



ORIGINAL ARTICLE

Prevalence, causes, and complications of acute kidney transplant rejection: survey in a single center

Mohsen Mohammad Rahimi¹, Ali Taghizadeh Afshar¹, Mansour Alizadeh¹, Atefeh Jafarzadeh Kohneeloo², Rohollah Valizadeh³, Roya Zakeri⁴, Sanam Fakour⁵, Mohammadreza Mohammadi Fallah^{1,*}

¹*Nephrology and Kidney Transplant Research Center, Urmia University of Medical Sciences, Urmia, Iran*

²*Department of Epidemiology and Biostatistics, Tehran University of Medical Sciences, Tehran, Iran*

³*Student Research Committee, Urmia University of Medical Sciences, Urmia, Iran*

⁴*Department of Pediatrics, Urmia University of Medical Sciences, Urmia, Iran*

⁵*Medicine Faculty and Student Research Committee, Urmia University of Medical Sciences, Urmia, Iran*

Corresponding author: Mohammadreza Mohammadi Fallah, E-mail: Mohammadifallah44@gmail.com

ARTICLE INFO*Article history*

Received: Jul 29, 2017

Accepted: Aug 29, 2017

Published: Oct 05, 2017

Volume: 2

Issue: 4

Conflicts of interest: None

Funding: None

Key words

Chronic renal failure,

Kidney,

Transplantation,

Transplant rejection

ABSTRACT

Backgrounds: Kidney transplantation has become a preferred surgical treatment for several renal disorders. To obtain information on acute transplant rejection and its complications, it is important to determine rejection prevalence and its potential causes. **Methods:** In this retrospective, 37-year study, 2,250 patients underwent conventional kidney transplantation. Patients who experienced graft loss, who underwent nephrectomy of the transplanted kidney during the first month after transplantation, or who died were enrolled the study. All required data were recorded in a designed questionnaire. **Results:** Of the 2,557 patients who underwent kidney transplantation, 86 (3.36%) experienced acute graft loss during the first month after transplantation; of these, 43 (50%) were men and 43 (50%) were women. The mean age of the patients who experienced acute graft loss was 40.09 ± 14.09 years. The most common underlying causes of acute graft loss were as follows: acute rejection of transplanted kidney (17.5%), renal vein thrombosis (13.9%), heart infarction (13.9%), and idiopathy (6.9%). Of these 86 patients, 33 underwent nephrectomy after rejection; however, 53 responded well to medical treatment. In addition, 33 patients (38.4%) underwent acute nephrectomy during the first month after transplantation, which constituted in 33 patients (1.2%) of the total graft losses. **Conclusion:** In our study, renal vein thrombosis was the most common underlying cause of graft loss in kidney transplantation patients that can be prevented using anticoagulants or other drugs to help prevent such outcomes, and graft rejection occurred most commonly in the first week after transplantation.

INTRODUCTION

Chronic kidney disease (CKD), defined as decreased glomerular filtration rate, increased renal albumin excretion, or a combination of decreased glomerular filtration rate and increased albumin loss, is a common clinical condition (1). Several complications are associated with CKD development, including increased cardiovascular complications, kidney disease progression, acute kidney injury, diminished cognition, anemia, mineral loss, and skeletal disorders and fractures (2). Diabetes mellitus is the most common cause of CKD, but other causes, such as herbal and environmental toxins, may be more common in some areas (3).

With thousands of surgeries performed during the past decade, kidney transplantation has become a preferred surgical treatment of several renal disorders (4). Surgical

transplantation techniques are well established, and the procedures have high success rates and few complications (5). However, surgical complications may develop in either the wound or the renal anastomoses. In terms of transplant stage, complications may arise during the back-table preparation of the allograft, the dissection of the renal bed and vascular anastomosis, and the restoration of the urinary tract (6).

Studies have shown different etiologies for renal transplant rejection. In 50% of cases, renal vein thrombosis was the underlying etiology leading to transplant rejection (7). Acute rejection of the transplanted kidney, especially during first weeks after transplantation, imposes irrevocable losses in terms of physical and mental conditions, in addition to economic effects (8). Despite numerous studies of post-transplantation side effects and chronic rejection of the transplanted kidney, few studies have evaluated the relation-

ship between acute rejection and early mortality. Since 1997, approximately 2,500 renal transplantations have been done at the Urmia Kidney Transplant Center. However, comprehensive studies are needed that investigate the probable relationship between acute rejection of the transplanted kidney and associated complications (1, 6, 7).

To obtain information on acute transplant rejection and its complications, it is important to determine rejection prevalence and its potential causes. Therefore, in this study, we investigated the prevalence of acute kidney transplant rejection and its causes.

METHODS

In this retrospective, 37-year study (conducted from 1988 to 2015), we analyzed 2,557 patients who received conventional kidney transplants performed at the Urmia Kidney Transplant Center in Urmia, Iran. The exclusion criterion was having incomplete medical records. The method of sampling was census, and all available records during the study period were selected. This study was approved by the Ethics Committee of the Research and Innovation Chancellor of the Urmia University of Medical Sciences. All transplantations were performed by members of a single transplant group, which was under the supervision of the department head.

Patients who experienced graft loss or nephrectomy of the transplanted kidney during the first month after transplantation or who died were enrolled in the study. All necessary information, including donor characteristics, recipient sex and age at the time of transplantation, underlying diseases, causes of allograft failure, and reasons for transplantation, were obtained from patient hospital admission records and operating room records and were recorded in a designed questionnaire. Data were analyzed using SPSS version 18 software (SPSS Inc., Chicago, IL, USA). To express quantitative values, we used mean \pm standard error. Comparison between groups was performed using independent t-tests for unpaired variables and the chi-squared test for qualitative variables. *P* values less than 0.05 were considered statistically significant.

RESULTS

Of the 2,557 patients who underwent kidney transplantation, 86 (3.36%) experienced acute graft loss during the first month after transplantation; of these, 43 (50%) were men and 43 (50%) were women. The mean age of the patients who experienced acute graft loss was 40.09 ± 14.09 years. Of 86 transplanted kidneys, 70 (81.4%) were left-side kidneys and 16 (18.6%) were right-side kidneys. The main cause of CKD was glomerulonephritis (Table 1). The most common underlying causes of acute graft loss were as follows: acute rejection of transplanted kidney (30 patients, 34.9%), renal vein thrombosis (15 patients, 17.5%), heart infarction (12 patients, 13.9%), idiopathy (6 patients, 6.9%), gastrointestinal bleeding (4 patients, 4.7%), sepsis (4 patients, 4.7%), bleeding of vascular anastomosis (4 patients, 4.7%), acute lung edema (3 pa-

tients, 3.5%), pulmonary embolism (2 patients, 2.3%), artery thrombosis (2 patients, 2.3%), intestinal perforation (2 patients, 2.3%), and emphysematous pyelonephritis (2 patients, 2.3%) (Table 2).

Of 86 patients, 33 underwent nephrectomy after transplant rejection, whereas 53 responded well to medical treatment. The causes of nephrectomy were as follows: vascular thrombosis (45.5%), graft rejection (15.2%), emphysematous pyelonephritis (6.1%), bleeding subsequent to anastomosis (6.1%), gastrointestinal bleeding (3%), sepsis (3%), and idiopathy (5.2%).

In our study, 33 patients (38.4%) underwent acute nephrectomy during the first month after transplantation, which constituted 1.2% of the total graft losses.

Furthermore, in our study, the most common reasons for nephrectomy in the first month after transplantation were vascular thrombosis (51.6%) and graft rejection (15.2%). The first week after transplantation included the most patients with graft loss (65.1%). During the second, sixth, and eighth weeks after transplantation, 18.6%, 7%, and 9.3% of patients, respectively, experienced graft loss.

Finally, during the first month after transplantation, 31 patients (36%) died after graft loss.

Table 1. Causes of chronic kidney disease in participating patients

Variable	Frequency	Percent
Diabetes	18	20.9
Glomerulonephritis	39	45.3
Chronic pyelonephritis	4	4.7
Polycystic kidney	7	8.1
Hypertension	11	12.8
Vesicoureteral reflux	3	3.5
Stone	2	2.3
Unknown	2	2.3
Total	86	100.0

Table 2. Causes of transplant rejection in participating patients

Variable	Frequency	Percent
Renal vein thrombosis	15	17.4
Rejection	30	34.9
Myocardial infarction	12	14.0
Renal arterial thrombosis	2	2.3
Intestinal perforation	2	2.3
Pyelonephritis	2	2.3
Hemorrhage due to surgery	4	4.7
Gastrointestinal bleeding	4	4.7
Sepsis	4	4.7
Acute pulmonary edema	3	3.5
Pulmonary embolism	2	2.3
Unknown	6	7.0
Total	86	100.0

DISCUSSION

In this descriptive analysis, we found that, in order of occurrence, rejection of transplanted kidney, thrombosis of renal kidney, and myocardial infarction were the most common causes of graft loss. Other causes were bleeding, sepsis, gastrointestinal perforation, and emphysematous pyelonephritis.

Previous studies showed that the most common cause of acute graft loss was vascular thrombosis. Acute rejection was the second most common complication that ultimately led to graft loss (7,8). However, in our study, acute renal rejection and vascular thrombosis were the most common, whereas, in similar studies, the primary causes were thrombosis and acute rejection (8).

It may seem that the high prevalence of rejection in our center was due to the lack of human leukocyte antigen laboratory testing, which are important screening and preoperative tests. However, the recent use of new-generation immunosuppressive drugs, such as mycophenolate mofetil, cyclosporine, and corticosteroids, has decreased the prevalence of rejection.

In this study, vascular thrombosis was the second most common complication that led to graft loss, and it was much lower than in similar studies. However, deaths, with normal functioning of transplanted kidneys, were higher than those reported in similar studies (44.1% vs. 15.6%, respectively) (8). This difference can be explained by a higher incidence of myocardial infarction (14%) in our study in comparison to that reported in other studies (7.3%). Therefore, strong criteria are needed for the screening of cardiac complications prior to kidney transplantation. Furthermore, scrutinizing risk factors for vascular thrombosis for patients and for prophylactic treatment is needed.

Patients who were candidates for transplantation, had a previous history of vein catheter implementation for hemodialysis, and all patients received angiography prior to surgery. In cases of atherosclerosis or stenosis, transplantation was performed at the contralateral iliac fossa (8).

Another reason for the statistical difference is lack of early graft loss of kidney transplantation in our center due to initial function of the transplanted kidney compared to similar study (12.8%) (9). In our study, only idiopathic causes were higher; other results, however, were approximately the same. The main reason for higher idiopathic causes of graft loss in our study was the lack of evidence recording.

In our center, 5.8% of early graft losses were attributed to pulmonary complications. This may be explained by cardiopulmonary disorders in three patients prior to transplantation. Also, in our study, two patients died because of intestine perforation. The main reasons may be intestine injury during abdominal wall reconstruction at the end of surgery and lack of a diagnosis.

Early nephrectomy was performed in 33 patients (1.2%). We found an obvious difference compared to previous studies (5,9). Johnston et al. showed that the prevalence of early nephrectomy after early graft loss was 56%, which was higher than our findings (38.4%). In addition, Johnston et al. reported more early nephrectomy in a period of less than a year, so that among 3707 patients with early transplant fail-

ure (graft survival <12 m), nephrectomy was performed in 56%, whereas we followed-up patients in less than a month/ Furthermore, Johnston et al. reported a nephrectomy incidence of 38.4%, which was higher than the incidence reported in our study (5). The main reason for this difference is that they considered both the early and late nephrectomy of transplanted kidneys, whereas we focused merely on the early nephrectomy of transplanted kidneys.

Reasons for nephrectomy within 1 month of kidney transplantation have been reported as follows: vascular thrombosis (51.6%), rejection (15.2%), and other causes (33.2%), which are in agreement with the findings of Ariyathenam et al. (5). Nevertheless, Zargar et al. found that the underlying causes of nephrectomy within 6 weeks of transplantation were as follows: rejection (57.1%), vascular thrombosis (28.4%), and sepsis (14.2%) (10). It seems that the significant differences between these two studies can be explained by attempts in our study to retain the transplanted kidney and not perform nephrectomy after rejection. However, approved vascular thrombosis in patients leads to nephrectomy.

In our study, all cases of vascular thrombosis led to nephrectomy, and we were not able to retain transplanted kidneys in cases of thrombosis. Panahi et al. found that the reasons for transplanted kidney nephrectomy within 10 weeks of transplantation were rejection (82%) and thrombosis (18%) (11). In comparison to our study, rejection was the most common cause of transplanted kidney nephrectomy, followed by vascular thrombosis.

In our study, most transplanted kidney losses occurred during the first week after transplantation (56 of 86 graft losses). In a similar study, Phelan et al. reported 57 graft losses of 92 cases during the first week (8).

CONCLUSION

Like previous studies, ours showed that renal vein thrombosis was the most common underlying cause of graft loss in kidney transplantation patients, and that the first week after transplantation was the most probable postoperative time for graft rejection. In light of these findings, we suggest intensive care to prevent renal vein thrombosis, especially during the early postoperative stages. In patients who undergo transplantation. We recommend that anticoagulants or other drugs be used to help prevent such outcomes.

ACKNOWLEDGMENTS

We thank the patients who contributed to this study and everyone who helped design and complete it.

AUTHOR CONTRIBUTIONS

All authors contributed equally to this study.

REFERENCES

1. Jha V, Garcia-Garcia G, Iseki K et al. Chronic kidney disease: global dimension and perspectives. *The Lancet* 2013;382:260-272.

2. Bonventre JV, Weinberg JM. Recent advances in the pathophysiology of ischemic acute renal failure. *Journal of the American Society of Nephrology* 2003;14:2199-2210.
3. Humar A, Matas AJ. Surgical complications after kidney transplantation. *Seminars in dialysis: Wiley Online Library*, 2005:505-510.
4. Hernández D, Rufino M, Bartolomei S et al. Clinical impact of preexisting vascular calcifications on mortality after renal transplantation. *Kidney international* 2005;67:2015-2020.
5. Ariyathenam A, Bamford A, Akoh JA. Transplant nephrectomy-A single-center experience. *Saudi Journal of Kidney Diseases and Transplantation* 2015;26:1108.
6. Sun I, Hong Y, Park H et al. Comparison of the Clinical Characteristics of Renal Transplant Recipients Who Underwent Early Versus Late Graft Nephrectomy. *Transplantation proceedings: Elsevier*, 2013:2953-2956.
7. Hernández D, Rufino M, Armas S et al. Retrospective analysis of surgical complications following cadaveric kidney transplantation in the modern transplant era. *Nephrology Dialysis Transplantation* 2006;21:2908-2915.
8. Phelan PJ, O'Kelly P, Tarazi M et al. Renal allograft loss in the first post-operative month: causes and consequences. *Clinical transplantation* 2012;26:544-549.
9. Johnston O, Rose C, Landsberg D, Gourlay W, Gill J. Nephrectomy after transplant failure: current practice and outcomes. *American Journal of Transplantation* 2007;7:1961-1967.
10. Zargar M, Kamali K. Reasons for transplant nephrectomy: a retrospective study of 60 cases. *Transplantation proceedings: Elsevier*, 2001:2655-2656.
11. Panahi A, Bidaki R, Mirhosseini SMM, Mehraban D. Renal allograft nephrectomy: Comparison between clinical and pathological diagnosis. *Nephro-urology monthly* 2013;5:1001.