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Post Renal Transplant Recurrence of IgA Nephropathy in a Tertiary Care Center

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ABSTRACT

Background: IgA nephropathy is a leading cause of chronic kidney disease. Recurrent IgA nephropathy in post renal transplant can cause proteinuria, hematuria and progressive renal dysfunction. In this study, we planned to evaluate the clinical course of patients with IgA nephropathy who underwent renal transplant. **Methods:** It is a retrospective study conducted in Madras medical college retrieved from the renal case records from the year 2006 to 2017. Patients who had IgA nephropathy as their native kidney disease or IgA nephropathy diagnosed in a post-transplant allograft biopsy when the native kidney disease was not known were included. **Results:** Of the 28 patients, 23 (82.1%) were males. The age of the recipients was 34.6±9.4 years while at the time of transplant the mean age was 28.7±7.7 years. The age of onset of native kidney disease was 26.7±7.9 years. The native kidney disease was biopsy proven IgA nephropathy in 24 (85.7%) patients .Twenty two (78.6%) underwent live related renal transplant. Six (21.4%) underwent deceased donor transplant. The mean age of donors was 43.6±9.2 years of which 17 (60.7%) were female. Seventeen (60.7%) received tacrolimus based regimen while 11 (39.4%) received cyclosporine based immunosuppression. Recurrence of disease was observed in 7 (25%) patients. The median time to recurrence after transplant was 67.3 (14.3 – 101.5) months. Graft loss was observed in 3 patients (42.8%). We did not find any significant risk factors associated with recurrence. **Conclusion:** Although post renal transplant recurrence was common with IgA nephropathy, significant association with risk factors are lacking in our study.

Keywords: IgA Nephropathy, Renal Transplant.

INTRODUCTION

IgA nephropathy is a leading cause of chronic kidney disease. As with native kidney disease, deposition of IgA in renal parenchyma can occur in the renal allograft and cause functional decline resulting in recurrent IgA nephropathy. Recurrent IgA nephropathy can cause proteinuria, hematuria and progressive renal dysfunction. In some it presents as completely asymptomatic where there is IgA deposition without any clinical manifestations.[1] The reported incidence of graft loss due to recurrent IgA nephropathy is approximately 7 to 10 percent at 10 years. The risk of graft loss is even higher among patients with graft dysfunction when the graft dysfunction is attributed to recurrent IgA disease. Thus recurrent IgA imposes a significant threat to the graft survival.[2] Although many of the risk factors have been postulated, none of them has been adequately validated in clinical studies. In this study, we planned to evaluate the clinical course of patients with IgA nephropathy who underwent renal transplant.

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MATERIALS AND METHODS

It is a retrospective study conducted in the Institute of nephrology of Madras medical college in South India. Patients who had IgA nephropathy as their native kidney disease or IgA nephropathy diagnosed in a post-transplant allograft biopsy when the native kidney disease was not known were included in the study. Demographic parameters and investigations were retrieved from the renal case records from the year 2006 to 2017. Statistical analysis was done using SPSS version 23. Continuous variables were expressed as mean± standard deviation or median (interquartile range) whereas categorical variables were expressed as absolute number (percentage).

RESULTS

Table 1: Demographics and clinical characteristics

Recipient characteristics	
Male (Number and percentage)	23(82.1)
Female (Number and percentage)	5(17.9%)
Mean age at diagnosis of IgA nephropathy (years)	26.7±7.9
Mean age at transplant (years)	28.7±7.7

Of the 28 patients included in the study, 23 (82.1%) were males. The age of the recipients was 34.6±9.4 years while at the time of transplant the mean age was 28.7±7.7 years. The age of onset of native

kidney disease was 26.7±7.9 years. The native kidney disease was biopsy proven IgA nephropathy in 24 (85.7%). The remaining had IgA nephropathy in the allograft biopsy and thus were presumed to have native kidney IgA nephropathy. The median time to progression to end stage renal disease was 12 months (0 – 23). Thirty percent of them presented with chronic kidney disease stage 5. The dialysis vintage before transplant was 15 (4 – 16) months.

Table 2: Donor characteristics

Parameters	Number and percentage
Male	11(29.3%)
Female	17(60.7%)
LRRT	22(78.6%)
DDRT	6(21.4%)
Tacrolimus based immunosuppression	17(60.7%)
Cyclosporine based immunosuppression	11(39.4%)

Twenty two (78.6%) underwent live related renal transplant. Six (21.4%) underwent deceased donor transplant. The mean age of donors was 43.6±9.2 years of which 17 (60.7%) were female. Seventeen (60.7%) received tacrolimus based regimen while 11 (39.4%) received cyclosporine based immunosuppression.

Table 3: clinical characteristics of post renal IgA recurrence patient

Parameters	
Male (Number and percentage)	7(100%)
LRRT (Number and percentage)	4(57.1%)
DDRT (Number and percentage)	3(28.6%)
Second transplant (DDRT)	1(14..3%)
Median time of recurrence in months	67.3
Mean duration of follow up in months	56 months
Graft loss (Number and percentage)	3(42.8%)

Recurrence of disease was observed in 7 (25%) patients. The median time to recurrence after transplant was 67.3 (14.3 – 101.5) months. The mean serum creatinine and urine protein creatinine ratio at the time of diagnosis of recurrent disease were 1.9±0.81mg/dl and 3.6 (1.9 – 4.8) respectively. The duration of follow up during post renal transplant period was 56 (32.3 – 103) months.

Graft loss was observed in 3 patients (42.8%). All three patients became dialysis dependent at the end of the follow up period. There was no significant difference in serum creatinine from disease recurrence to last follow up (p=0.21). We did not find any significant risk factors associated with recurrence like sex, native kidney disease, type of transplant, relationship, induction agent and types of immune suppressive drugs [Table 4]. Even though all who presented with recurrence were males, there is no statistical significance.

Table 4: Risk factors associated with recurrence of IgA nephropathy

Parameters	No. of events	No. of events	p value
Sex	Male (7/23)	Female (0/5)	0.21
NKD	Crescentic (1/8)	Chronic (6/20)	0.32
Type of transplant	LRRT (5/22)	DDRT (2/6)	0.48
Relationship	1st degree (3/17)	Others (2/11)	0.31
Induction agent	No induction (4/16)	Basiliximab (2/7), ATG (2/5)	0.69
Immunosuppression	Tacrolimus based (5/13)	Cyclosporine based (3/11)	0.58

DISCUSSION

Recurrence of IgA nephropathy post-transplant is a common problem encountered in nephrology practice. The reported recurrence rate both histologically and clinically varies and was between 21 and 58% when biopsies were done to find out the cause.[2] In our study, recurrence IgAN was seen in 25%. IgA recurrence was documented in 19% in other study.[3] Chaco et al. showed recurrence in 5 out of 20 biopsies (25%).[4] The risk of recurrence was found to increase with the duration of follow up.[5] In few reports from Japan, it was hypothesized that presence of IgA deposits in the donor kidneys is associated with increased risk of recurrence.[6]

The various risk factors proposed to be associated with IgA recurrence include live related donors, close HLA match between the donor and recipient, high serum IgA concentration, high levels of serum galactose deficient IgA1 specific IgG autoantibodies, the type of immunosuppressive regimen and genetic variants of complement factor H related protein 5.[7-10]

In our study, we did not find any significant risk factors predicting the recurrence of IgA nephropathy. Some studies found no recurrence risk in allograft whereas others had shown increased recurrence among living close related transplantation.[11-13] The type of posttransplant immunosuppression had no impact on IgAN recurrence.[14] Some studies reported a positive effect of ATG in preventing the recurrence,[15] but it needs prospective trial. Our study did not show any significant association of recurrent disease with induction immunosuppressive regimen probably to the lesser number of patients in each group.

Graft loss was 42.8% in our study and one among them was a recurrent crescentic IgA nephropathy.. One study by Singh T et al., recently reported no difference in graft loss in those with recurrence compared to those with acute rejection.[16] A recent ANZDATA publication showed that 60% of graft loss were due to allograft recurrence.[17] Recurrent and de- novo crescentic IgAN is a rare entity and was documented as 3–5%.[18,19] Few reports from

Japan hypothesized the higher rate of recurrence in allograft when the donated kidney had IgA deposits at the time of transplantation.[20]

The limitations of our study include its retrospective nature, lesser sample size and lesser duration of follow up since the median duration of follow up was 56 months. A prospective study with a larger sample size and duration of follow-up of more than 10 years will throw more insight into nature and impact on graft survival in allograft IgA nephropathy recurrence.

CONCLUSION

Although post renal transplant recurrence was common with IgA nephropathy, significant association with risk factors are lacking in our study.

REFERENCES

1. Kowalewska J, Yuan S, Sustento-Reodica N, Nicosia RF, Smith KD, Davis CL, et al. IgA nephropathy with crescents in kidney transplant recipients. Am J Kidney Dis. 2006;45:167-175.
2. Moroni G, Longhi S, Quaglini S, Gallelli B, Banfi G, Montagnino G, et al. The long-term outcome of renal transplantation of IgA nephropathy and the impact of recurrence on graft survival. Nephrol Dial Transplant. 2013;28(5):1305-14.
3. Nijim.S,Vujjini,V,Alasfar.S,Luo.X,Oranti.B,Delp.C,et al. Recurrent IgA Nephropathy After Kidney Transplantation. Transplantation. Proceedings,2016;48:2689-2694.
4. Chaco.B,George JT,Neelakantan N,Chako JK,Korula A.Outcomes of renal transplantation in patients with immunoglobulin A nephropathy in India. J Postgrad MED 2007;53;92-5
5. Ortiz F, Gelpi R, Koskinen P, Manonelles A, Räisänen-Sokolowski A, Carrera M, Honkanen E, GrinyóJM, Cruzado JM IgA nephropathy recurs early in the graft when assessed by protocol biopsy. Nephrol Dial Transplant. 2012 ;27(6):2553-8.
6. Moriyama T, Nitta K, Suzuki K, Honda K, Horita S, Uchida K, et al. Latent IgA deposition from donor kidney is the major risk factor for recurrent IgA nephropathy in renal transplantation. Clin Transplant. 2005;19 Suppl 14:41-8.
7. Andresdottir MB, Haasnoot GW, Doxiadis, II, Persijn GG, Claas FH. Exclusive characteristics of graft survival and risk factors in recipients with immunoglobulin A nephropathy: a retrospective analysis of registry data. Transplantation. 2005;80(8):1012-8.
8. Zhai YL, Meng SJ, Zhu L, Shi SF, Wang SX, Liu LJ, et al. Rare Variants in the Complement Factor H-Related Protein 5 Gene Contribute to Genetic Susceptibility to IgA Nephropathy. J Am Soc Nephrol. 2016;27(9):2894-905.
9. Clayton P, McDonald S, Chadban S. Steroids and recurrent IgA nephropathy after kidney transplantation. Am J Transplant. 2011;11(8):1645-9.
10. Berthoux F, El Deeb S, Mariat C, Diconne E, Laurent B, Thibaudin L. Antithymocyte globulin (ATG) induction therapy and disease recurrence in renal transplant recipients with primary IgA nephropathy. Transplantation. 2008;85(10):1505-7.
11. McDonald SP, Russ GR. Recurrence of IgA nephropathy among renal allograft recipients from living donors is greater among those with zero HLA mismatches. Transplantation. 2006;82(6):759-62.
12. Ponticelli C, Traversi L, Feliciani A, Cesana BM, Banfi G, Tarantino A. Kidney transplantation in patients with IgA mesangial glomerulonephritis. Kidney Int. 2001;60:1948–54
13. Wang AY, Lai FM, Yu AW, Lam PK, Chow KM, Choi PC, et al. Recurrent IgA nephropathy in renal transplant allografts. Am J Kidney Dis. 2001;38:588–96.
14. Mulay AV, van Walraven C, Knoll GA. Impact of immunosuppressive medication on the risk of renal allograft failure due to recurrent glomerulonephritis. Am J Transplant. 2009;9:804–11
15. Jennette JC. Rapidly progressive crescentic glomerulonephritis. Kidney Int. 2003;63:1164–77
16. Singh T, Astor BC, Zhong W, Mandelbrot DA, Maursetter L, Panzer SE. The association of acute rejection vs recurrent glomerular disease with graft outcomes after kidney transplantation. Clin Transplant. 2019;33(12):e13738.
17. Allen PJ, Chadban SJ, Craig JC, Lim WH, Allen RDM, Clayton PA, et al. Recurrent glomerulonephritis after kidney transplantation: risk factors and allograft outcomes. Kidney Int. 2017;92(2):461-9.
18. Recurrent Crescentic Immunoglobulin A Nephropathy in the Graft Kidney Indian J Nephrol2017 Sep-Oct; 27(5): 335–336
19. Tang Z, Ji SM, Chen DR, Wen JQ, Chen JS, Liu ZH, et al. Recurrent or de novo IgA nephropathy with crescent formation after renal transplantation. Ren Fail. 2008;30:611–6
20. Deng R, Dai Y, Zhang H, Liu L, Li J, Xiong Y, et al. Higher Incidence of Renal Allograft Glomerulonephritis in Living-Related Donor Kidney Transplantation. Transplant Proc. 2018;50(8):2421-5.

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