

Successful Usage of Extracorporeal Plasma Perfusion Adsorption Devices Columns for Desensitization Through Immunoabsorption in End-Stage Renal Disease Patients for ABO-Incompatible Kidney Transplant

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Abstract

Background: ABO-incompatible kidney transplantation (ABOiKT) has emerged as a viable solution to overcome donor shortages, particularly in countries with underdeveloped deceased donor programs. This study evaluated the efficacy of the SECORIM ABO immunoabsorption (IA) column (Vitrosorb AB, Malmo, Sweden) desensitization protocol in 21 end-stage renal disease (ESRD) patients undergoing live donor ABOiKT.

Methods: Patients underwent rituximab induction (375 - 500 mg), followed by individualized IA (1 - 3 sessions) using SECORIM ABO columns. Pre-transplant isoagglutinin IgG titers ranged from 1:32 to 1:1,024, successfully reduced to $\leq 1:8$ before transplantation. Post-operative immunosuppression included tacrolimus, mycophenolate mofetil, and corticosteroids.

Results: All recipients demonstrated stable graft function with no early rejection. The mean serum creatinine at discharge was 1.2 mg/dL (range 0.6 - 2.61 mg/dL), and tacrolimus trough levels varied between 6.19 and 24.9 ng/mL. There were no incidences of hyperacute rejection or graft loss.

Conclusion: The IA protocol proved effective in facilitating safe ABOiKT, ensuring optimal immunological modulation with favorable short-term outcomes, offering a reproducible framework for resource-constrained healthcare settings.

Keywords: ABO-incompatible transplant; SECORIM immunoabsorption

sorption column desensitization; Tacrolimus; Isoagglutinin titers; Kidney transplantation

Introduction

End-stage renal disease (ESRD) represents a growing global health burden, with kidney transplantation regarded as the definitive therapeutic modality that offers superior survival and enhanced quality of life over dialysis. However, the widening gap between the demand and availability of suitable organ donors, particularly in regions where deceased donor programs are underdeveloped, continues to pose a critical challenge. In countries like India, where live-related kidney donation predominates, ABO blood group incompatibility has historically been a major immunologic barrier, significantly limiting donor options and exacerbating waitlist mortality [1, 2].

ABO-incompatible kidney transplantation (ABOiKT) has emerged as a transformative approach to overcome this immunological hurdle, effectively expanding the donor pool. Despite early experiences with high rates of antibody-mediated rejection (AMR) and graft loss, advancements in desensitization strategies have substantially improved outcomes, making ABOiKT a viable alternative to ABO-compatible transplantation [3, 4]. These advancements primarily focus on mitigating hyperacute rejection caused by preformed anti-ABO isoagglutinins, which are naturally occurring antibodies capable of eliciting a potent immune response against incompatible grafts [5].

The evolution of desensitization protocols incorporating rituximab, plasmapheresis, intravenous immunoglobulin (IVIG), and, more recently, antigen-specific immunoabsorption (IA) has been pivotal in achieving successful ABOiKT. Rituximab, a monoclonal antibody targeting CD20⁺ B cells, plays a central role in reducing the production of isoagglutinins, thereby minimizing humoral immunity against the graft [6, 7]. Simultaneously, IA methods using antigen-specific columns have improved the selective elimination of antibodies while conserving vital plasma constituents [8].

The IA column protocol integrates these innovations into a streamlined, resource-efficient desensitization regimen

Manuscript submitted September 25, 2025, accepted October 18, 2025
Published online November 8, 2025

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doi: <https://doi.org/10.14740/wjnu1017>

Table 1. Overview of Immunological Strategy in ABOiKT

Step	Description
Donor-recipient mismatch	ABO blood group incompatibility
Pre-transplant evaluation	Blood group typing, HLA matching, antibody titers (IgG, IgM)
Desensitization initiation	Rituximab infusion, followed by IA or plasmapheresis
Surgical procedure	End-to-side vascular anastomosis under general anesthesia
Post-operative immunosuppression	Tacrolimus, mycophenolate, steroids, and monitoring of tac/titers/creatinine

ABOiKT: ABO-incompatible kidney transplantation; HLA: human leukocyte antigen; IA: immunoadsorption.

(Table 1). By combining rituximab-mediated B-cell depletion with targeted IA using an IA column and adjunctive hemodialysis (HD) sessions for metabolic optimization, the IA column offers a simplified yet effective approach to ABOiKT desensitization. Unlike traditional protocols that depend on multiple plasmapheresis sessions and high-dose IVIG, IA offers a more efficient approach by reducing procedural burden, minimizing non-specific plasma loss, and lowering overall cost factors that are especially critical in low- to middle-income countries [9-11]. Numerous studies have validated the efficacy of rituximab-based desensitization in preventing AMR, with 1-year patient and graft survival rates exceeding 90%, paralleling outcomes seen in ABO-compatible transplants [12-14]. Additionally, antigen-specific IA has demonstrated superior efficacy in isoagglutinin reduction with fewer sessions and lower complication rates compared to conventional plasmapheresis [15, 16]. The IA approach further refines these principles, promoting a modified, patient-centric desensitization model adaptable to various clinical settings. This study presents a retrospective case series of 21 patients who underwent ABOiKT using the IA desensitization protocol at a tertiary care center in India. The primary aim was to assess the efficacy of IA in achieving adequate isoagglutinin titer reduction, ensuring stable early graft function, and maintaining clinical safety across diverse donor-recipient pairs. By documenting clinical outcomes such as serum creatinine levels, tacrolimus trough concentrations, and absence of rejection episodes, this study underscores the clinical relevance and reproducibility of the IA protocol, advocating for its broader adoption in resource-constrained healthcare environments.

Materials and Methods

The renal transplant cases were retrospectively observed at a tertiary care transplant center in India between March 2021 and July 2024. The study enrolled 21 patients diagnosed with ESRD who underwent live donor ABOiKT. All patients received kidneys from first-degree relatives with incompatible ABO blood groups, necessitating pre-transplant desensitization. Informed consent was obtained from all patients before the initiation of desensitization and surgical procedures.

Pre-transplant evaluation

Each patient underwent a rigorous pre-transplant assessment,

which included a detailed clinical history, physical examination, and comprehensive laboratory workup. The workup included complete blood count (CBC), renal function tests (RFTs), liver function tests (LFTs), coagulation profile, and viral serologies (human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), and hepatitis C virus (HCV)). Blood group determination was confirmed via standard agglutination methods. Crucially, isoagglutinin titers (both IgG and IgM classes) against incompatible ABO antigens were measured using column agglutination technology. Human leukocyte antigen (HLA) matching and lymphocyte crossmatching were also performed to evaluate immunological compatibility.

Desensitization protocol: IA approach

Desensitization was initiated 2 - 3 weeks before the planned transplant using the IA protocol. This protocol integrated rituximab-based B-cell depletion with targeted antigen-specific IA and adjunctive HD, streamlining the desensitization process. The SECORIM® IA column setup used during desensitization is shown in Figure 1, illustrating the dual-column filtration system and plasma circulation pathway for antibody removal. All patients received a single intravenous dose of rituximab (375 - 500 mg) 2 weeks before transplantation. Depending on baseline isoagglutinin titers, patients underwent 1 - 3 sessions of IA therapy using IA columns, which selectively removed anti-A and anti-B antibodies without depleting essential plasma proteins. HD was employed as necessary to manage fluid overload, correct metabolic derangements, and enhance antibody removal. The target was to achieve anti-ABO



Figure 1. SECORIM® immunoadsorption column setup.

IgG titers of $\leq 1:8$ before proceeding to transplantation.

Unlike conventional desensitization protocols, which are heavily dependent on plasmapheresis and IVIG, IA employed a simplified yet highly selective approach, reducing the procedural burden and plasma loss. This methodology proved particularly advantageous in resource-constrained settings by offering a cost-effective and efficient desensitization strategy without compromising immunologic efficacy.

Transplant procedure

All 21 renal transplants were performed by the same surgical team using a standardized extra-peritoneal approach under general anesthesia. The donor kidney was anastomosed end-to-side to the recipient's external iliac artery and vein. Uretero-neocystostomy was performed with stenting based on intraoperative findings. The intraoperative course was uneventful in all cases, with satisfactory graft perfusion confirmed by Doppler assessment.

Immunosuppression and post-operative monitoring

The post-transplant immunosuppressive regimen included: 1) tacrolimus (starting dose: 0.1 mg/kg/day in two divided doses), titrated to maintain trough levels between 8 and 12 ng/mL; 2) mycophenolate sodium (720 mg/day); 3) oral prednisolone, initiated at 20 mg/day and tapered; and 4) anti-thymocyte globulin (ATG) induction (1 - 2 mg/kg) administered in all patients in view of high immunologic risk patients.

Patients were monitored intensively in the immediate post-operative period with daily assessments of urine output, hemodynamic stability, serum creatinine levels, and tacrolimus trough concentrations. Anti-A and/or anti-B isoagglutinin titers were rechecked post-operatively in selected patients to monitor for rebound responses.

Follow-up and outcome assessment

Patients were followed for 3 to 42 months. During the first month, weekly follow-ups included CBC, RFT, LFT, and tacrolimus monitoring. Doppler ultrasonography was performed within 1 week of transplantation and subsequently as required. Long-term surveillance involved periodic assessment of renal function, drug levels, and screening for infectious or immunological complications.

Outcomes

All 21 patients were successfully transplanted, with no episodes of hyperacute or biopsy-proven acute rejection during follow-up. No graft loss or severe infectious complications were documented. At discharge, all patients demonstrated stable renal function, with serum creatinine values ranging from 0.6 to 2.61 mg/dL.

Institutional Review Board (IRB) approval

The study protocol was reviewed and approved by the Institutional Ethics Committee of Aakash Healthcare Super Speciality Hospital, New Delhi.

Ethical compliance with human study

This study was conducted in compliance with the ethical standards of the responsible institutional and national committees on human experimentation and with the principles of the Helsinki Declaration.

Results

Demographics, desensitization protocol, and post-transplant outcomes

A total of 21 patients with chronic kidney disease (CKD) stage 5 underwent ABOiKT following a rituximab-based desensitization protocol. The group consisted of 15 males and six females with a mean age of 42.5 years (range, 28 - 61 years). All recipients received grafts from living-related donors. Parental donations were the most common donor category (42.8%), followed by spousal donations (33.3%), siblings (19.0%), and other relatives (4.7%). Regarding blood groups, recipients were predominantly O⁺ (47.6%) and B⁺ (33.3%) and A⁺ (19.0%), whereas donors were most commonly A⁺ (38%), reflecting the inherent ABO incompatibility. The detailed demographic and clinical features, including age, gender, donor relationship, blood groups, and transplant dates, are presented in Table 2. All patients successfully underwent desensitization, ensuring safe transplantation despite blood group barriers.

The desensitization strategy (Table 3) involved rituximab administration approximately 2 weeks before transplantation, followed by IA using ABO-specific columns. Each patient required between one and three IA sessions, with two sessions being most common (66.6%).

Pre-desensitization IgG titers demonstrated wide variability, from as low as 1:32 to as high as 1:1,024, indicating heterogeneous baseline sensitization. Following the protocol, most patients achieved substantial reductions in antibody levels, with post-IgG titers reduced to $\leq 1:8$ in the majority. Patient 1 achieved complete clearance (Nil), while most patients successfully reduced titers to 1:2 - 1:4. However, patients 5, 8, and 14 retained titers of 1:8, underscoring the variability in individual responses (Figs. 2 and 3).

Similarly, IgM titers, which often reflect early antibody-mediated activity, showed favorable declines. While pre-treatment titers were higher in several patients, most achieved a significant reduction to 1:2 - 1:8 before surgery. This decline in IgM is clinically important, as uncontrolled IgM levels may accelerate graft rejection. Overall, the protocol effectively reduced both IgG and IgM titers, ensuring safe progression to

Table 2. Demographic and Clinical Parameters at Discharge

Patient number	Transplant date	Age (years)	Gender	CKD stage	Donor relationship	Recipient blood group	Donor blood group	Transplant
1	12/11/2022	46	F	Stage 5	Husband	B+	A+	Successful
2	13/01/2023	41	M	Stage 5	Father	O+	A+	Successful
3	03/07/2024	51	M	Stage 5	Wife	O+	B+	Successful
4	14/03/2024	45	F	Stage 5	Mother	B+	A+	Successful
5	1/10/2024	42	F	Stage 5	Sister	B+	A+	Successful
6	20/10/2021	45	F	Stage 5	Mother	A+	AB+	Successful
7	01/10/2024	30	M	Stage 5	Wife	O+	B+	Successful
8	02/05/2024	33	M	Stage 5	Brother	O+	A+	Successful
9	12/10/2021	41	M	Stage 5	Sister	B+	AB+	Successful
10	21/03/2024	32	M	Stage 5	Brother	B+	AB+	Successful
11	16/09/2022	33	M	Stage 5	Wife	A+	B+	Successful
12	29/04/2022	28	M	Stage 5	Mother	O+	A+	Successful
13	20/10/2021	44	F	Stage 5	Mother	A+	AB+	Successful
14	7/09/2021	40	M	Stage 5	Mother	B+	AB+	Successful
15	19/02/2020	35	M	Stage 5	Maternal uncle	B+	A+	Successful
16	13/04/2022	33	F	Stage 5	Father	A+	AB+	Successful
17	7/02/2022	23	M	Stage 5	Father	O+	B+	Successful
18	23/09/2021	39	M	Stage 5	Wife	O+	AB+	Successful
19	16/07/2021	61	M	Stage 5	Wife	O+	B+	Successful
20	31/01/2020	48	M	Stage 5	Wife	O+	B+	Successful
21	13/01/2023	44	M	Stage 5	Father	O+	A+	Successful

CKD: chronic kidney disease.

ABO-incompatible transplantation, though certain patients required more intensive therapy.

Table 4 provides an overview of post-transplant graft function indicators among 21 patients, focusing on discharge creatinine and tacrolimus levels. The number of hospitalization days ranged from as short as 6 days to as long as 21 days, reflecting variations in individual recovery and clinical needs. Creatinine, a key marker of renal function, was within normal or near-normal limits for the majority of patients, ranging between 0.6 and 1.7 mg/dL. Notably, patients 12 and 19 presented with relatively higher values of 1.89 and 2.61 mg/dL, respectively, suggesting possible mild graft dysfunction that warranted closer monitoring. In contrast, most patients maintained stable creatinine values under 1.5 mg/dL, indicating satisfactory graft performance (Fig. 4).

Tacrolimus levels, critical for maintaining immunosuppression and preventing rejection, displayed wide interpatient variation, ranging from 6.19 to 24.9 ng/mL. While most patients remained within the therapeutic window of 6 - 16 ng/mL, some patients (2, 14, 15, and 21) showed higher levels (> 20 ng/mL), likely reflecting early post-transplant intensive immunosuppression regimens (Fig. 5).

To summarize, the IA-guided desensitization protocol successfully reduced anti-ABO antibody titers to permissible levels in most patients, facilitating successful transplan-

tation outcomes. Intensive IA and HD strategies were particularly crucial for patients presenting with high baseline titers. The post-transplant graft function indicators suggest that tailored desensitization protocols, even under resource constraints, can achieve favorable outcomes in ABOiKT recipients.

Discussion

The use of ABOiKT has transformed the field of kidney transplantation by enabling the use of a wider pool of living donors. Previously, the existence of preformed anti-A/B antibodies was a major stumbling block towards successful transplantation based on the threat of hyperacute and antibody-driven rejection. With the advent of advanced desensitization protocols, the threat of rejection has been eliminated, making ABOiKT a feasible option even in low-resource situations. Rituximab has been instrumental in desensitization protocols, being successful in depleting CD20⁺ B cells and thus decreasing the generation of anti-ABO antibodies [17]. Combination with antigen-specific IA via IA columns enables specific removal of isoagglutinins and is linked with fewer complications than standard plasmapheresis [18].

This group of 21 patients who received live donor

Table 3. Desensitization Protocol and Isoagglutinin Titers

Patient number	Immunoadsorption sessions	Column used	Pre-IgG titer	Pre-IgM titer	Post-IgG titer	Post-IgM titer
1	2	A	1:64	1:8	Nil	NA
2	2	A	1:128	1:32	1:2	NA
3	2	B	1:256	1:128	1:4	1:2
4	1	A	1:128	1:64	1:4	1:2
5	2	A	1:512	1:512	1:8	NA
6	1	B	1:32	1:4	1:2	Nil
7	2	B	1:1,024	1:512	1:4	1:4
8	2	A	1:512	1:512	1:8	1:2
9	1	A	1:32	Nil	1:2	NA
10	2	A	1:64	1:32	1:4	1:4
11	3	B	1:64	1:64	1:4	1:2
12	2	A	1:256	1:256	1:4	1:2
13	2	B	1:512	1:256	1:2	1:4
14	3	A	1:1,024	1:512	1:8	1:4
15	1	A	1:64	1:32	1:1	Nil
16	1	B	1:128	NA	1:2	NA
17	2	B	1:128	1:64	1:2	1:2
18	2	AB	-	-	-	-
		B	1:128	NA	1:2	NA
		A	1:64	NA	1:4	NA
19	2	B	1:128	1:128	1:2	1:1
20	2	B	1:128	1:64	1:2	1:2
21	2	A	1:128	1:256	1:2	1:2

NA: data not available.

ABOiKT at a tertiary care facility in India highlights the clinical efficacy and feasibility of standardized desensitization protocols. The IA column protocol was pivotal in this success by offering a systematic, tiered strategy of immunological preparation. IA brings together rituximab-mediated B-cell depletion with focused IA/plasmapheresis to achieve

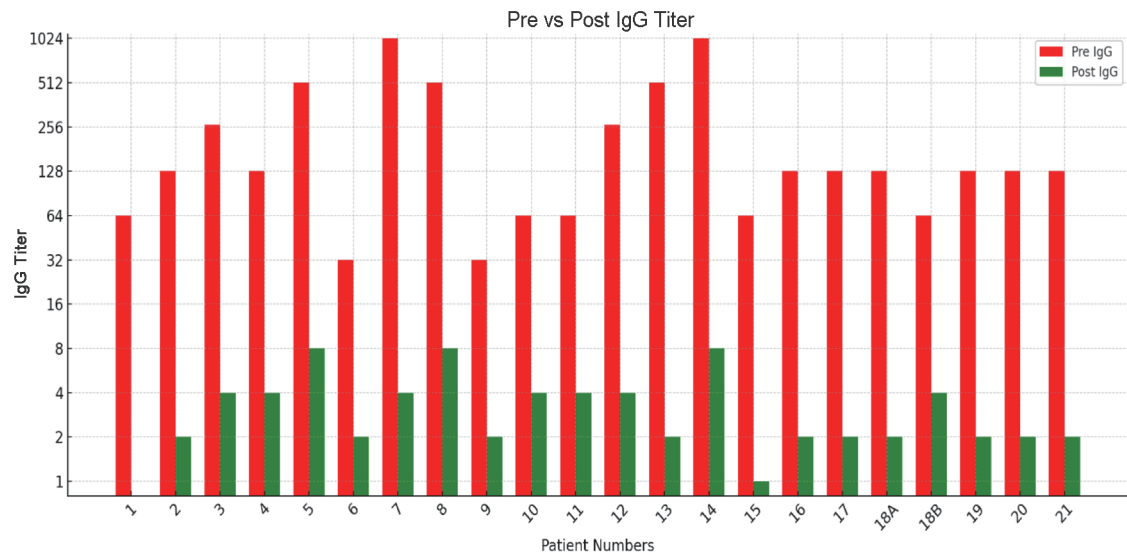


Figure 2. Pre- and post-desensitization IgG isoagglutinin titers across patients.

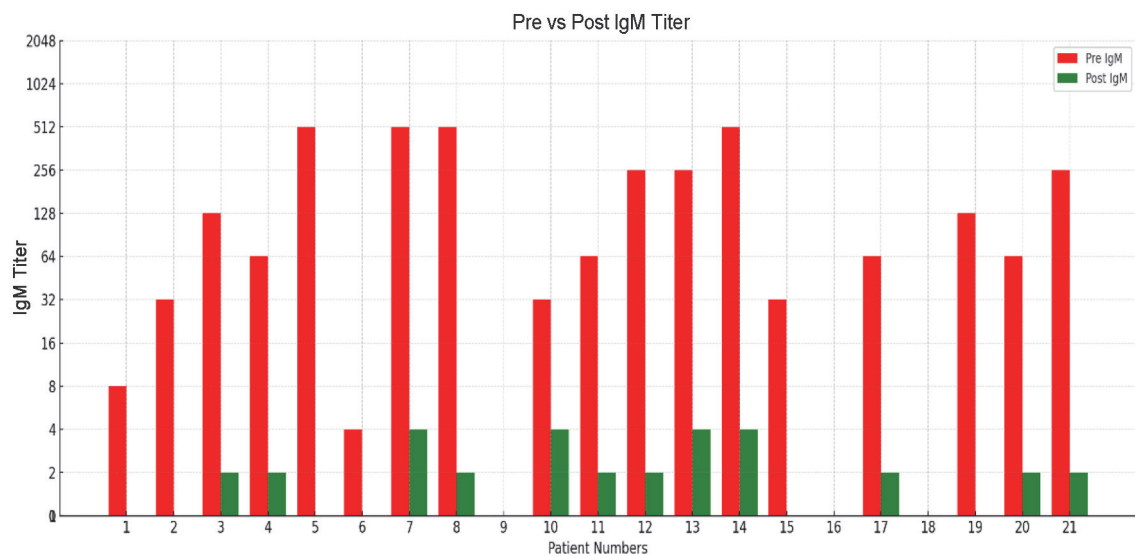


Figure 3. Pre- and post-desensitization IgM isoagglutinin titers across patients.

a further decline in isoagglutinin titers before transplant. Among the study, only one patient required post-transplant biopsy due to surgical re-exploration, showing partial cortical necrosis.

Table 4. Post-Transplant Graft Function Indicators: Creatinine and Tacrolimus Levels at Discharge

Patient number	Days from admission to discharge	Last creatinine (mg/dL)	Tacrolimus (ng/mL)
1	12	0.77	8.2
2	11	1.09	24.9
3	9	0.98	7.30
4	9	0.6	16.75
5	10	0.93	13.91
6	8	0.71	9.54
7	10	1.44	6.19
8	9	0.74	7.12
9	9	1.7	6.4
10	9	0.85	6.6
11	11	1.44	9.67
12	21	1.89	8.10
13	6	1.2	10.6
14	10	0.97	22
15	9	1.26	22
16	10	0.77	8.1
17	9	1.49	14.2
18	6	1.59	11.8
19	11	2.61	5.64
20	10	1.19	9.2
21	11	1.09	24.9

Procedural outcomes were significantly favorable, with all recipients having stable graft function at discharge. The lack of biopsy-proven rejection or premature graft loss is in line with recent reports emphasizing the efficacy of rituximab-based protocols. In addition, in spite of differences in baseline immunologic risk profiles as indicated by conflicting pre-treatment titers, clinical outcomes were consistent across the board. This confirms the malleability of the IA column to patient-specific needs [19, 20].

Serum creatinine levels at discharge were within safe ranges, and tacrolimus levels were carefully managed to maximize immunosuppression without nephrotoxicity. The broad variability of tacrolimus trough levels noted highlights the need for personalized dosing, particularly in the setting of variable IA needs and metabolic tolerance. The strategic addition of IA enhanced procedural predictability by normalizing pre-transplant immunologic modulation. In contrast to protocols dependent on plasmapheresis alone, IA column-based IA allowed for selective and target antibody removal with fewer procedural burdens and complications.

Yet, there were problems. One patient had delayed graft function due to intraoperative issues and required re-exploration. Notwithstanding this, eventual stabilization was evidence of the robustness of the protocol even under complex situations. Such situations underscore the importance of close perioperative surveillance and individualized post-operative care protocols. This experience is consistent with international data that reported 1-year graft survival rates of more than 90% in well-organized ABOiKT programs. It also makes IA an applicable, replicable model, which is specifically useful in areas where deceased donor programs are immature [21-27].

Conclusion

The clinical cases described here offer strong evidence that ABOiKT, supported by the IA desensitization protocol, is an

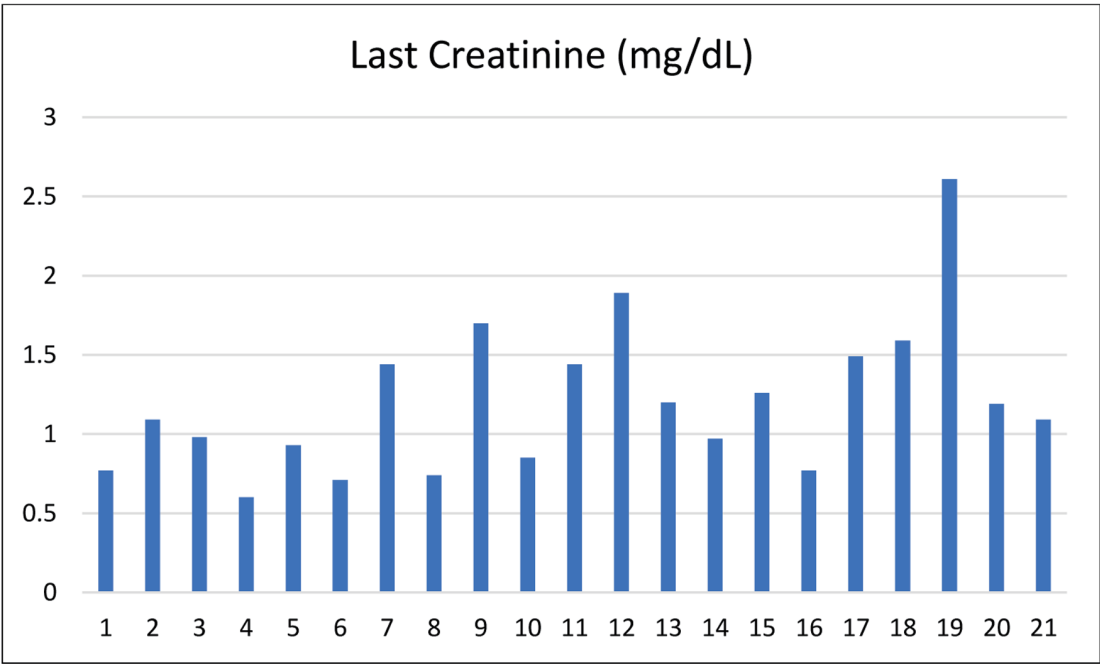


Figure 4. Last serum creatinine levels at discharge across patients.

effective and safe treatment for patients with ESRD threatened by donor incompatibility. The protocol was effective in overcoming immunologic barriers to allow successful engraftment without early rejection or graft loss in varied recipient-donor relationships. The clinical effectiveness of this regimen was reflected in the consistently positive short-term results, char-

acterized by stable serum creatinine concentrations, tolerably well-treated immunosuppression protocols, and freedom from episodes of acute rejection. The inclusion in the IA protocol of rituximab induction with selective IA demonstrates a sophisticated and highly responsive desensitization process amenable to use in developing regions.

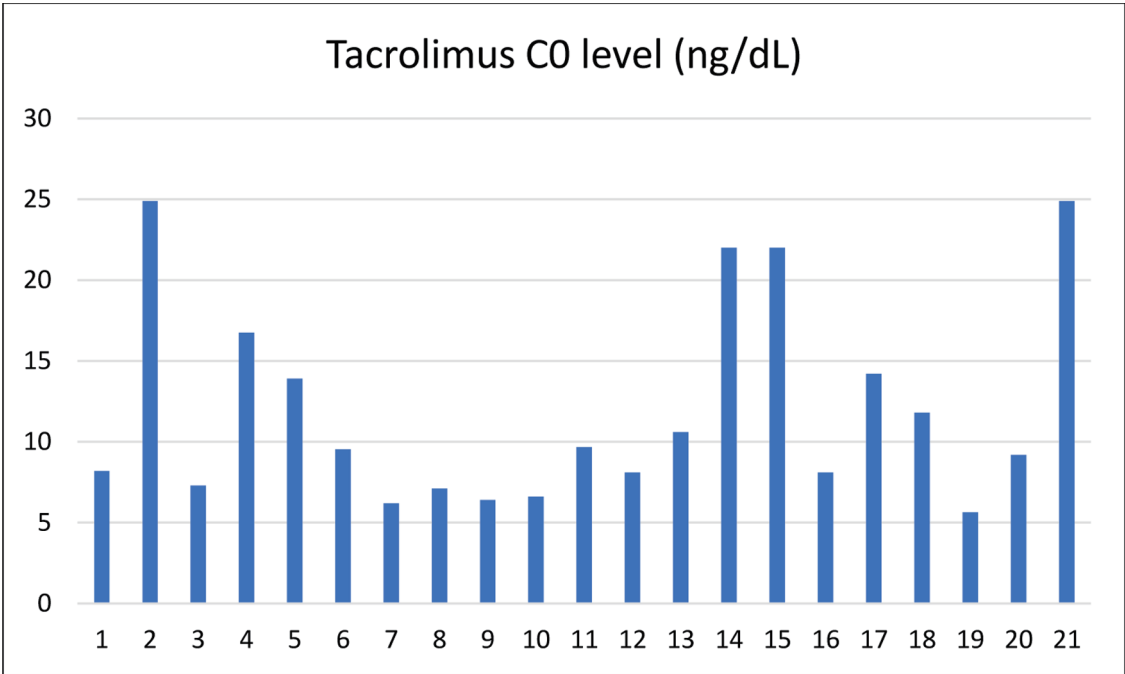


Figure 5. Last tacrolimus levels at discharge across patients.

Acknowledgments

The authors sincerely acknowledge the entire Nephrology and Urology transplant teams, laboratory staff, and nursing personnel for their unwavering support in patient care and data collection. Special thanks to the patients and their families for their trust and consent to share their medical records for academic purposes.

Financial Disclosure

No specific funding was received from public, commercial, or not-for-profit sectors for this study. The research was conducted as part of routine clinical practice.

Conflict of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Informed Consent

Written informed consent was obtained from all individual participants included in this study.

Author Contributions

All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Dr Vikram Kalra, Dr Anupam Roy, Dr Umesh Gupta, and Dr Ambar Khaira. Dr Vikram Kalra wrote the first draft of the manuscript, and all authors commented on previous versions. All authors read and approved the final manuscript.

Data Availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

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