

# Impact of Cost of Adverse Events After Kidney Transplantation

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## ABSTRACT

**Introduction:** Kidney transplantation is considered the best treatment of rehabilitation for chronic kidney disease (CKD) patients, because it increases quality of life and survival when compared to other modalities of renal replacement. However, after kidney transplantation may occur clinical and surgical complications. **Objectives:** To evaluate the main causes of adverse events associated with renal graft and their impact on cost after kidney transplantation in the public system in Brazil. **Methodology:** Follow-up, descriptive, retrospective, exploratory, cause and effect study with economic evaluation. We used data from the Departamento de Informática do Sistema Único de Saúde (DATASUS). We identified patients with register of kidney transplant in the states of northern and northeastern Brazil in 2013 and had adverse event associated with renal graft. These patients were followed up through the registers on DATASUS, specifically using the Sistema de Informação Hospitalar SIH/SUS from 2013 to 2017. **Results:** A total of 183 patients with a renal graft-related adverse event during the first four years of kidney transplantation who required hospitalization for treatment. Patients up to six months after transplantation had a higher frequency of

readmissions and longer hospitalization. The impact of the cost of treating these patients on the total cost of readmissions was US\$ 302,952.05.

**Conclusion:** Through the data analysis from SIH/SUS, it was possible to identify that the complications related to renal graft had significant impact of cost on the value of readmissions after kidney transplantation.

**Key words:** Adverse Events, Graft Rejection, Health Care Costs, Health Expenditures, Kidney Transplantation.

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## INTRODUCTION

Kidney transplantation is considered the best treatment of rehabilitation for chronic kidney disease (CKD) patients, because it increases quality of life and survival when compared to other modalities of renal replacement.<sup>1,2</sup>

The Sistema Único de Saúde (SUS) in Brazil provides universal and free coverage, including high complexity procedures, in which organ transplantation is granted.<sup>3</sup> Thus, SUS is responsible for all the transplant costs, since the search for potential donors, transplant procedure and follow-up after the surgery.<sup>4</sup> In Brazil, according to data of the Brazilian Association of Organ Transplantation (BAOT), 5,923 kidney transplants were done in 2018.<sup>5</sup>

Despite the significant advances, clinical and surgical complications after the surgery still represent important causes of morbidity and mortality. The most common complications are early graft dysfunction, rejections, infections caused by microorganisms, dyslipidemia, diabetes, hypertension and bone problems.<sup>6-8</sup>

In Brazil, initial expenditures with renal transplant are high, due to the surgical procedure, but the ones regarding the follow-up are low. In addition, transplant has shown to be the therapeutic alternative with lower cost than hemodialysis and peritoneal dialysis.<sup>9</sup> However, it is necessary the assessment of the after transplant complications, because the costs with adverse events correspond to a significant part of direct hospital costs, what represents a high impact in the budget of hospital admis-

sions.<sup>10</sup> Treatment of these events in the kidney transplant patient, most of the times, requires hospitalization.<sup>11</sup>

In Brazil, the Ministry of Health provides a Sistema de Informação Hospitalar (SIH/SUS), which stores data regarding the hospital internment provided by SUS, monthly reported by all the contracted public health-care institutions that offer hospital admissions. The data are consolidated by municipalities and states that send to DATASUS after their analysis and approval. The database is fed after filling out the Autorização de Internação Hospitalar (AIH).<sup>12</sup>

It is possible, through the data available on SIH/SUS, to evidence the cost and characteristics of the complications after kidney transplant in the different Brazilian regions and in different periods of time. Conducting a research about the complications after kidney transplant, assessing the cost in two different Brazilian regions, has important relevance for an efficient management of the resources and a better monitoring of patients. This study aimed to analyze the main causes of adverse events associated with renal graft and the impact of cost after kidney transplantation in the public system in Brazil.

## MATERIALS AND METHODS

This is follow-up, descriptive, retrospective, exploratory, cause and effect study with economic evaluation in which the universe were patients with register of kidney transplant in 2013 in the Northern and Northeastern

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Brazil. We assessed the adverse events related to the kidney graft during the four first years of transplant of these patients. Databases from different years and Brazilian states were associated through data linkage. We used the SIH/SUS as database, from the Information Department of SUS. The submission to the Human Research Ethics Committee was not required, as the research used publicly available information under law No. 12.527 / 2011 and without the possibility of individual identification, as provided for in Resolution No. 510/2016.<sup>13,14</sup> The sample consisted of readmissions between 2013 and 2017. The inclusion criteria were patients who had register of kidney transplant in the year of 2013 according to SIH/SUS in the Northern and Northeastern Brazil; whereas the exclusion criteria were patients with complications not related to kidney transplant.

## Analysed Variables

We analyzed the following variables in the study: sex; age, race/color, rate of adverse events associated with renal graft in the four first years after kidney transplant; International Classification of Diseases (ICD-10) and average of length of hospital stay for treatment of adverse event. Data were collected by a researcher from June to December 2018 on the DATASUS website (<http://www2.datasus.gov.br/DATASUS/index.php?area=0901&item=1&acao=25>) (BRASIL, 2017).<sup>15</sup>

## Economic Evaluation

This is a partial cost analysis, cost-consequence type, in which we analyzed the costs related to readmissions due to complications after kidney transplant. We only analyzed direct costs, in the Brazilian currency (US\$) and in the perspective of SUS. The real Brazilian currency was converted to the American dollar using the 2017 value for the last follow-up year. Data were also analyzed separately in the Northern and Northeastern regions of Brazil.

## Statistical Analysis

The files were extracted from the SIH / SUS base in .dbc format and expanded in the TabWin program to .dbf. Through the program convince to be exporting to Excel® version 2016. Statistical analysis was performed using the SPSS program. A crossover was performed between variables in which the causes and consequences were determined. In the analysis of numerical variables, the variance analysis test (three groups) were applied ( $p < 0,05$ ). All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) 21.0.0.0. Data were presented as graphs and tables.

## RESULTS

A total of 183 patients with kidney transplant register in 2013, which had adverse events related to the graft during the first four years after transplant, were included in the study. These patients correspond to 20,5% ( $n=183/893$ ) of those transplanted in 2013. The mean age of patients, during the occurrence of the adverse event, was 44 years old ( $\pm 13$  years) and 67.7% ( $n=124$ ) were male (Table 1). The total number of readmissions was 403 and each patient, in average, was readmitted twice for treatment of adverse event related to the graft.

The readmissions happened with higher frequency ( $n=240$ ; 59.7%) during the first six months of post kidney transplant. Besides that, the admissions in the period from 6 months until 2 years occurred in 25.4% ( $n=103$ ) of the times and they decreased when patients had more than two years of kidney transplant ( $n=60$ ; 14.9%).

ICD with higher frequency of readmissions was End-stage renal disease (N18.0) with 35.98% ( $n=145$ ) (Figure 1). During the follow-up period, we have found 9 death registers, in which 77.8% ( $n=7$ ) were in the first

six months of kidney transplant and 22.2% ( $n=2$ ) were in the period from 6 months to 2 years.

Main ICDs registered as cause of death were: Respiratory arrest (R09.2;  $n=5$ ; 55.6%), Acute Respiratory Failure (J96.0;  $n=1$ ; 11.1%), End-stage renal disease (N18.0;  $n=1$ ; 11.1%), Kidney Transplant Failure and Rejection (T86.1;  $n=1$ ; 11.1%) and Acute Kidney Failure, unspecified (N17.9;  $n=1$ ; 11.1%).

Regarding the length of stay of the admission, we analyzed that: 52.6% ( $n=212$ ) of the readmissions length less than 10 days, 43.4% ( $n=175$ ) length among 10 and 30 days and 4% ( $n=16$ ) a prolonged time longer than 30 days.

The average of the daily rate for treatment of the patient's clinical condition was US\$ 52.06, with a total spend of all readmissions of US\$ 302,952.05 in which 84.7% (US\$ 256,445.72) were hospital spends and 15.3% (US\$ 46,506.33) spends with human resources. The diagnosis with higher spend was End-stage kidney disease ( $n=145$ ) with an amount of US\$ 132,904.36 (25.2%) for 145 readmissions (Table 2). The average of length of stay with diagnosis N18.0 was 9 days (min: 1 day and max: 33 days).

The period after transplant in which the adverse event occurred ( $\leq 6$  months) and the length of the stay (among 10 and 30 days) for treatment had statistically significant correlation with total cost of the readmission (Table 3).

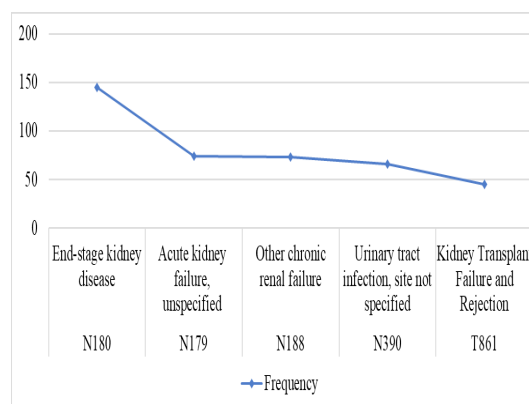
Regarding the kind of admission, 80.6% ( $n=325$ ) were urgency and 17.4% ( $n=70$ ) were elective, that is, most patients had graft complications that needed immediate assistance. 41.23% ( $n=134$ ) of the urgent care assistances were related to ICD N18.0, while 61.43% ( $n=43$ ) of the elective had as main diagnosis ICD N18.8. The average daily cost was very similar: urgency was US\$ 53.59 and the elective US\$ 46.6. Besides that, 88.89% ( $n=8$ ) of patients who died were in urgent care assistance.

The impact of the cost of the treatment of these patients in relation to total cost of readmissions (US\$ 528,329.50) was of 57.3% (US\$ 302,952.05).

## DISCUSSION

The analyses of health situations, in Brazil, can be carried out with aid of Health Information Systems of the Brazilian Ministry of Health.<sup>16,17</sup> Thus, by filling the Authorization for Hospital Admission (AIH) which is monthly sent by the municipal and/o state manager to DATASUS, it is possible to have individualized data by non-identified patient about admission, diagnose, procedures and costs.<sup>18</sup>

The occurrence of adverse events related to the renal graft was frequent in the period until 6 months after the kidney transplant, patients in this



**Figure 1:** Main diagnoses registered in the admissions during post kidney transplant ( $n=403$ ). Brazil, 2019. (Statement: at column width).

**Table 1: Epidemiological profile of patients followed up from 2013 to 2017 for assessment of adverse events after kidney transplant (n=183). Brazil, 2019. (Statement: at column width).**

Variables		N	%
Sex	Male	124	67.7
Race/color	Brown	96	52.4
	No Information	63	34.4
	White	14	7.6
Age	Black	10	5.6
	Max.	79 years old	
	Min.	5 years old	
	Mean ± SD	44 years old ± 13	
Readmissions	Max.	25	
	Min.	1	
	Mean	2	

**Table 2: Description of registered ICD as adverse event of kidney graft, frequency and cost (n=403). Brazil, 2019. (Statement: at column width).**

Main Diagnosis - ICD		N	Cost (US\$)
N18.0	End-stage kidney disease	145	132,904.36
N17.9	Acute kidney failure, unspecified	74	61,040.16
N18.8	Other chronic renal failure	73	40,177.34
N39.0	Urinary tract infection, site not specified	66	40,238.30
T86.1	Kidney Transplant Failure and Rejection	45	28,882.82
TOTAL		403	302,952.05

time range stayed longer at the hospital, as well as in the study conducted in Iran by Lankarani, Noorbala and Assari (2009).<sup>13</sup>

Just as found in another study conducted in Canada, age and male sex were not determinative for a higher frequency of adverse events.<sup>19</sup> In a study conducted by Gupta *et al.* (2019) the mean age was 35.61±10.64.<sup>19,20</sup> Besides that, the predominance of the male sex agrees with other studies, which point a higher prevalence of renal failure in men than in women.<sup>20,21</sup> In the assessment conducted by Carlotto and colleagues (2019) in Brazil, patients with complications also were male, although with mean age of 36.3±7.4. There is proximity of identified ages in the literature and the present study, reinforcing the profile of patients submitted to kidney transplant.<sup>22</sup>

Even with the transplant for treating the renal failure, the higher frequency of graft dysfunction was due to end-stage kidney disease. The development of a system that predicts the risk of renal graft loss is a reality due to the frequency of this event.<sup>23</sup> Associated to these factors, there is the occurrence of unspecified acute renal failure in the hospital readmission of the patients.<sup>24</sup>

Besides that, the incidence of infections also increased the readmissions of patients in the period up four years after transplant. During the initial period, patients use high doses of immunosuppressant drugs for preventing graft rejection, thus the pharmacotherapy of these patients includes antibiotics, antiparasitic and antiviral drugs as prophylaxis treatment for opportunistic infections.<sup>25</sup> In the study of Ruppel and colleagues (2018), it was shown that infection was the main cause of mortality in the first five years after kidney transplant.<sup>26</sup>

**Table 3: Correlation among main diagnosis of adverse event, time after transplant and length of stay (n=403). Brazil, 2019. p=0.031. (Statement: at column width).**

Main Diagnosis	≤ 6 Months		> 6 Months and ≤ 24 Months		> 24 Months		US\$	<10 Days		<30 Days		Total
	Months	Months	Months	Months	Months	Months		Days	Days	Days	Days	
N17.9	55	7	12	12	34	132,904.36	34	38	2	74	74	
N18.0	103	35	7	7	76	61,040.16	76	62	7	145	145	
N18.8	28	31	14	14	44	40,177.34	44	27	2	73	73	
N39.0	33	18	15	15	29	40,238.30	29	34	3	66	66	
T86.1	21	12	12	12	29	28,882.82	29	14	2	45	45	
TOTAL	240	103	60	60	212	302,952.05	212	175	16	403	403	

Legend: N18.1 End-stage kidney disease; N17.9 Acute kidney failure, unspecified; N18.8 Other chronic renal failure; N39.0 Urinary tract infection, site not specified; T86.1 Kidney Transplant Failure and Rejection.

The type of initial care to the patient may be decisive to the prognosis, in the cases, which involved adverse events regarding the renal graft, in this study, the great part of patients had graft complications that needed immediate care and deaths had occurred in these circumstances. However, there was not a higher cost when compared to elective care. Although the direct costs of patients who died were lower, there is a huge impact in the indirect costs such as the intangible costs for the society.

The treatment of patients with adverse events related to the renal graft had a significant cost impact in relation to the total cost spent in this period for hospital treatment of patients who underwent kidney transplant. The occurrence of readmissions after transplant and, in this case, consequent to adverse events increased the value of the transplant and in another study, it is possible to evidence this association.<sup>22,27</sup>

However, it can be evidenced that costs with adverse events decreased in the period of two years after the transplant, because there was a reduction in the readmissions and length of hospital stay. In the analysis lead by Zur-Mühlen *et al.* (2018), the costs with transplant dropped after one year and stayed stable until four years.<sup>28</sup>

Besides the costs generated with readmissions of post-transplant patients for treatment of adverse events, kidney transplant has shown the lower cost among the therapies for renal failure. Because the initial spend with transplant is elevated due to the surgical procedure, as well as the spends with maintenance in the normal course of follow up are reduced, however, dialysis therapy have its costs elevated with time, justified by the progressive loss of the organ.<sup>29,30</sup>

## CONCLUSION

By tracking the occurrence of adverse events, with aid of a Health Information System of the Brazilian Ministry of Health, it was possible to evidence the great impact of costs involved in the readmission of patients for treatment of adverse events related to the renal graft in the first four years. It was possible to identify that patients up to six months after transplant had higher frequency of readmissions and longer length of stay, thus, subsidize changes and specifications in the protocols of treatment after transplant, which could minimize this incidence.

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## CONFLICT OF INTEREST

The authors declare none.

## ABBREVIATIONS

**CKD:** Chronic Kidney Disease; **DATASUS:** Departamento De Informática Do Sistema Único De Saúde; **SIH/SUS:** Sistema De Informação Hospitalar; **SUS:** Sistema Único De Saúde; **BAOT:** Brazilian Association Organ Transplantation; **AIH:** Autorização De Internação Hospitalar; **ICD-10:** International Classification of Disease.

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