

RESEARCH ARTICLE (ORIGINAL) 

Clinical characterization of people undergoing kidney transplantation: immune sensitization

Caracterização clínica de pessoas submetidas a transplante renal: sensibilização imunológica

Caracterización clínica de las personas sometidas a un trasplante renal: sensibilización inmunológica

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Abstract**Background:** The kidney transplant is a foreign body in the patient's organism, thus constituting a procedure that triggers an intense inflammatory reaction.**Objective:** To assess the clinical characteristics of people undergoing kidney transplantation with immune sensitization.**Methodology:** A descriptive, documentary, and retrospective study with a quantitative approach to data treatment and analysis was carried out between June and August 2019.**Results:** The association between donor-specific antibodies (DSA) and graft dysfunction ($p < 0.03$) and pregnancy ($p < 0.04$) was statistically significant. The occurrence of complications was also associated with the length of hospital stay ($p < 0.00$) and serum creatinine levels in the first week after transplant ($p < 0.006$).**Conclusion:** The clinical characterization showed that most patients had graft dysfunction, DSA, and complications, meaning that transplanted patients require a critical and individualized follow-up.**Keywords:** nursing care; kidney transplantation; monitoring, immunologic**Resumo****Enquadramento:** O enxerto renal atua como um corpo estranho no organismo do doente, constituindo-se, assim, como um procedimento indutor de intensa reação inflamatória.**Objetivo:** Objetivou-se avaliar a caracterização clínica de pessoas submetidas a transplante renal com a sensibilização imunológica.**Metodologia:** Trata-se de um estudo descritivo, documental e retrospectivo, com abordagem quantitativa de tratamento e análise de dados, realizado de junho a agosto de 2019.**Resultados:** Evidenciou-se estatisticamente a relação do anticorpos doador-específicos (DSA) com a disfunção de enxerto ($p < 0,03$) e a gravidez ($p < 0,04$). Realizou-se também o cruzamento da ocorrência de complicação com tempo de internamento ($p < 0,00$) e o valor da creatinina sérica na primeira semana pós-transplante ($p < 0,006$).**Conclusão:** De acordo com as características clínicas, a maioria apresentou disfunção do enxerto, presença de DSA e complicações. Com isto, aponta-se a necessidade de um acompanhamento crítico e individualizado do paciente transplantado.**Palavras-chave:** cuidados de enfermagem; transplante renal; monitorização imunológica**Resumen****Marco contextual:** El injerto renal actúa como un cuerpo extraño en el organismo del paciente, por lo que constituye un procedimiento que induce una intensa reacción inflamatoria.**Objetivo:** El objetivo es evaluar la caracterización clínica de las personas sometidas a un trasplante renal con sensibilización inmunológica.**Metodología:** Se trata de un estudio descriptivo, documental y retrospectivo, con un enfoque cuantitativo en el tratamiento y el análisis de los datos, realizado de junio a agosto de 2019.**Resultados:** Se observó una relación estadística entre los anticuerpos específicos del donante (DSA) y la disfunción del injerto ($p < 0,03$) y el embarazo ($p < 0,04$). La aparición de complicaciones también se cruzó con la duración de la estancia hospitalaria ($p < 0,00$) y el valor de la creatinina sérica en la primera semana postrasplante ($p < 0,006$).**Conclusión:** Según las características clínicas, la mayoría presentó disfunción del injerto, presencia de DSA y complicaciones. Con esto, se apunta la necesidad de un seguimiento crítico e individualizado del paciente sometido a un trasplante.**Palabras clave:** cuidados de enfermería; trasplante de riñón; monitorización inmunológica**How to cite this article:** Saraiva, L. C., Nunes, A. C., Nascimento, M. V., Silva, A. C., Girão, C. M., & Studart, R. M. (2021). Clinical characterization of people undergoing kidney transplantation: immune sensitization. *Revista de Enfermagem Referência*, 5(6), e20121. <https://doi.org/10.12707/RV20121>

Introduction

Transplantation is one of the best therapeutic options for patients with chronic kidney disease (CKD) because it provides a better quality of life than other replacement therapies (Gonçalves et al., 2019). There is a worrying disproportion between the need for organs for transplantation and the number of transplants performed (Santos et al., 2015).

Transplanted patients are always at risk for organ rejection. Therefore, patients should receive adequate information to live with the real possibility of rejection and their new lifestyle, which will involve dependence on the daily use of immunosuppressive medication (Santos et al., 2015). Transplantation provides a better quality of life by freeing the patient from the hemodialysis machine, but it forces them to adopt a different lifestyle concerning their diet, hygiene, medications, and healthcare. Health education is essential for continuous care because it promotes the success of the surgery and minimizes rejection risks (Zhang, 2018).

Immune sensitization is defined by the presence of human leukocyte antigen (HLA) antibodies in the recipient's blood due to previous exposure to HLA, usually triggered by a history of organ transplant, pregnancy, or blood transfusion (Zhang, 2018).

Thus, sensitized recipients have an increased risk of antibody-mediated rejection (AMR) after kidney transplantation; however, subclinical AMR is suggested by the presence of donor-specific antibodies (DSA). Acute rejection can only be proven by biopsy (Vanhove et al., 2017).

Although T lymphocytes are often the most numerous infiltrating cells, several other mononuclear cells contribute to the development of the pathological process, such as B lymphocytes, Natural Killer Cells (NKC), dendritic cells, and monocytes/macrophages. The presence of NKCs, dendritic cells, and macrophages (elevated in more severe acute rejection and related to tubular dysfunction and chronic histological damage) confirms the indication of poor prognosis (Huang & Farkash, 2016).

The most current immunosuppressive therapies have reduced clinical rejection in the first year after transplant, while the diagnosis of subclinical rejections and the incidence of prior fibrosis markers have become important predictors of renal function and graft survival (Vanhove et al., 2017).

Given the complexity of the diagnosis and treatment of CKD, it is important to identify and assess the clinical outcome of patients undergoing kidney transplantation because it will provide useful data for more effective control of these patients and the success of their transplantation. In this context, the nurse plays a key role in the donation and maintenance of organs and tissues, as well as in the previous identification of patients who are at risk of immune sensitization to prevent AMR.

As it is a very complex therapeutic procedure, the nursing team must have technical-scientific expertise to provide systematized, specific, quality care.

Therefore, this study aims to assess the clinical character-

istics of people undergoing kidney transplantation with immune sensitization.

Background

The kidney transplant is a foreign body in the patient's organism, thus constituting a procedure that induces an intense inflammatory reaction. The immune responses of rejection of the transplanted organ are divided into cellular and humoral. Thus, cellular rejections are often acute, and T-cells are the main mediators of graft deterioration. Thus, in humoral immunity, the recipient's organ is damaged by DSA produced by the recipient against the donor's antigens (Sun & Yang, 2013).

Thus, antibody-mediated rejection has been defined as the main factor of graft dysfunction and graft loss after kidney transplant. DSAs identified before kidney transplantation (performed DSAs) can cause prior rejection, such as hyperacute rejection, accelerated acute rejection, antibody-mediated early acute rejection, and graft loss (Malheiro et al., 2017).

Presence of DSA, either performed or *de novo*, has become a well-established biomarker predicting poor transplant outcomes, including a high incidence of antibody-mediated rejection, graft dysfunction, and inferior graft survival. The increase in *de novo* DSAs after kidney transplant has been reported in 13%-30% of previously nonsensitized patients (Malheiro et al., 2017).

In this regard, the risk factors for DSA include high HLA mismatches, inadequate immunosuppression and non-adherence, graft inflammation, such as viral infection, cellular rejection, or ischemia injury, which can increase graft immunogenicity (Vanhove et al., 2017).

The evaluation of the renal function in the immediate postoperative period is related to urine formation (24-48 hours) and normalization of serum creatinine. Delayed graft function is defined as the need for dialysis within the first 7 days after transplantation, while tubular cell regeneration occurs (Motta et al., 2013). Therefore, it is important to assess the correlation between blood creatinine levels within the first week after transplantation and the occurrence of complications.

After transplantation, the major challenge is to avoid complications (early graft dysfunction, infection, urinary tract obstruction, thrombosis, stenosis) due to the high risks of rejection. Outpatient treatment is of utmost importance to avoid complications that can compromise graft function and lead to graft loss (Gill & Lowes, 2014).

Therefore, the following therapeutic strategies are used to reduce the progression of fibrosis in the kidney graft: immunosuppressive therapies without use or lower dosing of calcineurin inhibitors, renin-angiotensin-aldosterone system blockers, and treatment of subclinical rejections (Vanhove et al., 2017).

Nursing practice during this period aims to assess, detect, and intervene early in possible post-transplant kidney complications. Furthermore, the nursing team should possess at least basic knowledge, such as the patient's history, highlighting the evolution of the disease, current



status, and therapy applied to control and maintain the disease, as well as the patient's evolution during kidney transplantation and possible complications associated with the surgical procedure (Vanhove et al, 2017).

For Malheiro et al. (2017), the main nursing interventions in case of complications or rejection in the pre- and post-transplant period are to investigate the patient's history, risk of rejection, and living habits, monitor the results of laboratory tests, control diuresis, assess the presence and evolution of edema, assess signs and symptoms of fever, monitor blood pressure, administer immunosuppressant drugs as per medical prescription, and check the patient's and caregiver's education and adherence to therapy.

The nurses' contribution to the care delivered to patients during their treatment is indisputable as they are responsible for delivering individualized care to each patient and promoting and rehabilitating the recipients' health. They also play a key role minimizing the risks of graft rejection in transplanted patients (Gill & Lowes, 2014).

Research question

What is the correlation between the presence of DSA and the factors (graft dysfunction and pregnancy)?

What is the correlation between the occurrence of complications and the coefficients (length of hospital stay and serum creatinine level in the first week)?

Methodology

A descriptive, documental, and retrospective study was conducted with a quantitative approach to data treatment and analysis. Data were collected between June and August 2019 in a tertiary public hospital located in Fortaleza, Brazil, which has become a reference in kidney, pancreatic, liver, and corneal transplantation throughout the state of Ceará.

The sample consists of patients undergoing kidney transplantation. Three inclusion criteria were established for sample selection: a) to have been transplanted for at least one year; b) to be 18 years of age or more because transplantation in children has many specificities; and c) to agree to participate in the study. The exclusion criterion was a) double transplantations (kidney/liver or kidney/pancreas).

The study sample was calculated using the formula recommended for sample calculation in cross-sectional studies with finite populations (Hulley et al., 2008). The following parameters were used for sample calculation: a) 95% confidence level ($Z\alpha = 1.96$); b) sampling error of 5.3%; c) population size of 719 patients (number of transplants in 5 years); and d) a 90% prevalence of patients transplanted for more than one year.

Based on these parameters, the sample consisted of 356 patients who met the inclusion criteria. Data were collected using a form based on the transplanted patients' records. The form included sociodemographic, clinical, and laboratory data about the transplanted patients. Data were organized using Microsoft Excel and then transferred to IBM SPSS Statistics software, version 18.0. They were statistically analyzed using Pearson's test (correlation between length of hospital stay and graft dysfunction rate; correlation between cellular rejection and class I and class II panel reactive antibodies, and correlation between humoral rejection and class I and class II panel reactive antibodies) and Spearman's test (correlation between DSA and graft dysfunction) and based on the specific literature. The variables of interest were divided into pre-transplant characteristics and post-transplant characteristics.

The study was conducted in compliance with Resolution 466/12 of the National Research Ethics Committee (CONEP/CNS/MS). Data were collected after approval from the hospital's Research Ethics Committee (Opinion no. 2.435.893).

Results

The characteristics of kidney transplant recipients in this study were identified based on their clinical and immunological evaluation (Table 1).

Most patients were men (63.6%), and the majority of the women had already had at least one pregnancy (67.7%). Concerning age range, the mean age was 44.18 years, with the prevalence of the age range between 31 and 43 years (32.58%). Table 1 shows that most patients after undergoing kidney transplantation had no DSA (76.7%), graft dysfunction (65.3%), or complications (73.4%).

It should be noted that 42.1% of patients still had high serum creatinine levels three months after transplantation. As for the length of hospital stay, 44.6% of patients were hospitalized for 10 to 20 days.

Table 1*Distribution of kidney transplant recipients, according to post-transplant characteristics*

Variables	<i>f</i>	%
Presence of DSA ¹		
Yes	83	23.3
No	273	76.7
Graft dysfunction		
Yes	110	34.7
No	246	65.3
Length of stay (days)		
< 10	79	26.3
10-20	140	46.3
21-30	55	18.2
31-40	10	3.3
41 or +	18	5.9
Complications		
Yes	95	26.6
No	261	73.4
Creatinine		
Week 1		
<1.3 mg/dL	58	16.2
>1.3 mg/dL	298	83.4
Month 1		
<1.3 mg/dL	138	38.7
>1.3 mg/dL	218	61.3
Month 3		
<1.3 mg/dL	150	42.1
>1.3 mg/dL	206	57.9

Note. DSA¹ = Antibody preformed against the donor.

In Table 2, Spearman's correlation found a statistically significant association between DSA and graft dysfunction ($p < 0.03$) and between pregnancy and DSA ($p < 0.04$). Table 2 also shows a Spearman's cross-correlation between

length of hospital stay and occurrence of complications ($p < 0.00$) and a Spearman's correlation between serum creatinine levels in the first week and occurrence of complications ($p < 0.006$).

Table 2

Correlation between DSA/occurrence of complications with other factors, based on Spearman's Rank Correlation Test

	Correlation	Spearman's	Correlation	p-value
GD ²	DSA ¹	$p = 0.03$		$p < 0.05$
DSA ¹	PREGNANCY	$p = 0.04$		$p < 0.05$
COMPLICATIONS	LENGTH OF HOSPITAL STAY	$p = 0.00$		$p < 0.05$
COMPLICATIONS	SERUM CREATININE	$p = 0.006$		$p < 0.05$

Note. DSA ¹Antibody preformed against the donor. Graft dysfunction - GD.

Discussion

This study analyzed the profile and clinical outcome of patients undergoing kidney transplantation from a reference hospital for transplants in the state of Ceará, Brazil. A prevalence of men with CKD was confirmed (63.6%), with a disparity of 36.4%. This finding is in line with the study by Motta et al. (2013), in which the male gender is a risk factor for the development of CKD. Moreover, this higher prevalence of CKD in men is due to sedentary lifestyles, poor diet, stress, and other causes that contribute to the onset of the disease.

Regarding the transplanted patients' age, the 31-43 years age range (32.5%) prevailed, which is in line with Motta et al. (2013), who found a mean age of 36 years.

Coresh et al. (2007) also found a similar result. After the second decade of life, the GFT, whose normal value among young adults is around 120 mL/min/1.73m², progressively decreases on average 8-9 mL/min/1.73m²/decade.

Regarding the occurrence of pregnancy prior to transplantation, 67.7% of the women participating in the study had at least one pregnancy. Studies show that pregnancy prior to transplantation is a predisposing factor for DSA, which increases the likelihood of acute rejection and post-transplantation complications (Barbosa, 2014).

Barbosa (2014) calculated the likelihood of sensitization with a previous pregnancy and found an odds ratio of 5.81, that is, the likelihood of sensitization was 5.81 times higher in women in the group with previous pregnancies. A statistically significant association was also found between previous pregnancy and the presence of DSA ($p < 0.05$), which shows that a previous pregnancy has a strong influence on the presence of DSA.

Concerning the duration of dialysis prior to transplantation, 39.4% of transplanted patients had been doing dialysis for five years or more, and a small number of patients (5.9%) had undergone a preemptive transplant. These data may reflect the delay in undergoing the transplant or the lack of information and referral from the clinics to undergo a transplant. Evidence shows that the

longer the pre-transplant dialysis, the greater the number of comorbidities and the limitation imposed by the treatment (Frota et al., 2010).

With regard to the type of donor, there was a predominance (97.3%) of deceased donors, which is in line with the study by Motta et al. (2013), where 90.6% of transplants were performed with organs from deceased donors. Two of the advantages of living donors are that there is usually a higher HLA matching and a shorter ischemia time between organ removal and reimplantation, usually minutes. With deceased donors, HLA matching is partial or absent, and the time between organ removal from the donor and reimplantation into the recipient is longer, usually a few hours (Takemoto et al., 2004).

Prolonged tissue ischemia is known to facilitate the exposure of antigens of the transplanted organ to the recipient's immune system, favoring immune recognition and increasing the likelihood of triggering a rejection process (Guyatt et al., 2008).

Regarding preformed anti-HLA or DSA antibodies, 76.7% of patients were not at risk for rejection, while 23.3% had a preformed antibody for rejection. Regarding the prognosis of transplanted patients, the results show that a large part of implanted grafts was not dysfunctional (Moura et al., 2009).

The study showed a statistically significant association between DSA and graft dysfunction ($p < 0.05$), meaning that the presence of DSA has a strong influence on kidney graft dysfunction.

Sellarés et al. (2013) report DSA against donor HLA antigens produced by the recipient can attack the graft. These antibodies may be present in the recipient before transplantation, so rejection may occur in the first days or weeks after transplant or at a later time, occurring progressively and chronically and culminating in a new CKD. Kidney transplantation is the best alternative for patients with CKD. However, a substantial number of grafts are lost due to acute and chronic rejection. Humoral and cellular mechanisms have proven to be involved in rejection episodes.

Regarding Delayed Graft Function (DGF), 246 (65.3%) of patients had no problems with the function of the transplanted graft.

DGF is defined as the need for dialysis in the first week after transplantation (Butala et al, 2013).

The mean length of hospital stay was 10 to 20 days (46.3%). Motta et al. (2013) report that the mean length of hospital stay in cases of kidney transplantation is 24.6 ± 18.2 days.

A statistically significant association was found between the length of hospital stay and the presence of complications ($p < 0.01$), showing that the longer the length of hospital stay, the greater the risk of transplant-related complications.

Moreover, a statistically significant association was found between the occurrence of complications and serum creatinine levels in the first postoperative week ($p < 0.01$), meaning that complications strongly influence the normalization of serum creatinine levels and good graft function. Based on laboratory tests, this study shows that serum creatinine levels reduce after the first week, and 42.1% of patients had serum creatinine levels below 1.3 mg/dl in the third month. Data on graft function as assessed by the serum creatinine levels proved satisfactory, which is similar to the results found by Carvalho et al. (2010), where, on average, patients maintained a stable renal function at 3, 6, and 12 months after kidney transplantation.

In view of the above, it is important to understand the patient's clinical manifestations after transplantation and implement health plans based on each patient's needs.

Conclusion

The patients' clinical characterization shows that the majority of them had graft dysfunction, DSA, and complications. The length of hospital stay was 10 to 20 days, corroborating other studies. Serum creatinine levels reduced in the first week and were less than 1.3 mg/dL in most patients by the sixth month, which means a satisfactory post-transplant clinical evolution.

These results point to the need for a critical and individualized professional follow-up of transplanted patients to ensure the long-term success of the transplantation. Thus, these findings are expected to contribute to the implementation of health strategies for a successful transplantation and to the development of care plans, as this subject is understudied. They will serve as a basis for future research, providing nurses with a broader theoretical and scientific basis on the subject.

Author contributions

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