

Clinical and Immunological Assessment of Renal Transplant Recipients

Avaliação Clínica e Imunológica dos Receptores de Transplante Renal

Evaluación Clínica e Inmunológica de los Receptores de Trasplante Renal

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ABSTRACT

Objective: The study's purpose has been to assess both clinical and immunological characteristics of renal transplant recipients. **Methods:** It is a documentary and retrospective study that was performed at the renal transplantation ambulatory from the *Hospital Geral de Fortaleza (HGF)*, Fortaleza city, Ceará State, with patients hospitalized from June 2012 to June 2014. The sample consisted of 300 patients submitted to renal transplantation. The predictive variables of interest were subdivided in the following categories: pre-transplant characteristics, post-transplant characteristics and immunological characteristics. Pearson and Spearman tests were used to evaluate the correlation between variables. **Results:** There was a predominance of male patients (65%), with ages ranging from 44 to 56 years (31.4%). A statistically significant relationship was found between the Donor-Specific Antibody and Delayed Graft Function ($p < 0.04$), Cellular Rejection and Panel-Reactive Antibody class I ($p < 0.05$), duration of hospitalization and Delayed Graft Function ($p < 0.001$) and also between the Human Leukocyte Antigen and MISMATCH. **Conclusion:** It is pointed out the need for a critical and individualized follow-up of the transplanted patient by the professionals to guarantee the long-term transplantation success.

Descriptors: Assessment, kidney transplantation, Nursing.

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RESUMO

Objetivo: Avaliar as características clínicas e imunológica dos receptores de transplante renal. **Métodos:** estudo documental e retrospectivo, realizado em um Ambulatório do Hospital Geral de Fortaleza, Fortaleza, Ceará, Brasil, com pacientes internados no período de junho de 2012 a junho de 2014. A amostra foi composta por 300 pacientes submetidos ao transplante renal. As variáveis preditoras de interesse, foram subdivididas em: características pré-transplante, características pós-transplante e características imunológicas. Utilizou-se testes de Pearson e Spearman para avaliar correlação entre variáveis. **Resultados:** Houve predomínio de pacientes do sexo masculino (65%), com faixa etária entre 44 e 56 anos (31,4%). Demonstrou-se relação estatisticamente significativa entre o DSA e a disfunção do enxerto ($p < 0,04$), Rejeição celular e Painel Reativo classe I ($p < 0,05$), o tempo de internação e a disfunção do enxerto ($p < 0,001$) e entre o entre o HLA e o MISMATCH. **Conclusão:** Aponta-se a necessidade de um acompanhamento crítico e individualizado do paciente transplantado por parte dos profissionais para garantir o sucesso do transplante a longo prazo.

Descritores: Avaliação, Transplante de Rim, Enfermagem.

RESUMEN

Objetivo: Evaluar las características clínicas e inmunológicas de los receptores de trasplante renal. **Métodos:** estudio documental y retrospectivo realizado en una clínica del Hospital General de Fortaleza, Fortaleza, Ceará, Brasil, con pacientes ingresados desde junio de 2012 a junio de 2014. La muestra fue de 300 pacientes sometidos a trasplante de riñón. Las variables predictoras de interés, fueron subdivididas en: características pre-trasplante, características post-trasplante y características inmunológicas. Se utilizaron pruebas de Pearson y Spearman para evaluar la correlación entre variables. **Resultados:** Hubo un predominio de pacientes del sexo masculino (65%), con edades comprendidas entre 44 y 56 años (31,4%). Se demostró una relación estadísticamente significativa entre el DSA y la disfunção del injerto ($p < 0,04$), el rechazo celular del panel reactivo clase I ($p < 0,05$), el tiempo de internación y la disfunção del injerto ($p < 0,001$) y entre el HLA y el MISMATCH. **Conclusión:** Se apunta la necesidad de un acompañamiento crítico e individualizado del paciente trasplantado por parte de los profesionales para garantizar el éxito del trasplante a largo plazo. **Descritores:** Evaluación, Trasplante de Riñón, Enfermería.

INTRODUCTION

Transplantation consists of a surgical procedure in which an organ or tissue is transferred from one individual to another, in order to replace or compensate for a lost function. In kidney transplantation, a healthy kidney is implanted in a person with chronic end-stage renal disease as the most effective replacement therapy.¹

According to the National Transplant Registry in the first quarter of 2015 compared to the data for 2014, there was a reduction in the number of transplants, registering a drop of 1.4% of potential donors and 0.8% of effective donors. Kidney transplantation fell by 7.6%, with a drop of 20.3% in live donors, and 3.4% in deceased donors. About 40% of families refuse to be organ donors.²

Renal transplantation is seen as an inducing process of intense inflammatory reaction where the transplanted organ functions as a foreign body in the recipient's organism,

filled with immunogenic antigens that are presented to their complex immune system, always determining an immunity reaction.³

After transplantation, the huge challenge is to avoid complications that could compromise the functioning of the graft and lead to its loss, especially rejection leading to a decline in renal function and requiring rapid intervention to avoid transplant failure.

Graft rejections are immunological processes that can be classified into cellular and humoral. In cellular rejections are generally acute and T lymphocytes are the main mediators of graft damage. In humoral rejections, the graft is assaulted by Donor-Specific Antibody (DSA) against donor antigens, produced by the recipient. These DSAs can also be produced later in life after transplantation, and thus rejection occurs progressively and chronically, culminating with a new chronic kidney disease.⁴⁻⁶

In order for renal transplantation success to occur, there must be ABO blood group compatibility, a Human Leukocyte Antigen (HLA) histocompatibility typing, and Crossmatch recognition, which is capable of predicting hyperacute rejection episodes.¹

Another factor that has substantially contributed to the fact that kidney transplantation is considered the best option for patients with chronic kidney disease is the technological advance with regard to immunosuppressive therapy. The main purpose of this therapy is to increase graft survival, avoiding acute and chronic rejections of the transplanted organ.^{7,8} With the advent of new immunosuppressive drugs, acute rejection rates decreased significantly, although the impact on the graft half-life has been less important.⁹

Renal graft monitoring is currently performed by measuring its function, and blood creatinine, whose variations are not specific for rejection, and renal biopsy are routinely determined. Hence, the identification of molecules by non-invasive, sensitive methods, useful in clinical practice, so-called biomarkers, has been the object of extensive studies by several groups of researchers.¹⁰

The nurses' contribution to the success of transplantation is undeniable since it provides specialized care in the protection, promotion, and rehabilitation of the health of candidates, recipients and their families, as well as of living and family donors throughout the life cycle.¹¹

Bearing in mind this framework, the study aimed to assess both clinical and immunological characteristics of renal transplant recipients.

METHODS

It is a documentary and retrospective study that was performed at the renal transplantation ambulatory from the *Hospital Geral de Fortaleza (HGF)*, Fortaleza city, Ceará State, with patients hospitalized from June 2012 to June 2014. It is a tertiary public hospital of reference in the

whole s Ceará State regarding the execution of transplantation of kidney, pancreas, liver, and corneas. The justification of this temporal cut is due to the access to complete data for the analysis of graft function.

The sample consisted of 300 patients submitted to renal transplantation. The data were collected from July to October 2016, using a form, based on the data recorded on the medical records of transplanted patients, regardless of gender or donor type. Children and double transplants were excluded from the study since their physiology and hemodynamics differ from adults and elderly people. The form contained sociodemographic data, clinical and laboratory aspects of transplant recipients.

The data were organized using the Excel program and then transferred to the Statistical Package for Social Sciences (SPSS) program version 21.0. Pearson's tests (the correlation between hospitalization time and graft dysfunction rate, the correlation between cellular rejection and panel-reactive antibody class I and class II, and the correlation between humoral rejection and panel-reactive antibody class I and class II) and Spearman (Correlation between DSA and graft dysfunction) for data analysis. Concerning the predictive variables of interest, they were subdivided in the following categories: pre-transplant characteristics, post-transplant characteristics, and immunological characteristics.

The study was carried out in agreement with the Resolution No.466/12 from the National Commission of Research Ethics. The data were collected after obtaining a favorable Legal Opinion No.754.462.

RESULTS AND DISCUSSION

There was a predominance of male patients (65%), within the age group from 44 to 56 years old (31.4%), with a weight range between 56 and 74 kg (53.6%), the most prevalent underlying disease being undetermined (64.1%), hemodialysis time between one and two years (35.8%), and the majority presenting a reactive panel in both classes of less than 10%, class I (69.4%) and class II (81%), and most recipients had a deceased donor transplant (97.3%).

It was evidenced that the majority of patients after renal transplantation did not have DSA (66.3%), Delayed Graft Function (DGF) (65.3%), cellular rejection (95.0%) and humoral rejection (91.3%), as well as complications (71.3%). In relation to the serum creatinine value, a constant decline was observed from the first week after renal transplantation, but only after the third month, the majority (55%) had a result lower than 1.3 mg/dL, constituting the threshold of normality (Table 01).

Table 01 - Distribution of renal transplant recipient according to post-

Variable	n	%
Presence of DSA¹		
Yes	101	33.7
No	199	66.3
Graft dysfunction		
No	196	65.3
Yes	104	34.7
Hospitalization time (days)		
<10	83	27.6
10 to 20	134	44.6
21 to 30	45	15
31 to 40	13	4.3
41 or more	25	8.2
Cellular rejection		
Yes	15	5.0
No	285	95.0
Humoral rejection		
Yes	26	8.7
No	274	91.3
Complications		
No	214	71.3
Yes	86	28.7
Creatinine		
week 1		
<1.3mg/dL	40	13.3
>1.3 mg/dL	260	86.7
Month 1		
<1.3 mg/dL	113	37.6
>1.3mg/dL	187	62.4
Month 3		
<1.3 mg/dL	165	55.0
>1.3 mg/dL	135	45.0

Note: 1Preformed antibody against the donor.

Spearman's correlation showed a statistically significant correlation between DSA and DGF (p=0.04).

rel	DSA	Spearman's correlation	p-value
DGF		p=0.04	p<0.05
DSA		p=0.04	p<0.05

Figure 01 - Correlation between the DSA and DGF (Spearman's correlation significance test).

Pearson's correlation showed a statistically significant difference between cellular rejection and Panel-Reactive Antibody (PRA) class I (p<0.05). The correlation showed significant results between humoral rejection with both re-

	Cellular rejection	Pearson's correlation	Significant p-value
PRA			
PRA I		0.038	<0.05
PRA II		0.613	<0.05

Figure 02 - Correlation between cellular rejection and PRA class I and class II (Pearson's correlation significance test). Fortaleza city, Ceará State, 2017. n = 300

Considering the **Figure 03** and through the Pearson's correlation, it is possible to reject the null hypothesis that there is no correlation between the variables, since the p-value is less than 0.001 and concludes in favor of the alternative hypothesis ($p \neq 0$) that there is a correlation. This result confirms the relationship between the duration of hospitalization and

	Hospitalization time	Pearson's correlation	Significant p-value
DGF		0.000	<0.001
	Hospitalization time	0.000	<0.001

	MISMATCH	Pearson's correlation	Significant p-value
HLA			
HLA A		$p=0.000$	<0.01
HLA B		$p=0.000$	
HLA DR		$p=0.000$	

Figure 04 - Correlation between hospitalization time and graft dysfunction rate - DGF (Pearson's correlation significance test). Fortaleza city, Ceará State, 2017. n = 300

The clinical and immunological characteristics of the renal graft function of the recipients of a reference hospital in renal transplantation were analyzed. Regarding the evaluation of reactivity against panel class I was of 209 (69.4%) <10% and that of class II presented 243 (81%) <10%, patients. The Panel-Reactive Antibody (PRA) test indicates the degree of HLA sensitization of the organ transplant recipient to the population of potential donors.¹² This panel is selected to represent the distribution of HLA antigens from the population and therefore the positivity against this panel reflects the reactivity against the population.¹³

Thus, the degrees of sensitization of a receptor will be considered sensitized when the reactivity is below 10%, sensitized when 10-50% and hypersensitized when the reactivity is above 50%. This definition may vary from center to center, and in some places, it is defined as hypersensitizing the one that reacts with more than 70 or 80% of panel cells.¹³

The PRA has great importance in the induction of immunosuppression and in the clinical follow-up of the transplanted patient, since guided by the PRA dosage, the physician decides for a more powerful immunosuppressant or in a

larger dose. Moreover, PRA discharge is a good indication of the risk of chronic rejection by DSA once again produced in a patient previously with a low PRA dose.¹⁴

Anti-HLA or DSA preformed antibody was found to be 66.3% not at risk for rejection. In contrast, 33.7% had preformed antibody for rejection. Regarding the prognosis of transplanted patients, the results indicate that a large part of implanted grafts did not present any dysfunction.¹⁵

The study presented a statistically significant relationship between DSA and graft dysfunction ($p < 0.05$), in order to express that the presence of DSA has a strong influence on renal graft dysfunction. A study⁵ addresses that the graft can be assayed by specific antibodies (DSA) against the donor's HLA produced by the recipient. These antibodies may be present in the recipient prior to transplantation, and thus, rejection may occur within the first few days or weeks after transplantation and may be produced later in the transplant period, and thus rejection occurs in a progressive and chronic manner, culminating with a new chronic renal disease.

Renal transplantation is currently the therapy of choice for patients with end-stage renal disease. Nonetheless, a considerable number of grafts are still lost due to acute and chronic rejection. There is evidence that humoral as well as cellular mechanisms are involved in rejection episodes. This leads us to believe that, although renal transplantation is the best treatment for end-stage renal disease, if there are no technologies in the detection of these antibodies the receptor may be being exposed to serious risks of triggering rejection process.^{16,17}

Considering the graft dysfunction (DGF), it was observed that the majority of the patients did not present problems with the development of the transplanted graft function. DGF is defined as the need to undergo dialysis within the first week after transplantation. It is a condition closely associated with the morbidity and significant economic burden of procedures necessary for the diagnosis and/or treatment of rejection and the long-term high rates of graft failure and mortality.¹⁸

There was a significant relationship between the length of hospital stay and renal graft dysfunction ($p < 0.01$), demonstrating that the longer the hospital stay plus the risk of graft dysfunction, the patient may present, a result corroborated in the literature.¹⁹

The study demonstrated a significant reduction in rejection rates, as the literature bring changes in detection and treatment directly contributing to this reduction. It is worth noting that a statistically significant relationship between cellular rejection and PRA class I ($p < 0.05$) and between humoral rejection and PRA class I and class II ($p < 0.05$) was evidenced.

In clinical practice, the main signs and symptoms that characterize the rejection are fever, systemic arterial hypertension, increased volume and pain on the graft, decrease in urinary volume and increase in the value of serum creatinine with no other explanation for the ascent.²⁰

Early diagnosis of acute rejection is crucial for graft function and survival, which requires the care team, especially nursing, to critically evaluate patients in the search for signs and symptoms for intervention in a quick and efficient manner.²¹

Regarding the HLA immunological characteristics, 46% of the patients had an HLA A compatibility, 47% had two compatibilities in HLA B and 52.3% had one in HLA DR. With regards to the MISMATCH, 26.3% of recipients presented three incompatibilities. The study demonstrated a significant relationship between HLA A, B, and DR, and MISMATCH ($p < 0.01$).

Class I HLAs are basically responsible for the signaling to the immune system of the internal state of the cell's protein machinery, among them the HLA A, B, C antigens. Class II HLAs are present in antigen-presenting cells of the defense system, notably HLA DR, DQ, and DP.²²

Some factors contribute to a greater risk of developing graft immune rejection, such as situations in which the organism is exposed to extraneous HLA, such as in blood transfusions and gestations, the greater the chance of producing a DSA, in other words, an antibody that can attach to the donor's HLA.²³

Nursing and all interdisciplinary teams play a key role in the care and monitoring of patients with chronic renal disease in the post-renal transplantation and should be performed in a coherent, responsible, humanized and directed to their singularity, based on scientific research, to ensure the best service. It is worth mentioning that this study contributes to the expansion of the knowledge of primary care professionals, in order to better follow-up on patients with chronic diseases, mainly in adherence to treatment, lifestyle change and early detection of complications, such as chronic renal disease (by calculating the filtration rate of all patients with hypertension and diabetes).

This study has limitations. It is worth noting that this is a cross-sectional study, which by the design itself does not allow a follow-up of the subjects, which would allow the identification of risk and/or protection factors. Furthermore, this is a documentary research, then predisposed to information bias.

CONCLUSIONS

Male participants within the age group from 44 to 56 have predominated. Most had no risk of rejection, but had graft dysfunction, rescue therapy complications, cellular and humoral rejection, and infections. The time of hospitalization was 10 to 20 days, demonstrating a reduction in rejection rates. Regarding the creatinine, in the first week there was a decay and in the sixth month, the creatinine result was lower than 1.3 mg/dL, this result means satisfactory post-transplant clinical evolution.

Hence, the need for a critical and individualized follow-up of the transplanted patient by the professionals to ensure the long-term transplantation success, then guaranteeing

that they return their activities with sufficient knowledge to maintain the graft and with self-care skills, enabling an adequate lifestyle and safety for professionals.

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