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Research Article

# ABO INCOMPATIBLERENAL TRANSPLANTATION -OUR INSTITUTIONAL EXPERIENCE

**Periasamy Ponnusamy[1], Senthilvel Arumugam[2]*, Balaraman V[3] and Vipin Sharma[4]**

[1,2]Department of Urology, Government Kilpauk Medical College Hospital, Chennai, Tamilnadu
[3]Department of Nephrology, Government Kilpauk Medical College Hospital, Chennai, Tamilnadu
[4]Government Kilpauk Medical College Hospital, Chennai, Tamilnadu

**A R T I C L E I N F O**

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**A B S T R A C T**

**Introduction:** ABO incompatible Kidney Transplant (ABOi-Kidney Transplant) was previously considered to be an absolute contraindication for patients with end-stage kidney disease (ESKD) due to hyperacute rejection related to immunological barrier. Intensified immunosuppression and immunological understanding has helped to shape current desensitization protocols. This study provides an overview of the history, outcome, protocol, advantages and disadvantages in ABOi-Kidney Transplant.

**Aim of The Study:** To define

- Desensitization modalities and protocols for ABO Incompatible Kidney Transplant and Post-transplant immunologic surveillance.
- Factor affecting Antibody-mediated rejection in ABO incompatible kidney allograft transplantation. And Outcome of ABO incompatible kidney allograft transplant.

**Materials and Methods:** This is a retrospective and prospective analysis of case series of ABO in Kidney Transplant which were done in our institute (KILPAUK MEDICAL COLLEGE HOSPITAL) from August 2015 to March 2019.Total 6 cases of ABO incompatible Kidney Transplant were done. Preop and post op protocol defined and strictly follow during the study, vessels and ureteric anastomosis done as per standard technique. Success rate or outcome is measured in term of graft survival or graft rejection.

**Results /Outcome:** In our institute all the six patients were strictly evaluated pre operatively and post operatively. The creatinine came down to less than 2 mg /dl within 4 th POD and the urine output was adequate for all the six patients .No patients were required hemodialysis post operatively in more than 2.5 year follow up .No graft biopsy done till date. There was no signs and symptoms of rejection to any patients. All the six patients are under follow.

**Conclusion:** As the pre-transplant and post-transplant desensitization protocols have developed and changed in many different fields, satisfactory results have been observed. The allograft outcomes have been enhanced. Graft survival is comparative to ABO compatible transplant. It is good option to increase the donor pool, especially country like India where cadaver Kidney Transplant is still low.



## INTRODUCTION

ABO incompatible Kidney Transplant (ABOi-Kidney Transplant) was previously considered to be an absolute contraindication for patients with end-stage kidney disease (ESKD) due to hyperacute rejection related to immunological barrier. Intensified immune suppression and immunological understanding has helped to shape current desensitization protocols. In ABOi-Kidney Transplant, there is an additional residual immunological risk that may lead to allograft damage, despite using current diverse but usually intensified immunosuppressive protocols at the expense of increasing risk of infection and possibly malignancy reassuringly, there has been an evolution in ABOi-Kidney Transplant leading to a simplification of protocols over the last decade. This study provides an overview of the history, outcome, protocol, advantages and disadvantages in ABOi-Kidney Transplant.[1]

**Corresponding author:* **Senthilvel Arumugam**
Department of Urology, Government Kilpauk Medical College Hospital, Chennai, Tamilnadu

### *Aim of the Study*

***To Define***

- Desensitization modalities and protocols for ABO Incompatible Kidney Transplant and Post-transplant immunologic surveillance.\
- Factor affecting Antibody-mediated rejection in ABO incompatible kidney allograftransplantation.
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## MATERIALS AND METHODS

This is a retrospective and prospective analysis of case series of ABO inKidney Transplant which were done in our institute (KILPAUK MEDICAL COLLEGE HOSPITAL) from August 2015 to March 2019.Total 6 cases of ABO incompatible Kidney Transplant were done.Proper written explanatory consent taken from patients and relative and explained the risk associated with Kidney Transplant , available option, Side effect of immunosuppression and post operatively complications. Approval from transplant committee taken. Preop and post op protocol defined and strictly follow during the study, vessels and ureteric anastomosis done as per standard technique. Success rate or outcome is measured in term of graft survival or graft rejection.

### *Pre-Operative Methodology of Desensitization Followed in our Institution*

1. Rituximab is a monoclonal antibody against the protein CD 20, 375 mg/m2 given 14 days before transplantation.
2. Plasmapheresis done about 2 liters pre operatively .average Four sessions done in alternate day before transplantation depends on ABO antibody titer.
3. Immunoglobulins 100 mg/kg has been given every alternate day after each plasmapheresis.
4. Immunosuppressant started in low dose pre operatively T.Tacrolimus 1 mg bd, T.MMF 500 mg bd before 48 hour of surgery.
5. Basiliximab anti CD 25, 20 mg IVbolus given 2 hours prior to transplantation.
6. Pre-operative anti ABO antibody titer was monitored and maintained below 1; 8.which was done by gel agglutination method.

### *Post-operative Monitoring Methodology*

1. Immunosuppressant dose has been increased to T.Tacrolimus 2 mg bd, T.MMF 500 mg bd, and Prednisolone started.
2. 2.Anti ABO antibody titer monitored two days once post operatively and maintained below 1;8.
3. Antibiotics inj cefoperazone sulbactum 1.5 g bd was given.
4. USG Doppler study was done on 4 Th POD to look for the vascular status and resistive index of the transplanted kidney.
5. Graft biopsy was planned for diagnosis of graft rejection on basis on derange renal parameter after transplant, but none of recipient till date required.
6. Post-operative plasmapheresis was planned as optional procedure but none required.

## RESULTS /OUTCOME

In our institute all the six patients were strictly evaluated pre operatively and post operatively. The creatinine came down to less than 2 mg /dl within 4 th POD and the urine output was adequate for all the six patients .No patients were required hemodialysis post operatively in more than 2.5 year follow up.No graft biopsy done till date. There was no signs and symptoms of rejection to any patients. All the six patients are under follow.

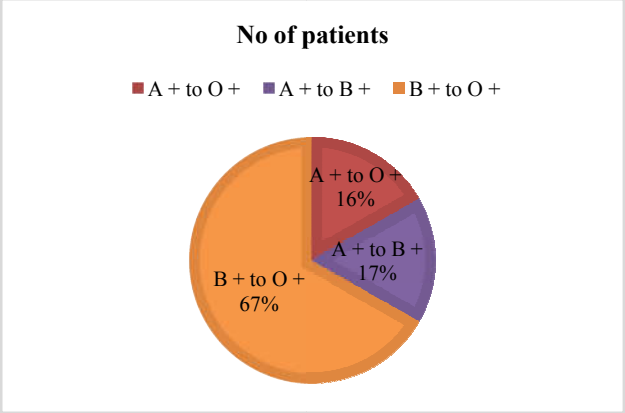
### *Master table*

| S no | | Case 1 | Case 2 | Case 3 | Case 4 | Case 5 | Case 6 |
|---|---|---|---|---|---|---|---|
| Age in years | Donor | 58 | 55 | 58 | 48 | 62 | 56 |
| | Recipient | 40 | 52 | 39 | 27 | 38 | 27 |
| Gender | Donor | F | F | F | F | F | F |
| | Recipient | M | F | M | M | M | M |
| Blood group | Donor | A + | A + | B + | B + | B + | B + |
| | Recipient | O + | B + | O+ | O + | O + | O + |
| Donor Kidney selected | | Left | Left | Left | Left | Left | Left |
| Donor kidney | Artery | 1 | 2 | 1 | 1 | 2 | 2 |
| | Vein | 1 | 1 | 1 | 1 | 1 | 1 |
| ABO Titer | Pre op | 1:256 | 1:256 | 1:128 | 1:256 | 1:128 | 1:128 |
| | At time of surgery | 1:8 | 1:4 | 1:8 | 1:4 | 1:4 | 1:4 |
| No of plasmapheresis | | 5 | 6 | 4 | 5 | 4 | 4 |

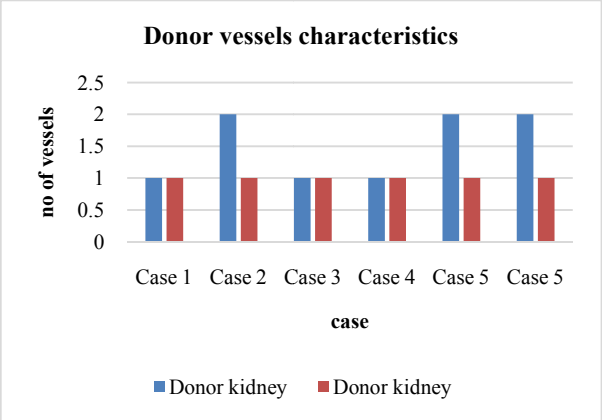
Mean age of recipient is 56.16 years while recipient mean age is 37.16 years, all donor were female while out of 6 recipient only 1 female was there. All are related donor, in all case left kidney is selected, and 3 cases donor have double vessels, and single vein were there. While other cases having single artery and single vein.Average follow up is 2.5 years, no rejection noted in follow up period till now. One patient died because of opportunistic infection (noncompliance of patient).

### *Blood Group Combination*

| Blood group combination | No of patients |
|---|---|
| A + to O + | 1 |
| A + to B + | 1 |
| B + TO O + | 4 |




### *Donor Vessels Characteristics*




## DISCUSSION

### *Current Status of ABO-Incompatible Kidney Transplantation*

### *General Methodology of Desensitization*

For the successful performance of ABOi Kidney Transplant, the antibody-mediated response must be understood and targeted. These strategies, or desensitization, are all based on the same principles , including not only the removal of preexisting antibodies that are directed at the donor ABO antigen, but also waiting to transplant until the anti-ABO antibody titer is below a set target. Additionally, the prevention of further production of new recipient anti-ABO antibodies before and after transplantation is another founding principle. Ordinarily, several pretransplant apheresis sessions are required for antibody removal. To prevent reformation of the antibody, apheresis is followed by intravenous immunoglobulin, a mixture of immunosuppressive therapies, and erasable splenectomy .This procedure usually occurs over a period of one to two weeks.

***Plasmapheresis***

The simplest and most common method to remove antibody from plasma is therapeutic plasma exchange, in which large amounts of plasma are withdrawn and replaced with colloid solutions. This procedure eliminates approximately 20% of the anti-ABO antibodies with each session. However, this technique is not sufficiently selective to remove only protective antibodies and also removes coagulation factors, hormones, and antiviral and antibacterial immunoglobulin G (IgG) and immunoglobulin M (IgM).The removal of these factors increases the risk of bleeding or infection .However, this technique is by far the least expensive means of removing antibodies.

The selective techniques of double-filtration plasmapheresis or antigen-specific immunoadsorption are safe and more effective and are therefore usually the first choice.

Because no coagulation factors are eliminated, large plasma volumes can be processed, and the resultant efficacy is increased compared to that of therapeutic plasma exchange.

Using a second filter, double-filtration plasmapheresis is capable of eliminating the plasma fraction containing the immunoglobulins and decreases the amount of plasma discarded. Using the process of immunoadsorption, the plasma is processed through a Glycosorb ABO immunoadsorbent column and re-infused into the patient. There are no volume losses, and thus the number of adsorption cycles has no limit.

***Intravenous Immunoglobulin***.

*Intravenous immunoglobulin* plays a role in the down regulation of the antibody mediated immune response. The immunoglobulin blocks not only the Fc receptor on the mononuclear phagocyte, but also the direct neutralization of the alloantibody. Further, it inhibits the CD19 expression on the activated B cell, as well as that of the complement and the alloreactive T cell. Although alloantibody rebounds within days of the discontinuation of plasmapheresis, the benefit of intravenous immunoglobulin may continue for many months after drug administration.

***Splenectomy***

*Traditionally, concurrent splenectomy* was an important prerequisite of the desensitization protocol for ABOi Kidney Transplant, based on the idea that it contributed to the reduction of the antibody-producing B-cell pool. Alexandre *et al*., the early investigator of ABOi Kidney Transplant[2], suggested that the splenectomized recipient had a much smaller risk of antibody-mediated rejection

However, whether splenectomy is essential for successful ABOi Kidney Transplant remains unproven. Sonnenday *et al*. Found that the suppression of anti-ABO antibody after splenectomy was not significantly different from that of nonsplenectomized patients[3]. Sonnenday *et al*. reported that splenectomized recipients had a 25% greater mortality at 84 months compared with that of non-splenectomized recipients. Gloor *et al*. reported that splenectomy is not necessary even for patients with high-baseline anti-ABO antibody titers. Takahashi *et al*. demonstrated that splenectomy is not necessary to inhibit antibody production because significant numbers of memory cells exist in the bone marrow.[4]

***Graft Accommodation and B-Cell Tolerance.***

*If anti-ABO* antibodies are removed prior to transplantation, one of three types of immune response may occur:

- Rejection,
- Immune tolerance, or
- Accommodation.

About 2–5% of patients produce antibodies to the incompatible ABO antigen, which mediate allograft rejection. Some recipients seem to have immunologic tolerance to the incompatible ABO antigen because they do not reject the allograft or produce anti-ABO antibody against it. Antibody-mediated damage can result in rapid and irreversible graft thrombosis due to complement activation or contributes to long-term graft dysfunction However, as the anti-ABO antibody usually reaccumulates and persists after successful ABOi Kidney Transplant, the recipient maintains satisfactory graft function. This resistance of allograft to antibody-mediated rejection despite the significant presence of anti-ABO antibodies in the recipient serum is known as accommodation.

***Criteria of Accommodation in ABOi Kidney Transplant to Include***

1. detectable anti-ABO antibody in the recipient serum,
2. normal graft histology according to light microscopy,
3. the presence of A or B antigen in the graft, and
4. Renal function similar to that of ABO compatible patients (GFR greater than 45mL/min at one year after transplant).

***Post-transplant Monitoring and Desensitization (Post transplant Immunologic Surveillance)***

***The Monitoring of anti-*** ABO antibody titer is critical for determining the effectiveness of desensitization and the optimum time to permit graft implantation. After transplantation, the anti-ABO antibody level must be monitored to detect its reaccumulation, which may indicate or induce antibody-mediated rejection. In patients with a higher rebound in serum antibody production after the incompatible transplant, desensitization therapy, especially antibody-depletion procedures, should be repeated.

All patients whose post-transplant antibody titer remained below 1: 8 exhibited stable renal function. Those patients who had an increased titer above 1: 64 experienced allograft failure. Recommended initiating plasmapheresis if the antibody titer increases to 1: 16 in the first two weeks after transplantation,

showed that humoral rejection was rare when the antibody level was maintained less than 1: 8 in the first week and 1: 16 in the second week after transplantation. They then allowed antibody titers to rise if the graft function and surveillance biopsies were normal. Most centers performing ABOi Kidney Transplant have adhered to the guideline that serum anti-ABO antibody titers should be 1: 16 or lower before transplantation.

***Antibody-Mediated Rejection.***

*Antibody-mediated rejection* (ABMR) is known as the primary cause of graft loss in ABOi Kidney Transplant. It is clear that ABMR has a negative influence on short-term outcome following ABOi Kidney Transplant. Recent studies have reported that ABMR occurred in 17.9% up to 30% of ABO-incompatible Kidney Transplant s. Demonstrated that anti-ABOIgG antibody titers of 1: 32 at the time of transplantation and the presence of donor specific anti-HLA antibodies were independent risk factors for ABMR.

survival was 97% for the ABOi Kidney Transplant compared with 95% for the ABO-compatible Kidney Transplant in their three-centre experience at their five-year follow-up. Patient survivals were 98% in both Kidney Transplant groups.

In the analysed UNOS data of Gloor and Stegall[12], they concluded that a long-term immunological response against ABO incompatibility has little effect on graft survival with current immunosuppressive protocols and patient monitoring. Tanabe[13] summarized the outcomes of 851 ABOi Kidney Transplant performed in 82 institutions in Japan between 1989 and 2005. The five-year graft survival in their study was 79%, with patient survival at 90%. Fuchinoue *et al*.[14]report the five-year outcome of ABOi Kidney Transplant as a graft survival rate of 100%, whereas Ishida *et al*.[15] achieved a graft survival of 57% and patient survival of 89% at ten years postoperatively for more than 130 cases of ABOi Kidney Transplant.

| Ref | Type of study | Study population | ABOi population | Desensitization | Outcome |
|---|---|---|---|---|---|
| Hume *et al* | Observational | 9 | 1 | No treatment | Graft nephrectomy day 17 |
| Ota *et al* | Observational, comparative | 51 | 51 | DFPP and/or IAs/SPx | 2-yr graft survival: 87% *vs* 84.6% *vs* 50% ( A- *vs* B- *vs* ABO-incompatible) |
| Alexandre *et al* | Observational | 23 | 23 | PE/SPx | 2-yr graft survival: 88% (related donor), 50% (unrelated donor) |
| Takahashi *et al* | Observational, comparative | 1496 | 441 | DFPP or PE or IAs/SPx | 9-yr graft survival: 59% *vs* 57% (ABOi *vs* ABOc |
| Futagawa *et al* | Observational, comparative | 378 | 191 | NA | 5-yr graft survival: 66.2% *vs* 79.5% (ABOi *vs* ABOc |
| Shimmura *et al* | Observational, comparative | 167 | 167 | DFPP and/or IAs/SPx | 5-yr graft survival: 74.3% *vs* 78.5% ( CYA with AZ *vs* TAC or MMF) |
| Our study | Observational | 6 | 6 | PE and IVig | 2.5 years graft survival 100% , |

Although the development of desensitization protocols has improved graft survival, the outstanding results are largely due to aggressive surveillance, early detection, and an enhanced therapeutic approach for ABMR

***Literature Review***

In 1987, Alexandre and colleagues published a historic series of 23 recipients of ABOi Kidney Transplant s from living donors; 1-year graft survival was 79%, with 88% survival among living-related donor recipients[5] .A study from the Mayo Clinic by Gloor *et al*. described 89% 1-year graft survival among 18 patients treated with plasmapheresis, intravenous immunoglobulin, Thymoglobulin induction, three-drug immunosuppression (tacrolimus, mycophenolate mofetil, and corticosteroids), and splenectomy,[6] while in our study 1 year graft survival is 100 %.

Short-term results from the protocol described above have been notable. For instance, in the study of Tydén *et al*.[7], recipients with a baseline anti-A or -B IgG titer of up to 1: 128 were successfully transplanted with no episode of acute rejection. Montgomery [8] reported one-year patient and graft survivals of 96.3% and 98.3%, respectively, in a cohort of 60 consecutive ABOi Kidney Transplant using a variety of protocols. Oettl *et al*.[9] demonstrated a 100% survival rate of both patients and grafts at one-year after transplant. Genberg *et al*.[10] reported that ABOi Kidney Transplant had no negative impact on long-term graft function compared to that of ABO-compatible Kidney Transplant in terms of patient survival, graft survival, or incidence of acute rejection after a mean follow-up of three years. Tydén *et al*.[11] found that graft

while in our study after 2.5 years follow up no graft rejection noted till now, success rate is 100 % which is comparable to literature.

***Abbreviation***

(PP: plasmapheresis, IA: immunoadsorption, TPE: therapeutic plasma exchange, DFPP: double-filtration plasmapheresis, IVIG: intravenous immunoglobulin, CMV-IVIG; CMV hyperimmune IVIG, ABMR: antibody mediated rejection, IS: immunosuppression, FK: tacrolimus, MMF: mycophenolate mofetil, MPD: methylprednisolone).

***Pros and cons of ABO Incompatibility Kidney Transplant***
***Pros***

1. Reducing waiting list and time for transplant
2. Expanding living donor pool
3. Improvement of patient's prognosis
4. Excellent graft survival (comparable with ABOc-KIDNEY TRANSPLANT )

***Cons***

1. Comparative high immunological risk
2. Higher incidence of acute AMR
3. Intensified immunosuppression
4. Antibody depletion therapy
5. Increasing expenditure

## CONCLUSION

As the pre-transplant and post-transplant desensitization protocols have developed and changed in many different fields, satisfactory results have been observed. As the body of immunologic knowledge including that regarding antibody-

mediated rejection has grown, the allograft outcomes have been enhanced. Due to the surprising result, the pool of potential ABOi Kidney Transplant candidates has increased. Although cost of Kidney Transplant is increased by plasmapheresis and addition immunosuppression, but still is good option to increase the donor pool, especially country like India where cadaver Kidney Transplant is still low. Overall success rates are now comparable with those of ABO-compatible Kidney Transplantation, more case and comparative study should be done for better statistical analysis.

## References


1. Masaki Muramatsu*et al* ABO incompatible Kidney Transplant s: Good or bad? World J Transplant. 2014 Mar 24; 4(1): 18–29
2. Milljae Shin and Sung-Joo KimJournal of Transplantation Volume 2011, Article ID 970421, 11 pages
3. Sonnenday CJ *et al* Plasmapheresis, CMV hyperimmune globulin, and anti-CD20 allow ABO-incompatible Kidney Transplantation without splenectomy, Am J Transplant. 2004 Aug;4(8):1315-22
4. Takahashi KRecent findings in ABO-incompatible Kidney Transplantation: classification and therapeutic strategy for acute antibody-mediated rejection due to ABO-blood-group-related antigens during the critical period preceding the establishment of accommodation. *Clinical and Experimental Nephrology*. 2007; 11(2):128–141. *Clin Exp Nephrol. 2007 Jun; 11(2):128-141*
5. Alexandre, GP, Squifflet, JP, De Bruyere, M*et al*. Present experiences in a series of 26 ABO-incompatible living donor renal allografts. *Transplant Proc*1987; **19**: 4538– 4542.
6. Gloor, JM, Lager, DJ, Moore, SB*et al*. ABO-incompatible Kidney Transplant using both A2 and non-A2 living donors. *Transplantation*2003; **75**: 971– 977.
7. G. Tydén, G. Kumlien, H. Genberg, J. Sandberg, T. Lundgren, and I. Fehrman, "ABO incompatible Kidney Transplantations without splenectomy, using antigen-specific immunoadsorption and rituximab," American Journal of Transplantation, vol. 5, no. 1, pp. 145–148, 2005.
8. R. A. Montgomery, "Kidney Transplantation across HLA and ABO antibody barriers: integrating paired donation into desensitization protocols," American Journal of Transplantation, vol. 10, no. 3, pp. 449–457, 2010.
9. T. Oettl, J. Halter, A. Bachmann *et al*., "ABO blood group-incompatible living donor Kidney Transplantation: a prospective, single-centre analysis including serial protocol biopsies," Nephrology Dialysis Transplantation, vol. 24, no. 1, pp. 298–303, 2009.
10. H. Genberg, G. Kumlien, L. Wennberg, U. Berg, and G. Tydén, "ABO-incompatible Kidney Transplant using antigen-specific immunoadsorption and rituximab: a 3-year follow-up," Transplantation, vol. 85, no. 12, pp. 1745–1754, 2008.
11. Tydén, J. Donauer, J. Wadström *et al*., "Implementation of a protocol for ABO-incompatible Kidney Transplantation—a three-center experience with 60 consecutive transplantations," Transplantation, vol. 83, no. 9, pp. 1153–1155, 2007.
12. J. M. Gloor and M. D. Stegall, "ABO incompatible Kidney Transplantation," Current Opinion in Nephrology and Hypertension, vol. 16, no. 6, pp. 529–534, 2007.
13. K. Tanabe, "Japanese experience of ABO-incompatible living Kidney Transplant," Transplantation, vol. 84, supplement 12, pp. S4–S7, 2007.
14. S. Fuchinoue, Y. Ishii, T. Sawada *et al*., "The 5-year outcome of ABO-incompatible Kidney Transplant with rituximab induction," Transplantation, vol. 91, no. 8, pp. 853–857, 2011.
15. H. Ishida, K. Tanabe, H. Toma, and T. Akiba, "Therapeutic apheresis therapy for ABO-incompatible Kidney Transplantations," Therapeutic Apheresis, vol. 7, no. 6, pp. 520–528, 2003.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