Evaluation of Graft Outcome and Patient Survival in Children after Renal Transplantation: A Single Center Experience

Hadi Sorkhi^{1*}, Abazar Akbarzadeh Pasha², Farshid Oliaei², Mohammad Mahdi Rajabpour², Mustafa Taghavi²

¹Non-Communicable Pediatric Diseases Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, IR Iran. ²Departments of Kidney Transplantation, Babol University of Medical Sciences, Babol, Iran

***Corresponding Author** Dr. Hadi Sorkhi, **Email:** hadisorkhi@yahoo.com

Abstract

Background and Aim: Quality of life has been improved by kidney transplantation (KT), especially in pediatric patients. Children have a higher risk of rejection and graft loss compared to adults. It is important to determine the pediatric graft outcome and prevent early graft loss, if possible. This study was done to evaluate graft and patient survival in pediatric patients after kidney transplantation.

Methods: This cross-sectional study was done on all children below 18 years old that underwent kidney transplantation in Shahid Beheshti Kidney Transplant Center. Sex, time of transplantation, serum creatinine, acute rejection, viral infection (cytomegalovirus), and graft survival and patient survival were recorded. **Results:** Fifty-eight patients underwent kidney transplantation. The mean serum creatinine level was 0.89 ± 0.88 mg/dl, 0.7 ± 1.29 mg/dl, 058 ± 0.92 mg/dl, 0.9 ± 0.83 mg/dl and 1.32 ± 0.91 mg/dl on day 1, 2, and 3 post KT, discharge day, and the last follow-up visit, respectively. Graft survival was 93.1%, 89.5% and 86.5% at 1, 5 and 10 years, respectively. During the study, five patients expired and therefore patient survival was 99.6%, 92.3% and 92.3% at 1, 5 and10 years, respectively. **Conclusion:** This study, compared to other studies, showed that the graft and patient survival were acceptable. More attention should be paid to improve the outcome.

Keywords: Children; Adolescents; Kidney Transplantation; Graft Survival; Live Survival.

Received: January, 2021Conflict of interest: The authors declare no conflict of interest.Revised: March, 2021Please cite this article as: Sorkhi H, Akbarzadeh Pasha A, Oliaei F, Rajabpour MM,
Taghavi M. Evaluation of Graft Outcome and Patient Survival in Children After Renal
Transplantation: A Single Center Experience. J Ped Nephrol 2021;9(3):1-5.
https://doi.org/10.22037/jpn.v9i3.33662

Introduction

The quality of life has improved with kidney transplantation (KT) in both adults and children. It is the best treatment modality in any patient with end-stage renal disease (ESRD) (1-7). In pediatric patients, kidney transplantation is associated with better growth and routine lifestyle (2-3). Graft and life survival outcomes have improved with the advent of newer drugs used in pediatric kidney transplantation (8). In Iran, the rate of kidney transplantation is 7.2 in million pediatric patients (9). The factors that influence graft and patient survival include immunosuppressive regimen, donor's selection criteria, recipient's primary

disease, and surgical procedure. In addition, other factors that could affect graft and patient survival are the acute rejection rate, preemptive KT, median duration of dialysis before KT, etiology of ESRD, median bodyweight at KT, and donor's characteristics (age and sex) (10-12).

Some authors have reported a lower graft survival rate in children compared to adult due to a higher risk of infections, acute rejection, and rejection of medication use (13-15).

The 1-year and 5-year graft survival rates are 90% and 81%, respectively (16). Patients with acute rejection and primary hyperoxalouria have lower

graft survival rates (16). In one study, the graft survival rate was lower in black recipients during 3- and 5-year follow-ups (17).

Since there are different reports and there is a paucity of data about long-time outcomes of renal transplantation in children, especially in Iran, this study was conducted to determine the graft and patient survival outcomes in children in the north of Iran.

Methods

This cross-sectional study was done in all children below 18 years old that received kidney transportation in Shahid Beheshti Kidney Transplant Center, north of Iran during 2000-2010. The inclusion criteria were age under 18 years, a GFR (glomerular filtration rate) of below 15 ml/min/1.73^{m2} before transplantation, and at least 10 years regular follow-up. The exclusion criteria were transfer to other centers and lack of a good followup. The major limitation of our study was missing of some data related to patients who were transferred to other centers.

All of the patients were treated with hemodialysis. The donors were non-related and were all evaluated for kidney diseases and infections such as hepatitis B and C, cytomegalovirus infection (CMV), and human immune deficiency virus (HIV) using serological testes.

In addition, all recipients were evaluated for infections and gastrointestinal tract disorders, cardiovascular diseases and predisposing urological abnormalities. After normal white blood cell count, cross-match and panel study, a donor was selected for a recipient.

The induction drugs included intravenous methylprednisolone for 5 days (2 days before and 3 days after transplantation) followed by oral prednisolone, cyclosporine (one day before the operation, postoperative administration was resumed when the serum creatinine level was below 2 mg/dl), azathioprine, or mycophenolate mofetil (MMF). All cases with acute rejection were treated with methylprednisolone or anti-thymoglobulin (ATG).

Age, sex, time of transplantation, serum creatinine level after transplantation, and graft survival and patient survival rates at 1, 5 and 10 years after transplantation were recorded. Five patients expired due to non-kidney-related causes. In addition, acute rejection and CMV infection during 3 and 6 months after transplantation were recorded. The data were analyzed with the SPSS 18 and using chi-square, ttest and Kaplan Meier tests. P<0.05 was significant.

Results

Fifty-eight patients were evaluated in this study of whom 32 (55%) were boys and the rest were girls (45%) with a mean age of 13.53 ± 3.26 years.

Nine (15.5%) patients were below 10 years old (6 boys and 3 girls) and 49 (84.5%) were 10-18 years old (26 boys and 23 girls).

After transplantation, the mean urine volume was 11.43 ± 5.48 ml/kg/hr on day one and 10.7 ± 10.33 ml/kg/hr on day 2.

The mean serum creatinine level was 0.89 ± 0.88 mg/dl, 0.7 ± 1.29 mg/dl, 058 ± 0.92 mg/dl, 0.9 ± 0.83 mg/dl and 1.32 ± 0.91 mg/dl on day 1, 2, and 3 post KT, discharge day, and last follow-up visit, respectively.

The mean serum creatinine level was 0.76 ± 0.77 mg/dl, 1.25 ± 0.32 mg/dl, $0.89\pm0.43\pm$ mg/dl, 2.07 ± 078 , and 1.1 ± 0.32 mg/dl in male patients and 1.04 ± 1.1 mg/dl, 0.96 ± 1.34 mg/dl, 0.74 ± 0.99 mg/dl, 0.96 ± 0.9 mg/dl, and 1.55 ± 1.24 mg/dl in female patients at day 1, 2, and 3 post KT, discharge day, and the last follow-up visit, respectively (p>0.05).

The rate of acute rejection was 8.6% in the first three months after transplantation.

In addition, five (8.6%) patients had CMV infection in the first six months after transplantation of whom four were male and only one was female.

The graft survival rate was 93.1% at 1 year, 89.5% at 5 years, and 86.5% at 10 years.

Five patients died from unknown causes during this study; therefore, the patient survivals rate was 99.6%, 92.3% and 92.3% at 1, 5 and10 years, respectively.

Discussion

According to this study, graft survival was 93.1%, 89.5% and 86.5% at 1, 5, and 10 years, respectively. With introduction of new drugs and protocols for induction and maintenance of immunosuppression therapy in recent years, graft and patient survival have improved in children and adults.

In children, graft survival depends on some factors such as the recipient's age at transplant time, race, induction and maintenance drug protocol, primary kidney disease, live or deceased kidney donor, and prior panel reactivity (18-20). The 3-year and 5-year graft survival have been reported to be 80% and 75% in some studies, respectively (18, 21-22). In addition, the 10-year group survival is reported to be 66% (23).

The 1-, 3-, 5-, 10-, and 20-year kidney transplant survival are 90%, 82%, 81%, 62% and 62%, respectively (16). In this study, the graft survival was higher in children above 7-10 years old. The graft survival at 3 and 5 years are lower in black pediatric recipients (70.9% vs. 83.3% and 59.9 vs. 77.7%) (17).

In a study conducted in children after kidney transplantation, the graft survival rate was 95%, 84%, 97% and 62% after 1, 2, 5 and 10 years, respectively (24).

According to these studies, the graft survival was high after one year while the rate was different after the first year. The reason for this difference may be the drug protocol for induction and maintenance therapy, primary kidney disease, recipient age, etc.

The present study found no difference in the graft survival rate between boys and girls (P>0.05). However, one study reported a higher graft survival rate in girls (14.8 ± 0.7 vs 11.8 ± 0.5 years) but the difference was not significant (16). Therefore, it seems that sex may not have an important effect on the graft survival rate.

The risk of acute rejection within three months after transplant was (8.6%). Acute rejection may cause graft failure in 13-21% of the children (25-26). Some studies reported that the number and severity of rejections and response to corticosteroids during the first six months after transplant may be significant factors to determine the graft survival (26-28). Hummer et al found that the risk of acute rejection was lower in living donors and one-year after transplantation (29). Seventy-eight (24.8%) children experienced one episode of acute rejection and 5.8% had more than one episode of rejection during follow-up in a study by Naderi G et al (16). Smith JM et al reported that the rate of acute rejection was 15.02% one year after KT and decreased over time. In this study, the risk of rejection was higher in children above 12 years old (30). In addition, a study by Tejani AH, et al showed the risk of delayed graft failure (DGF) was higher in children with acute rejection (31% vs. 23%) (31).

The risk of acute rejection was higher in children during first month after transplant, which could affect graft survival. Therefore, more attention should be paid to prevent acute rejection, especially in the first month after transplant.

The patient survival rate was 93.1%, 89.4% and 86.5% at 1, 5, and10 years, respectively.

The patient survival rate was 100%, 99.4%, 97.8% and 96.5% at 1,5,10, and 20 years in a study by Naderi G et al, respectively (16). In another study, the 1-year, 3-year and 5-year patient survival rate was 98.2%, 97.4% and 95.6% in living donor (LD) recipients, respectively. In deceased donor (DD) recipients, however, the survival rate was 97.1%, 96%, and 92.6% at 1, 3, and 5 years, respectively (P<00.1). Therefore, children with LD had higher patient survival rates (32).

In another study, the 5-, 10-, and 20-year patient survival rates were 96%, 93% and 88%, respectively (33). In this study, children with LD had higher patient survival rates than DD children (P<0.05).

In the present study, although the graft survival rate was lower than the patient survival rate, the patients had the opportunity to receive a second transplant.

Conclusion

According to this study, the graft and patient survival rates were high. More attention should be paid to selection of donors. New drug choices may improve graft and patient survival rates.

Acknowledgments

The authors are grateful to the Clinical Research Development Committee of Amirkola Children's Hospital, Research Council and Non-Communicable Pediatric Diseases Research Center, Health Research Center, Babol University of Medical Sciences and Kidney Transplantation Ward for their support and cooperation (No:1142).

Conflict of Interest

The author declares no conflicts of interest.

Financial Support

The author declares no financial support.

References

- 1. Offner G, Latta K, Hoyer PF, et al. Kidney transplanted children come of age. Kidney Int 1999;55:1509-17.
- 2. Mir S, Erdogan H, Serdaroglu E, et al. Pediatric renal transplantation: single center experience. Pediatr Transplant 2005;9:56-61.

- Tejani A, Harmon WE. Clinical transplantation. In: Barrat TM, Avner ED, Harmon WE, eds. Pediatric Nephrology. Baltimore: Lippincott, Williams & Wilkins, 1999:1309-37.
- Mendley SR, Zelko FA. Improvement in specific aspects of neurocognitive performance in children after renal transplantation. Kidney Int 1999;56:318-23.
- 5. Qvist E, Narhi V, Apajasalo M, et al. Psychosocial adjustment and quality of life after renal transplantation in early childhood. Pediatr Transplant 2004;8:120-5.
- Maxwell H, Haffner D, Rees L. Catch-up growth occurs after renal transplantation in children of pubertal age. J Pediatr 1998;133:435-40.
- 7. Harambat J, Cochat P. Growth after renal transplantation. Pediatr Nephrol 2009;24:1297-306.
- Filler G,Webb NJ, Trompeter R. Four-year data after pediatric renal transplantation: a randomized trial of tacrolimus vs. cyclosporin microemulsion. Pediatr Transplant 2005;9:498-503.
- Gheissari A, Hemmatzadeh S, Merrikhi A, et al. Chronic kidney disease in children: A report from a tertiary care center over 11 years. J Nephropathol 2012;1:177-82.
- Dharnidharka VR, Fiorina P, Harmon WE. Kidney transplantation in children. N Engl J Med 2014;371:549-58.
- 11. Van Arendonk KJ, Boyarsky BJ, Orandi BJ, et al. National trends over 25 years in pediatric kidney transplant outcomes. Pediatrics 2014;133:594-601.
- 12. Assadi F. Pediatric kidney transplantation: kids are different. Iran J Kidney Dis 2013;7:429-31.
- 13. Schurman SJ, McEnery PT. Factors influencing short-term and long-term pediatric renal transplant survival. J Pediatr 1997;130:455-62.
- Sert I, Yavascan O, Tugmen C, et al. A retrospective analysis of long-term graft survival in 61 pediatric renal transplant recipients: a single-center experience. Ann Transplant 2013;18:497-504.
- 15. Torkaman M, Khalili-Matin-Zadeh Z, Azizabadi-Farahani M, et al. Outcome of living kidney transplant: pediatric in comparison to adults. Transplant Proc 2007;39:1088-90.
- Naderi G, Latif A, Karimi S, Tabassomi F, Esfahani ST. The Long-term Outcome of Pediatric Kidney Transplantation in Iran: Results of a 25-year Single-Center Cohort Study. Int J Organ Transplant Med. 2017;8(2):85-96. Epub 2017 May 1.
- Omoloja A, Mitsnefes M, Talley L, Benfield M, Neu A. Racial differences in graft survival: a report from the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS). Clin J Am Soc Nephrol. 2007 May;2(3):524-8. Epub 2007 Apr 11.
- Hwang AH, Cho YW, Cicciarelli J, et al. Risk factors for short- and long-term survival of primary cadaveric renal allografts in pediatric recipients: a UNOS analysis. Transplantation 2005;80:466-70.
- 19. Benfield MR, McDonald RA, Harmon W, et al. Changing trends in pediatric transplantation: 2001 annual report of the North American Pediatric Renal

Transplant Cooperative Study. Pediatr Transplant 2003;7:321-35.

- 20. Gjertson DW, Cecka JM. Determinants of long-term survival of pediatric kidney grafts reported to the United Network for Organ Sharing kidney transplant registry. Pediatr Transplant 2001;5:5-15.
- Loirat C, Ehrich JH, Geerlings W, et al. Report on management of renal failure in children in Europe, XXII. Nephrol Dial Transplant 1994;9(Suppl 1):26-40.
- 22. Mehls O, Rigden S, Ehrich JH, et al. Report on management of renal failure in Europe, XXV, 1994. The child-adult interface. The EDTA-ERA Registry. European Dialysis and Transplant Association-European Renal Association. Nephrol Dial Transplant 1996;11(Suppl 1):22-36.
- 23. Englund M, Berg U, Tyden G. A longitudinal study of children who received renal transplants 10-20 years ago. Transplantation 2001;76:311-8.
- 24. Mahdavi R, M. Naghibi M. KIDNEY TRANSPLANTATION IN CHILDREN: RESULTS OF TEN YEARS EXP ERIENCE IN IMAM REZA HOSPITAL. Medical Journal of the Islamic Republic of Iran. 2002 :16 (3):145-149
- 25. North American Pediatric Renal Transplant Cooperative Study (NAPRTCS). Annual report 2005, available from https://web.emmes.com/study/ ped/annlrept/annlrept.html (accessed February 17, 2012).
- Cransberg K, van Gool JD, Davin JC, et al. Pediatric renal transplantation in the Netherlands. Pediatr Transplant 2000;4:72-81.
- 27. Guyot C, Nguyen JM, Cochat P, et al. Risk factors for chronic rejection in pediatric renal allograft recipients. Pediatr Nephrol 1996;10:723-7.
- 28. Humar A, Hassoun A, Kandaswamy R, et al. Immunological factors: the major risk for decreased long-term renal allograft survival. Transplantation 1999;68:1842-6.
- 29. Seikaly M, Ho PL, Emmett, Tejani A, et al. The 12th annual report of the North American Pediatric Renal Transplant Cooperative Study: Renal transplantation from 1987 through 1998. Pediatr Transplant 2001;5:215-31.
- Smith JM, Martz K, Blydt-Hansen TD. Pediatric kidney transplant practice patterns and outcome benchmarks, 1987-2010: a report of the North American Pediatric Renal Trials and Collaborative Studies.Pediatr Transplant. 2013 Mar;17(2):149-57.
- Tejani AH, Sullivan EK, Alexander SR, Fine RN, Harmon WE, Kohaut EC. Predictive factors for delayed graft function (DGF) and its impact on renal graft survival in children: a report of the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS). Pediatr Transplant. 1999 Nov;3(4):293-300.
- 32. Smith JM, Stablein DM, Munoz R, Hebert D, McDonald RA. Contributions of the Transplant Registry: The 2006 Annual Report of the North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS). Pediatr Transplant. 2007 Jun;11(4):366-73.

Outcome of Renal Transplantation

 Honda M, Sakai K, Shishido S. Long-term outcomes of pediatric kidney transplantation: A single-center experience over the past 34 years in Japan. Int J Urol. 2020 Feb;27(2):172-178.