association of UTIs and recurrent UTIs with the risk factors described in literature, (ii) to identify renal graft complications, namely graft loss related to chronic failure and episodes of acute rejection, in patients with UTIs and recurrent UTIs and (iii) to characterise UTIs and recurrent UTIs regarding major aetiological agents.

MATERIAL AND METHODS

An observational retrospective cohort study has been carried out in the patients who underwent renal transplantation between the 1st January 2004 and 31st December 2005 at the Hospital of Santa Cruz and were subsequently followed in the outpatient setting. The clinical records of these patients were analysed, from the date of the transplant up to five years of follow-up or up to the date of allograft loss, death or loss to follow-up.

UTI was considered when the clinical record included at least one of the following criteria: (i) positive urine culture with over 10^5 colonies/mL; (ii) clinical signs of UTI, including constitutional symptoms (malaise and fever with or without chills and/or nausea and vomiting) and/or local symptoms (including dysuria, polyuria, mictional urgency, nocturia, supra-pubic tenderness, macroscopic haematuria and/or ipsilateral low back pain to the renal graft) in patients with a complete blood count showing leukocytosis and/or biochemistry analysis with increased PCR and/or characteristic urine analysis (usually including leukocyturia, possibly with acidic pH, pyuria and/or nitrite present in the urine test). Recurrent UTI was considered when three or more UTI episodes occurred over a 12-month period or when two episodes over a six-month period.

The following independent variables and variables for general characterisation were analysed for each patient: transplantation date, age at that transplantation date, gender, renal failure aetiology, type and duration of pre-transplant renal replacement therapy (RRT), type of kidney donor (deceased or living), presence of diabetes mellitus at the time of transplantation and its progression over follow-up, induction immunosuppressive and maintenance regimen, prophylactic induction regimen, dates of post-transplantation UTI, micro-organisms isolated in urine culture, nadir creatinine level (12 months post-transplant) and at the end of follow-up. The causes and dates of graft losses were recorded, as well as the causes and dates of death (when applicable).

Clinical data were entered in an anonymous and confidential database (Microsoft Excel®). Upon the initial descriptive analysis of global data of our group of patients, UTI frequency at follow-up was assessed. A 5% significance level has been considered for all tests – Chi-square test for categorical variables or t-Student test for continuous variables – using SPSS® for Windows (version 20.0; SPSS Inc., Chicago, IL, United States) software. The relative risk and 95% confidence intervals (CI) were estimated for statistical significant variables. Our study has been carried out with the approval by the Ethics Commission of the CHLO.

RESULTS

Socio-demographic and clinical characteristics of our group of patients

A 127-patient cohort has been studied, based on 593 person years of follow-up. Table 1 shows data referred to our group of patients grouped according to non-recurrent and recurrent UTIs. Patients' average age (± standard deviation) at the date of transplantation was 43.0 ± 15.0 and 58.3% of the patients were male. At the time of transplantation, 9.4% of the patients had diabetes mellitus and 5.5% developed it upon transplantation. Chronic kidney disease (CKD) was most commonly caused by chronic glomerulonephritis (26.8%), followed by graft loss (11.8%) and vasculopathy (11.8%). Before transplantation, haemodialysis was the most frequently used RRT (77.2%) and on average RRT duration was 41.9 ± 36.8 months. Most patients (77.2%)

Table 1 - Characterisation of our group of patients and comparison a) between those not having and having developed at least one UTI episode and, from the latter (*n* = 53), the comparison b) between those having developed non-recurrent and recurrent UTI

			a)		b)	
		Total Population (*) (*n* = 127)	**No UTI group (*n* = 74)**	**UTI group (*n* = 53)**	**Non-recurrent UTI (*n* = 32)**	**Recurrent UTI (*n* = 21)**
Pre-transplantation	Age in years, mean ± sd	43.0 ± 15.0	42.8 ± 14.8	42.9 ± 15.0	45.0 ± 14.0	40.0 ± 16.0
	Gender, n (%)					
	Male	*74 (58.3)*	***57 (77.0)***	***17 (23.0)***	***14 (82.4)***	***3 (17.6)***
	Female	*53 (41.7)*	***17 (32.1)***	***36 (67.9)***	***18 (50.0)***	***18 (50.0)***
	Diabetes mellitus, *n* (%)	12 (9,4)	7 (58,3)	5 (41,7)	4 (80,0)	1 (20,0)
	CKD aetiology, *n* (%)					
	Diabetes mellitus	10 (7.9)	6 (60.0)	4 (40.0)	3 (75.0)	1 (25.0)
	Polycystic kidney disease	12 (9.4)	6 (50.0)	6 (50.0)	4 (66.7)	2 (33.3)
	Previous transplant failure	8 (6.3)	4 (50.0)	4 (50.0)	3 (75.0)	1 (25.0)
	Chronic glomerulonephritis	15 (11.8)	5 (33.3)	10 (66.7)	5 (50.0)	5 (50.0)
	Interstitial nephritis	34 (26.8)	29 (85.3)	5 (14.7)	5 (100.0)	0 (0.0)
	Vasculopathy	15 (11.8)	9 (60.0)	6 (40.0)	3 (50.0)	3 (50.0)
	Others	33 (26.0)	15 (45.5)	18 (54.5)	9 (50.0)	9 (50.0)
	Previous RRT, *n* (%)					
	Haemodialysis	98 (77.2)	57 (58.2)	41 (41.8)	22 (53.6)	19 (46.4)
	Peritoneal dialysis	19 (15.0)	12 (63.2)	7 (36.8)	5 (71.4)	2 (28.6)
	Pre-emptive	2 (1.6)	2 (100.0)	0 (0.0)	--	--
	More than one of the above	8 (6.3)	3 (37.5)	5 (62.5)	5 (100.0)	0 (0.0)
	Duration of RRT in months, mean ± sd	41.9 ± 36.8	37.5 ± 36.2	48.2 ± 37.0	51.0 ± 42.0	44.0 ± 29.0
Transplant	Donor, *n* (%)					
	Deceased	98 (77.2)	58 (59.2)	40 (40.8)	23 (57.5)	17 (42.5)
	Living	29 (22.8)	16 (55.2)	13 (44.8)	9 (69.2)	4 (30.8)
Post-transplantation	Imunossupressão inicial, *n* (%)					
	CsA + MMF + Pred	99 (78.0)	62 (62.6)	37 (37.4)	23 (62.2)	14 (37.8)
	Tac + MMF + Pred	26 (20.5)	11 (42.3)	15 (57.7)	9 (60.0)	6 (40.0)
	Outros	2 (1.6)	1 (50.0)	1 (50.0)	0 (0.0)	1 (100.0)
	Initial immune suppression, *n* (%)					
	None	68 (53.5)	43 (63.2)	25 (36.8)	17 (68.0)	8 (32.0)
	ATG	23 (18.1)	11 (47.8)	12 (52.2)	7 (58.3)	5 (41.7)
	Basiliximab	33 (26.0)	19 (57.6)	14 (42.4)	6 (42.8)	8 (57.2)
	Combination therapy	3 (2.4)	1 (33.3)	2 (66.7)	2 (100.0)	0 (0.0)
	Use of mTor inhibitor, *n* (%)					
	No	87 (68.5)	50 (57.5)	37 (42.5)	22 (59.4)	15 (40.6)
	Yes	40 (31.5)	24 (60.0)	16 (40.0)	10 (62.5)	6 (37.5)
	Serum creatinine in mg/dL, mean ± sd					
	At 12 months (nadir)	1.42 ± 0.65	1.43 ± 0.56	1.41 ± 0.76	1.51 ± 0.75	1.25 ± 0.77
	At 5 years	1.69 ± 1.41	1.65 ± 1.24	1.75 ± 1.64	1.88 ± 1.97	1.53 ± 0.85
	Post-transplant diabetes mellitus, *n* (%)	7 (5.5)	5 (71.4)	2 (28.6)	2 (100.0)	0 (0.0)

Percentages refer to each line, except those outlined (*) referring to the total population – the percentages obtained in comparison a) relate to the number of patients presenting each factor in the total population, while those obtained in comparison b) relate to the number of patients with each factor in the group presenting at least one UTI. The single statistically significant association between gender and the occurrence of UTI (*p* value < 0.001) and recurrent UTI (*p* value < 0.001) is outlined in bold. sd, standard deviation. CKD, Chronic Kidney Disease. RRT, Renal Replacement Therapy. CyA, Cyclosporin-A. MMF, Mycophenolate Mofetil. Pred, Prednisolone. Tac, Tacrolimus. ATG, Anti-thymocyte globuline. mTor, Mammalian target of rapamycin.

received their kidney graft from a deceased donor. The most frequently used initial immune suppression regimen was the association of cyclosporin A, mycophenolate mofetil and prednisolone (78.0%) and 46.5% of the patients underwent immunosuppressive induction therapy with anti-thymocyte globulin (ATG), basiliximab or both. The use of mTor inhibitors, on any moment of follow-up, occurred in 31.5% of the patients. The serum creatinine nadir was on average 1.42 ± 0.65 mg/ dL and 1.69 ± 1.41 mg/ dL by the end of follow-up.

UTI and recurrent UTI frequency and associated factors evaluation

Our group of patients was divided in two main groups: one group of patients without any UTI over the follow-up and another group with at least one UTI event. The latter was subdivided in two groups according to recurrent UTI criteria..

Over the follow-up, 53 (41.7%) patients presented at least one UTI event, corresponding to an incidence rate of 3.73 UTI episodes per patient/year. Considering this group of patients, 21 (39.6%) presented recurrent UTI (corresponding to 16.5% of the total). Gender was the only risk factor for which we found a statistically significant association with the occurrence of UTI and recurrent ITU (*p* value < 0.001 on both situations). Women presented a

higher probability of developing UTI, corresponding to a relative risk of 2.96 (95%CI: 2.02-4.03) for the occurrence of UTI and 2.83 (95%CI: 0.96-8.32) for recurrent UTI.

The average time of pre-transplantation RRT was higher in the UTI group of patients (48.2 ± 37.0 months) *vs.* no-UTI patients (37.5 ± 36.2 months). UTI was found in 41.8% of the patients who were on haemodialysis (*n* = 98) and in 36.8% of those on peritoneal dialysis (*n* = 19) and recurrent UTI occurred in 11.4% and 10.5%, respectively. Patients submitted to pre-emptive kidney transplantation (no previous dialysis) (*n* = 2) did not present any UTI.

Average creatinine levels were similar at 12 months between both groups (1.43mg/ dL in the no-UTI group and 1.41mg/ dL in the UTI group) with a higher creatinine level at five years, although not significant, in the UTI group (1.65 mg/ dL in the no-UTI group and 1.75 mg/ dL in the UTI group). We found a lower creatinine level at 12 months and at five years in the recurrent UTI group (1.25 mg/ dL and 1.53 mg/ dL, respectively) when compared to the non-recurrent UTI group. Nevertheless, the differences between creatinine nadir and at five years level were similar (0.37 mg/ dL in non-recurrent UTI group and 0.28 mg/ dL in recurrent UTI group).

Global clinical results in UTI and no-UTI groups

As shown in Table 2, 11.0% of the patients suffered allograft loss during follow-up principally caused by acute rejection 35.7%). From the patients in which chronic failure was the cause for allograft loss, 75.0% of the patients presented at least one UTI over the follow-up period. Regarding the patients who suffered allograft loss, the average duration of kidney graft was 24.1 ± 19.3 months. During the five-year follow-up, only one patient died (four years after transplantation) of undetermined cause but with no UTI. None of the patients in our group was lost to follow-up.

Clinical and aetiological aspects of recurrent and non-recurrent UTI

Twenty-five percent of the UTI episodes occurred during the first post-transplant semester (Fig. 1). Medium time interval to first UTI episode was 13.06 ± 14.43 months.

Hospital admission related to acute pyelonephritis was needed in 30.6% of the UTI episodes and in 28.3% of recurrent UTI episodes. UTI was the main cause for admission to the Nephrology Department (Fig. 2).

Considering all UTI episodes (Fig. 3), the most frequently isolated micro-organism in the urine culture was *Escherichia coli* (51.6%), followed by *Klebsiella pneumoniae* (15.5%) and *Enterobacter spp.* (9.9%). A higher number of UTIs caused by *Escherichia coli* were recorded in non-recurrent UTI group (59.7%) *vs.* recurrent UTI group (46.5%), as well as *Proteus mirabilis* (4.8% *vs.* 1.0%). A higher number of UTIs caused by *Enterobacter spp.* (12.1%), *Enterococcus faecalis* (9.1%), *Klebsiella pneumoniae* (18.2%) and *Staphylococcus spp.* (4.0%) were recorded in the recurrent UTI group.

DISCUSSION

Over a 5-year follow-up, 41.7% of kidney transplant recipients at the Hospital of Santa Cruz in 2004-2005 presented at least one UTI episode, in line with current literature.[1,2,6,9] The 16.5% recurrent UTI incidence is also similar to previous reports[5,9] and with a recent study carried out at the *Centro Hospitalar e Universitário de Coimbra* that described a 20.6% recurrent UTI incidence.[10]

Table 2 - Clinical results of patients in total population and in the group with at least one UTI over the follow-up period

Clinical results	Total (*n* = 127)	a) No UTI group (*n* = 74)	a) UTI group (*n* = 53)	b) Non-recurrent UTI (*n* = 32)	b) Recurrent UTI (*n* = 21)
With functioning graft, *n* (%)	112 (88,2)	65 (87,8)	47 (88,7)	29 (90,6)	18 (85,7)
Graft loss, *n* (%)	14 (11,0)	8 (10,8)	6 (11,3)	3 (9,4)	3 (14,3)
*Cause for graft loss, n (%)**					
Acute rejection	5 (35,7)	4 (50,0)	1 (16,7)	1 (33,3)	0 (0,0)
Chronic graft failure	4 (28,6)	1 (12,5)	3 (50,0)	1 (33,3)	2 (66,7)
Vascular complications	2 (14,3)	2 (25,0)	0 (0,0)	--	--
Disease relapse	1 (7,1)	1 (12,5)	0 (0,0)	--	--
Others / Undetermined	2 (14,3)	0 (0,0)	2 (33,3)	1 (33,3)	1 (33,3)
Death, *n* (%)	1 (0,8)	1 (1,4)	0 (0,0)	--	--

Percentage calculated on each column, referred to the total of patients for each group, except when outlined (*) where the percentages calculated referred to the patients with graft loss, for each group

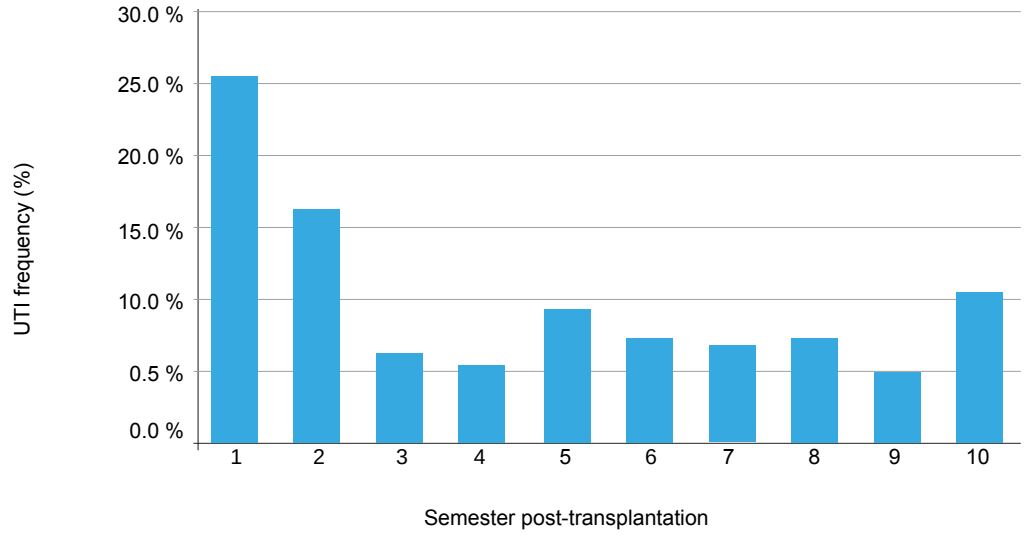

Figure 1 - Number of UTIs over the follow-up semesters

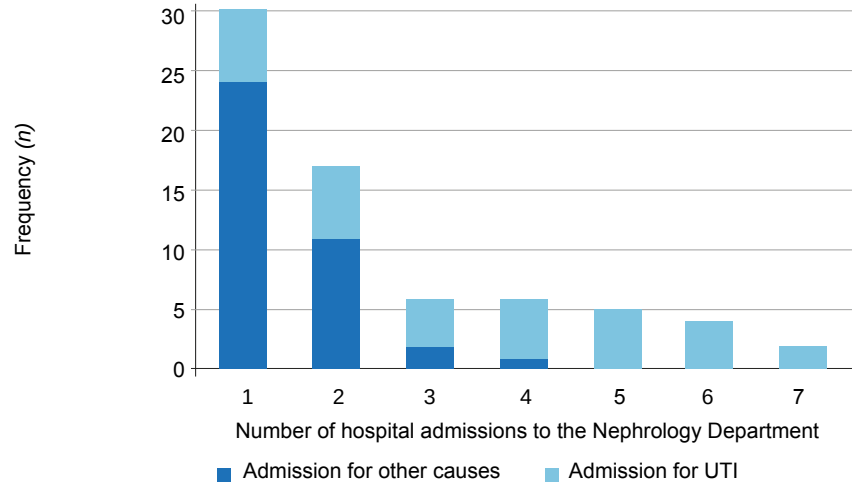

Figure 2 - Total number of hospital admissions to the Nephrology Department at the Santa Cruz Hospital per patient

Several factors have been associated to a higher UTI incidence, namely peri-operative factors and patient's clinical and social characteristics.[1,2,5,7,11] However, we only found a statistically significant association between female gender and the occurrence of UTI and recurrent UTI, frequently recognized in this group of patients.[1,2,6,11]

Despite the presence of diabetes and its progression over the follow-up as risk factors for UTI[1-3,9] described in other studies,[1,6,12] we were not able to establish this association. Only 5.5% of our group of patients developed diabetes during follow-up, lower than expected when compared to the previously described 13% frequency at five years upon transplantation.[13] Although some aetiologies related to CKD are associated to a higher occurrence of UTI, such as interstitial pyelonephritis associated to non-obstructive vesico-ureteric reflux (VUR), neurogenic bladder and obstructive uropathy,[1-3,5,11] such a relationship was not found in our study. Even though pre-transplant RRT duration was slightly higher in the UTI group, this difference did not reach statistical significance. It is known that a longer time of RRT may lead to a decrease or total loss of residual diuresis, possibly associated to severe anatomical abnormalities of the urinary tract, predisposing to UTI.[5,9]

Interestingly, the patients who underwent pre-emptive transplantation did not develop UTI (n = 2), which may reflect their best clinical condition, as they did not suffer any of the complications usually associated to dialysis in addition to presenting with excellent pre-transplant diuresis. However, it is not possible to draw any conclusions from this tendency due to the small number of patients in this specific group of patients.

Most patients received their graft from a deceased donor (77.2%), which also reflects the Portuguese reality[8] and the described positive association between graft origin from a deceased donor and the occurrence of UTIs, possibly due to graft being subject to a longer period of ischaemia and more easily contaminated.[1-4,6]

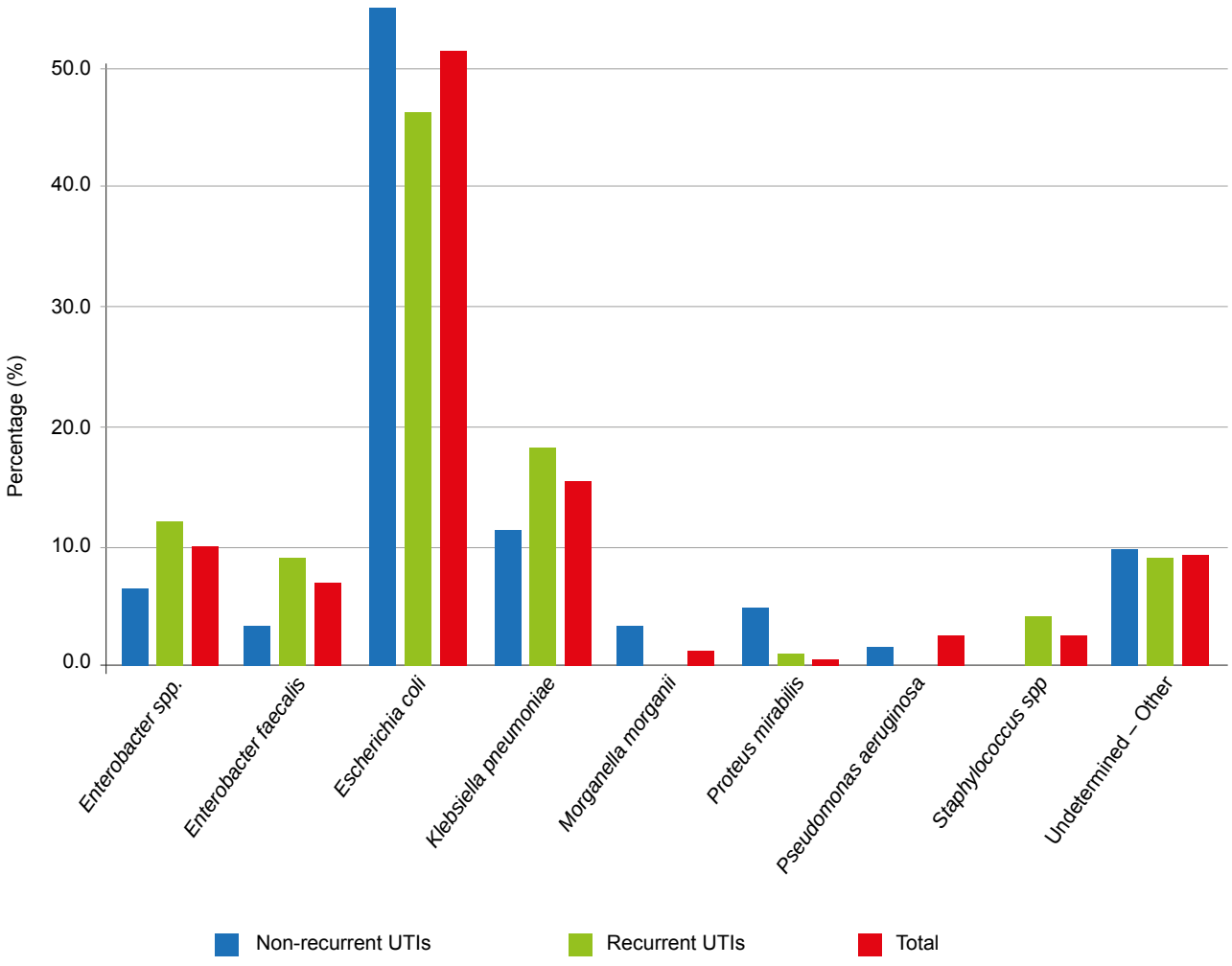

Figure 3 - Comparison between aetiological agents of non-recurrent, recurrent UTI and the total of UTI episodes

Regarding the immunosuppressive regimen, we were not able to establish any statistically significant association between the use of certain drugs and a higher incidence of UTI, neither in the patients in whom the use of drugs for immunosuppression induction was needed, nor in those patients in whom mTor inhibitors were used. In line with what has been described in other studies regarding maintenance therapy,[14] we found a higher UTI and recurrent UTI incidence rate in the group of patients under tacrolimus therapy (57.7% and 23.1%, respectively *vs.* 37.4% and 14.8% in the group of patients under cyclosporine, respectively). It has been described that clinical consequences related to immunosuppressive drugs (namely infections and neoplasms) are more related to the intensity of immune suppression than to the drugs themselves.[4] Similarly, regarding induction therapy, we found a higher number of UTI episodes in the group under ATG when compared to those under basiliximab and once again this tendency is in line with what has been described in literature[1,2,4,9] as ATG therapy acting through lymphocyte depletion is more immunosuppressive.

We also assessed the lowest serum creatinine level, usually described as nadir level, as well as the creatinine level at the end of the follow-up, in order to provide a rough estimate of the function of the kidney graft. As expected, we found an increase of the creatinine levels over the follow-up, with a higher level in the UTI group of patients. Although without a statistically significant relationship, this difference may be explained by a possible lesion of the renal parenchyma caused by the occurrence of infections.[1,2] Therefore, a higher creatinine level at five years would be expected in the recurrent UTI group. However, both groups show similar levels (0.37mg/ dL in the non-recurrent UTI and 0.28mg/ dL in the recurrent-UTI group).

Although an increase in mortality has been described related to the occurrence of UTIs,[1,2,5,6,9,15] this was not found in our study. In line with other series we found kidney allograft loss an average of 11.0% of our patients, ranging from5 to17%.[11] We did not observe any statistically significant association between UTI occurrence during follow-up and renal graft loss although we found that it occurred in 1 of 5 patients presenting allograft loss caused by acute rejection

versus 3 out of 4 with chronic graft failure. In patients presenting renal allograft loss related to chronic failure, infection alone may represent a major contributing factor for rejection events due to the exposure of renal parenchyma to released inflammatory mediators such as cytokines and free radicals.[1,2,12]

Regarding other clinical issues related to UTIs, we found that these mostly occur over the first semester post-transplantation (25.5%), once again in line with what was expected.[1-3,6] Pre-operative factors, namely surgical instrumentation of the urinary tract, as well as higher immune suppression regimens, mainly with higher steroid dosages, contribute to a higher risk of UTI.[1-3,5] These data reinforce the importance of early antibiotic prophylaxis.[1,5] The European guidelines recommend a UTI prophylaxis with trimethoprim-sulfametoxazole for renal transplant patients [1,2,5,7,9] which, beyond preventing *Pneumocystis jirovecci* infection, seems to contribute to a reduction of UTI frequency, duration of symptomatic disease, bacteraemia occurrence and need for hospital admission.[1,2,4,5] The optimal duration for this prophylaxis has not yet been determined.[5]

Although most UTI episodes have not needed hospital admission (corresponding to 69.4% non-recurrent UTI patients and to 71.7% recurrent UTI patients), these were the main cause for admission to the Nephrology Department. However, we should not assume that UTI is a minor health issue, potentially related to deadly complications.[1,6,13] Reassuringly, the absence of mortality related to UTI in our group of patients, even in patients with severe immune suppression and clinical manifestations, confirms the need for a low threshold for hospital admission and for an early start of appropriate therapy.

Regarding bacterial isolates, *Escherichia coli* (51.6%) was the most frequently isolated agent in the urine culture, followed by *Klebsiella pneumoniae* (15.5%) and *Enterobacter spp*. (9.9%), as previously reported.[1,2,5,9,16,13] This ranking was also observed for recurrent UTIs. Recently, another Portuguese study described *Klebsiella pneumoniae* as the most frequent agent in recurrent UTIs.[10]

Some of the associations already described have not been found in our study; this fact may be partly explained by the small number of patients in our study, preventing adequate statistical power. In addition, data related to a single Portuguese clinical centre limits a generalisation to other centres, with other models of follow-up. Furthermore, in our study, we were not able to study some of the variables described in literature, as some important information was not correctly described on patient's clinical records, namely the number of days patients required post-transplant urinary catheterization, the presence of double-J catheters and the need for early dialysis after the transplantation procedure. Information bias regarding the remaining collected variables is not expected and neither is the presence of unreported UTI.

To our knowledge, as a long follow-up cohort study, this has been the only study carried out in Portugal allowing for short and long-term clinical results regarding post-transplantation UTIs and recurrent UTIs to be obtained.

CONCLUSION

In our group of patients, female gender was the only risk factor for the development of recurrent or non-recurrent UTIs. Most UTIs (25.5%) occurred during the first semester post-transplantation and *Escherichia coli* was the aetiological agent most commonly found.

The long follow-up period of our study produced relevant information and raised new issues. Prospective, ideally multi-centric studies are needed, with a higher number of patients, in order to allow for a better characterisation of the Portuguese reality. On the basis of this study, we conclude that the results of renal transplantation, measured in terms of patient's survival and graft duration, have progressively improved but intercurrences, mainly infectious, remain a major problem in transplantation medicine.

ACKNOWLEDGEMENTS

The authors wish to acknowledge the *Secretariado da Consulta da Unidade de Transplantação Renal do Hospital de Santa Cruz* and all the personnel who made this study possible.

CONFLICTS OF INTEREST

The authors have declared no conflicts of interest in the writing of this manuscript.

FINANCIAL SOURCES

The authors have declared no external financial sources for the writing of this manuscript.

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Acta Med Port 2014:27:364-371

Publicado pela **Acta Médica Portuguesa**, a Revista Científica da Ordem dos Médicos

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www.actamedicaportuguesa.com
ISSN:0870-399X | e-ISSN: 1646-0758