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Feasibility and Short-Term Outcomes of Desensitization in Sensitized Kidney Transplant Candidates: A Prospective Single-Center Observational Study From India

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Abstract

Background: Sensitization to human leukocyte antigens (HLA) remains a major barrier to kidney transplantation, leading to prolonged waiting times and increased risk of antibody-mediated rejection (ABMR). Prospective data on desensitization from Indian programs are limited.

Objectives: To assess the feasibility and 12-month outcomes of desensitization in sensitized patients (those with preformed anti-HLA antibodies) undergoing living donor kidney transplantation (LDKT) with an HLA-incompatible donor or awaiting deceased donor kidney transplantation (DDKT). The primary outcomes were the change in immunodominant anti-HLA antibody mean fluorescence intensity (MFI) after desensitization and the proportion of patients transplanted. Secondary outcomes were patient- and death-censored graft survival, graft function, biopsy-proven acute rejection, and infections over 12 months of follow-up.

Methods: This prospective, single-center observational study enrolled 13 consecutive sensitized adults (single-antigen bead MFI > 2,000 against a living donor, or panel-reactive antibody (PRA) > 30% or an immunodominant antibody MFI > 5,000 for waitlisted candidates) who underwent desensitization between May 2023 and April 2025 and were followed for 12 months after transplantation: 11 deceased-donor waitlisted candidates (rituximab and high-dose intravenous immunoglobulin (IVIG)), with plasmapheresis for repeat courses) and two HLA-incompatible living-donor recipients (plasmapheresis with low-dose IVIG). All transplanted recipients received rabbit anti-thymocyte globulin (r-ATG) induction and were followed for 12 months.

Results: Eight of 13 patients (61.5%) were transplanted: six of 11 (54.5%) deceased-donor candidates and both living-donor recipients. In the paired data, Class I MFI fell from a median of 11,434 (IQR 7,175-12,892) to 2,900 (1,882-4,325) ($p = 0.004$), and Class II MFI from 3,535 (1,667-5,947) to 1,318 (1,031-1,672) ($p = 0.002$). Class II levels remained above 10,000 in two patients, neither of whom was transplanted. Two waitlisted patients (18%) developed serious infections during desensitization and were withdrawn. Delayed graft function (DGF) occurred in five of six deceased-donor recipients; both living-donor recipients had immediate function. Biopsy-proven acute rejection occurred in two of eight recipients (25%; one antibody-mediated, one T-cell-mediated). Patient and graft survival at 12 months were 100% (8/8), and mean serum creatinine was 1.14 ± 0.10 mg/dL.

Conclusion: In this small, uncontrolled single-center cohort, desensitization was feasible and was associated with a reduction in Class I antibody strength and promising short-term outcomes in carefully selected sensitized patients. Class II antibodies responded less. These preliminary findings need confirmation in larger controlled studies with longer follow-up.

Categories: Transplantation, Nephrology
Keywords: donor specific antibodies, highly sensitized, hla desensitization, kidney transplant, therapeutic plasmapheresis

Introduction

Kidney transplantation remains the most effective renal replacement therapy for patients with end-stage renal disease (ESRD), offering superior survival, better quality of life, and reduced long-term healthcare burden when compared with maintenance dialysis [1]. Sensitization to human leukocyte antigens (HLA) develops as a consequence of prior immune exposure, most commonly following blood transfusions, pregnancies, or previous kidney transplantation. The presence of donor-specific antibodies (DSA) in sensitized recipients substantially increases the risk of antibody-mediated rejection (ABMR), early graft dysfunction, and inferior graft survival [1,2]. As a result, these patients often experience prolonged waiting

times, limited donor options, and, in many cases, exclusion from conventional transplant programs [3].

Desensitization protocols aim to reduce circulating alloantibodies and modify the recipient's humoral immune response, thereby lowering immunological risk prior to transplantation. Plasmapheresis facilitates the physical removal of donor-reactive antibodies from the circulation, resulting in an immediate but transient reduction in antibody burden. Intravenous immunoglobulin (IVIG) exerts broader immunomodulatory effects, including attenuation of antibody-mediated injury and regulation of immune effector pathways [4]. Rituximab, a B-cell-depleting agent, reduces antibody production by targeting CD20-expressing B lymphocytes and limiting their contribution to ongoing alloimmune activation [5]. When used in combination, these modalities allow effective antibody reduction and immune modulation in carefully selected high-risk recipients.

In clinical practice, desensitization is employed either to broaden transplant eligibility by lowering sensitization levels in waitlisted patients or to permit planned transplantation in the presence of known DSA. In the latter setting, pre-transplant antibody reduction is particularly important to mitigate the risk of hyperacute or early ABMR in crossmatch-positive or immunologically incompatible transplants.

However, desensitization is resource-intensive and may be associated with infection, rejection, and early graft dysfunction. In India, most kidney transplants are from living donors, and deceased donation remains low. Sensitized patients therefore face very long waiting times because both a compatible living donor and a deceased donor offer are unlikely. Several factors shape sensitization and its management in India: frequent blood transfusion in patients on dialysis, limited availability of paired kidney exchange, and the high cost of IVIG and newer agents such as imlifidase or eculizumab. In addition, the high background prevalence of tuberculosis and other infections raises concerns about intensifying immunosuppression. Most published desensitization outcomes come from Western centers with different donor pools, allocation systems, and resources. Indian reports are few, mostly retrospective and largely limited to living-donor HLA-incompatible transplantation. Prospective data on desensitization for deceased-donor candidates within an Indian point-based allocation system are, to our knowledge, lacking.

We therefore conducted a prospective, single-center observational study at a high-volume Indian transplant center. We hypothesized that individualized desensitization would reduce the strength of the immunodominant anti-HLA antibody enough to permit transplantation with a negative flow cytometry crossmatch in a substantial proportion of sensitized candidates, with acceptable 12-month outcomes. The primary objectives were to describe the change in immunodominant anti-HLA antibody mean fluorescence intensity (MFI) after desensitization and the proportion of enrolled patients who proceeded to living-donor HLA-incompatible or deceased-donor kidney transplantation. Secondary objectives were to describe 12-month patient and graft survival, early graft function, biopsy-proven acute rejection, infectious complications, and serum creatinine at 12 months.

Materials And Methods

Study design, setting, and ethics

This was a prospective, single-center observational cohort study conducted at the Institute of Kidney Diseases and Research Centre-Institute of Transplantation Sciences (IKDRC-ITS), Ahmedabad, India, a tertiary referral transplant center performing approximately 500 kidney transplants per year, between May 2023 and April 2025. The study was approved by the Institutional Ethics Committee of IKDRC-ITS and Gujarat University of Transplantation Sciences (GUTS) (approval no. Guts/Ec-06/Nephro-06, dated 20/06/2023) and was conducted in accordance with the Declaration of Helsinki and the Declaration of Istanbul. All participants gave written informed consent before enrollment, both for desensitization and for the use of their data for research and publication. All living-donor transplants were approved by the hospital authorization committee as required under the Transplantation of Human Organs and Tissues Act (THOTA).

Study population, sampling, and eligibility

Sampling

We used consecutive sampling: every patient who met the eligibility criteria and started desensitization at our center during the study period was invited to participate.

Inclusion Criteria

The study included patients whose age was ⩾ 18 years; had end-stage kidney disease on maintenance dialysis; had HLA sensitization, defined as at least one anti-HLA antibody with MFI ⩾ 1,000 on single-antigen bead testing; had either a living, ABO-compatible (related/spousal/unrelated) donor with a DSA MFI > 2,000 (living-donor pathway) or active registration on the deceased-donor waitlist with an allocation score > 10 and either a panel-reactive antibody (PRA) > 30% (Class I or II) or an immunodominant antibody with MFI > 5,000 (deceased-donor pathway); was medically fit to receive IVIG, rituximab, and plasmapheresis; and had provided written informed consent.

Exclusion Criteria

The study excluded patients whose age is < 18 years; those with active hepatitis B, or hepatitis C or HIV infection, defined as detectable viral load/HBsAg positive without suppression; active tuberculosis or other active infection; and had active malignancy, ABO-incompatible donor, positive complement-mediated cytotoxicity (CDC) crossmatch with the living donor, previous severe reaction to IVIG or rituximab, or pregnancy.

Allocation Score Threshold

In Gujarat, deceased-donor kidneys are allocated by a point-based score under the Gujarat Deceased-donor Organ Transplantation (G-DOT) program of the State Organ and Tissue Transplant Organization (SOTTO) [6]. The score is based on listing the components, e.g., waiting time on dialysis, PRA, age, and prior donation by a relative. At our center, most deceased-donor kidneys during the study period went to candidates with a score of 12-14. We therefore offered desensitization only to candidates with a score > 10, who had a realistic chance of an organ offer while antibody levels were reduced. This criterion introduces selection, which is acknowledged in the Limitations.

Donor Types

Living donors were ABO-compatible (related/spousal/unrelated) donors. Deceased donors were brain-dead donors, classified as standard-criteria (SCD) or expanded-criteria donors (ECD) using the United Network for Organ Sharing/Organ Procurement and Transplantation Network (UNOS/OPTN) definition (ECD: age ⩾ 60 years, or age 50-59 with at least two of hypertension, terminal creatinine > 1.5 mg/dL, or cerebrovascular cause of death).

Study objectives, outcomes, and definitions

Primary Outcomes

Change in MFI of the immunodominant anti-HLA antibody in each class, from the pre-desensitization sample to the last sample before transplantation, or to the end of the desensitization course for patients not transplanted. Proportion of enrolled patients transplanted within the study period.

Secondary Outcomes

Patient survival; death-censored graft survival (graft loss defined as return to maintenance dialysis or re-transplantation); early graft function; biopsy-proven acute rejection; infections; and serum creatinine at 12 months. Infections during desensitization were recorded in all enrolled patients.

Immunological Definitions

Sensitization is the presence of preformed antibodies against HLA antigens, detected by single-antigen bead assay at MFI ⩾ 1,000. PRA is the percentage of a reference panel of HLA antigens against which the patient's serum reacts. It was measured separately for Class I and Class II. MFI is a semi-quantitative measure of antibody binding to an individual HLA-coated bead in the single-antigen bead assay; it is not a titre. DSA is an anti-HLA antibody directed against an HLA antigen present in a specific, known donor. An immunodominant antibody is found in deceased-donor candidates without a defined donor; it is the anti-HLA antibody with the highest MFI in each class.

Clinical Definitions

Immediate graft function (IGF): serum creatinine < 3 mg/dL by post-operative day 5 without dialysis; slow graft function (SGF): serum creatinine ⩾ 3 mg/dL on day 5 without dialysis; and delayed graft function (DGF): need for dialysis within the first post-transplant week.

Desensitization protocols

Living Donor ABO-Compatible, HLA-Incompatible Transplantation

Desensitization was offered when DSA exceeded 2000 MFI (using Luminex xPONENT developed by Luminex Corporation, Texas, USA). Patients were offered two to four alternate-day plasmapheresis sessions (1.5 plasma volume exchange) followed by IVIG 100 mg/kg after each session. Tacrolimus and mycophenolate mofetil were started with plasmapheresis initiation. Renal transplant was done within 48 hours of the last plasmapheresis. Flow cytometry (FCM) was done (using a BD FACSCalibur flow cytometer developed by Becton Dickinson (BD) Biosciences, Franklin Lakes, New Jersey, USA) pre-transplant.

Deceased Donor Waitlisted Patients

Patients with PRA >30% or immunodominant antibody >5000 MFI were offered desensitization. Inj. rituximab 375 mg/m² on days 0 and 14 was given, followed by IVIG 2 g/kg on days 28 and 42. Repeat desensitization with plasmapheresis (four to six sessions) and IVIG (100 mg/kg after each plasmapheresis session) was performed if a transplant did not occur within six months (Table *1*).

Feature	Living-donor (ABO-compatible, HLA-incompatible)	Deceased-donor waitlisted
Patients (study ID)	n = 2 (patients 12, 13)	n = 11 (patients 1–11)
Antibody measured	DSA against the known donor	Immunodominant anti-HLA antibody (donor not yet known)
Indication	DSA MFI > 2,000	Allocation score > 10 AND (PRA > 30% OR immunodominant MFI > 5,000)
Rituximab	Not given	375 mg/m² on days 0 and 14
IVIG	100 mg/kg after each plasmapheresis (low dose)	2 g/kg on days 28 and 42 (high dose)
Plasmapheresis	2–4 alternate-day sessions, 1.5 plasma volumes, replacement fluid (albumin / FFP)	Only in a repeat course: 4–6 sessions, each followed by IVIG 100 mg/kg
Timing of transplant	Planned; within 48 h of last plasmapheresis	On receiving an organ offer; repeat course if no transplant within 6 months
Maintenance drugs started	Tacrolimus + MMF from first plasmapheresis	At transplant / during desensitization
Target to proceed	DSA MFI <1000 and negative T- and B-cell FCXm	Immunodominant MFI <5000 and negative T- and B-cell FCXm with the actual donor
Induction	r-ATG, total 2.5–3 mg/kg	r-ATG, total 2.5–3 mg/kg

TABLE 1: Desensitization protocol

DSA: donor-specific antibodies; MFI: mean fluorescence intensity; r-ATG: rabbit anti-thymocyte globulin; PRA: panel-reactive antibody; IVIG: intravenous immunoglobulin; FFP: fresh frozen plasma; MMF: mycophenolate mofetile; FCXm: flow cytometric crossmatch; HLA: human leukocyte antigen

Immunosuppression and Follow-up

All recipients received induction therapy with rabbit anti-thymocyte globulin (r-ATG), given the high immunological risk in this sensitized cohort. Maintenance immunosuppression included standard triple immunosuppression (tacrolimus, mycophenolate mofetil, and prednisolone). All patients were given routine post-transplant antimicrobial prophylaxis. Post-transplant DSA was not routinely monitored. Patients were followed for graft function, rejection, and infectious complications. Routine screening for BKV and Parvo B19 was not done in view of resource constraints.

Data collection

Patients were enrolled prospectively at the start of desensitization and followed in real time according to a predefined schedule. Study variables were defined before enrollment and recorded on a structured case record form at each visit. Laboratory values (HLA antibody MFI, crossmatch, creatinine, and tacrolimus levels) were transcribed from the institutional electronic laboratory system, and clinical events were verified against the case files.

Outcomes and statistical analysis

No formal sample-size calculation was performed; all consecutive eligible patients during the study period were enrolled. The study was therefore not powered for hypothesis testing, and the analyses are exploratory. Continuous variables are summarized as mean ± standard deviation or median (interquartile range), as appropriate, and categorical variables as number (percentage), with the denominator stated. Proportions are reported with exact (Clopper-Pearson) 95% confidence intervals. Pre- and post-desensitization MFI values were compared separately for Class I and Class II in patients with paired measurements using the Wilcoxon signed-rank test, given the small sample and skewed distribution. Clinical outcomes in transplanted

recipients (n = 8) are reported descriptively. Because of the small number of patients and events, no comparison between living- and deceased-donor recipients and no multivariable or adjusted analyses were performed. A two-tailed $p < 0.05$ was considered statistically significant. Missing data were not imputed. Analyses were performed with IBM SPSS Statistics for Windows, Version 26 (Released 2018; IBM Corp., Armonk, New York, United States). This study is reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline for cohort studies.

Results

Thirteen patients were enrolled: 11 in the deceased-donor pathway and two in the living-donor pathway. Eight (61.5%) were transplanted: six of 11 deceased-donor candidates (54.5%) and both living-donor recipients. Of the five deceased-donor candidates who were not transplanted, two were withdrawn after developing serious infections during desensitization (pulmonary tuberculosis and recurrent pneumonia), one was lost to follow-up, and two remained on the waitlist because of inadequate reduction of the immunodominant antibody. No patient received off-protocol desensitization agents.

Patient demographics of included patients are summarized in Table 2. The mean age was 38.5 ± 9.6 years. In this study, out of the total 13 patients, nine were male, accounting for 70%, whereas four were female, comprising only 30% of the study population. Chronic kidney disease (CKD) of unknown etiology was the most common cause of ESRD (46%), while chronic glomerulonephritis (CGN-CKD), diabetic kidney disease (DKD), and post-transplant CKD were each responsible for 15% (n=2) of the cases. Around 40% of patients had a dialysis duration ≤24 months. In these sensitized patients, nine patients had a history of multiple blood transfusions; two patients had a history of previous renal transplant and multiple pregnancies.

Patient	Age(Years)	Gender	Dialysis Vintage(Months)	Native Kidney Disease	Sensitization History	Comorbidity
1	20	Male	14	Post-Tx CKD	Previous Transplant	Nil
2	38	Female	17	CKD-UE	Multiple Pregnancy	Nil
3	39	Male	54	CKD-UE	Blood Transfusion	Nil
4	55	Female	62	CKD-UE	Multiple Pregnancy	IHD
5	31	Female	38	CKD-UE	Blood Transfusion	Nil
6	50	Male	61	DKD	Blood Transfusion	DM-II
7	35	Male	45	CTIN	Blood Transfusion	Nil
8	38	Male	31	CGN-CKD	Blood Transfusion	Nil
9	32	Male	28	Post Tx CKD	Previous Transplant	Nil
10	48	Male	28	DKD	Blood Transfusion	DM-II
11	28	Male	23	CKD-UE	Blood Transfusion	Nil
12	42	Female	9	CGN-CKD	Blood Transfusion	Nil
13	45	Male	6	CKD-UE	Blood Transfusion	Nil

TABLE 2: Patient's demographics

Post-Tx CKD: post-transplant chronic kidney disease; CKD-UE: CKD of unknown etiology; DKD: diabetic kidney disease; CTIN: chronic tubulointerstitial nephropathy; CGN-CKD: chronic glomerulonephritis chronic kidney disease; IHD: ischemic heart disease; DM II: diabetes mellitus type 2

Immunological profile of patients described in Table 3. The PRA reflects the degree of sensitization prior to transplantation. A total of 13 patients are represented in this dataset, stratified according to their PRA. In Class I, a significant proportion of patients (six out of 13; 46%) had PRA values in the range of 61%-90%, which corresponds to high sensitization. Overall, this distribution shows that the majority of transplant recipients in this study were moderately to highly sensitized, with 76% (10 out of 13) having PRA Class I levels above 30%. Six patients (46%) had PRA Class II values ranging from 1% to 30%, five patients (39%) had PRA Class II between 31% and 60%, and two patients (15%) had PRA Class II in the 61%-90% range. Overall, 84% (11 out of 13) of the transplant recipients in this study had PRA Class II levels between 1%-60%.

Patient	Number of HLA Mismatches*	PRA Class I	PRA Class II	Pre-treatment MFI Class I	Pre-treatment MFI Class II	Post-treatment and Pre-transplant Class I MFI	Post-treatment and Pre-transplant Class II MFI	Pre-Tx FCM	Induction Agent
1	5	72%	32%	12,568	3400	3400	1200	-VE	r-ATG
2	3	85%	34%	15,454	1029	2130	988	-VE	r-ATG
3	4	88%	45%	12,368	6700	3500	1677	-VE	r-ATG
4	6	60%	35%	10,500	3670	4600	1655	-VE	r-ATG
5	4	67%	28%	14,689	3689	5300	1435	-VE	r-ATG
6	6	49%	15%	9800	1289	1800	890	-VE	r-ATG
7	NA	87%	75%	13,000	12,390	5200	10,188	NA	NA
8	NA	20%	80%	2300	18,787	2400	16,400	NA	NA
9	NA	81%	5%	17,000	1678	ND	ND	ND	NA
10	NA	56%	24%	8980	5389	ND	ND	ND	NA
11	NA	28%	35%	6790	3600	ND	ND	ND	NA
12	4	38%	5%	6300	1200	1500	800	-VE	r-ATG
13	2	25%	12%	4500	2800	1324	1159	-VE	r-ATG

TABLE 3: Immunological profile of patients

NA: not available; ND: not done; PRA: panel-reactive antibody; MFI: mean fluorescence intensity; Pre-Tx FCM: pre-transplant flow cytometry; r-ATG: rabbit anti-thymocyte globulin

The distribution of HLA mismatches among transplanted recipients is shown. Most patients exhibited three to five mismatches (>70%). A smaller proportion of patients had a lower mismatch burden.

Class I and Class II highest MFI levels were evaluated both at baseline and post-desensitization in deceased donor and living related renal transplant recipients to assess the immunological response to desensitization (Table *4*). Reductions in Class I and Class II MFI were observed post-desensitization. Mean Class I MFI is reduced from 10,327 ± 4,429 to 3,115 ± 1,490. However, in Class II there is only a slight reduction in antibody value from baseline 5048 ± 5128 to 3239 ± 5093 post-desensitization, specifically in patients with high baseline titer (>10,000). Similarly, two patients who didn't receive a transplant also had higher baseline Class II antibody MFI even after desensitization. A pre-transplant T- and B-cell flow cytometry crossmatch with the actual donor was performed in all eight recipients (two living donor kidney transplantations (LDKT), six deceased donor kidney transplantations (DDKT)) and was negative in all.

Group/antibody class	Pre-desensitization, median (IQR); mean ± SD	Post-desensitization, median (IQR); mean ± SD	p (Wilcoxon)
All with paired data: Class I	11,434 (7,175–12,892); 10,148 ± 4,425	2,900 (1,882–4,325); 3,115 ± 1,512	0.004
All with paired data: Class II	3,535 (1,667–5,947); 5,495 ± 5,773	1,318 (1,031–1,672); 3,639 ± 5,303	0.002
Transplanted (n = 8): Class I	11,434 (8,925–13,098); 10,772 ± 3,843	2,765 (1,725–3,775); 2,944 ± 1,488	0.008
Transplanted (n = 8): Class II	3,100 (1,267–3,675); 2,972 ± 1,885	1,180 (964–1,490); 1,226 ± 335	0.008

TABLE 4: Paired MFI analysis

MFI of the immunodominant antibody in each class.

Median percentage reduction: Class I ≈ 72%, Class II ≈ 44%.

In DDKT patients, four had SCD and two had ECD. All DDKT patients had a cold ischemia time of less than 18 hours. In the studied transplant group, the preferred induction agent was r-ATG (rabbit anti-thymocyte globulin), administered at a total dose of 2.5-3 mg/kg to all recipients in view of high immunological risk.

The graft and patient outcomes of the included patients are summarized in Table *5*. Both living-donor recipients had IGF. Among the six deceased-donor recipients, five had DGF, and one had SGF. With only two living-donor recipients, the two groups were not formally compared. Renal biopsy was performed in all six deceased-donor recipients for DGF or SGF. It showed acute tubular necrosis in four, ABMR in one, and T cell-mediated rejection in one. Biopsy-proven acute rejection therefore occurred in two of eight transplanted recipients (25%; 95% CI 3.2-65.1%), both deceased-donor recipients. After transplantation, two of eight recipients developed infections (fungal pneumonia and graft pyelonephritis). At 12 months, all eight recipients were alive with functioning grafts (patient and death-censored graft survival 100%; 95% CI 63.1-100%), and mean serum creatinine was 1.14 ± 0.10 mg/dL.

Patient	Graft Function	Renal Biopsy Finding	Management	Infection Episode	S. Creatinine (12 months)	Patient Survival
					(mg/dl)	(12 months)
1	DGF	ATN	Conservative	Nil	1.12	Alive
2	DGF	ATN	Conservative	Fungal Pneumonia	1.3	Alive
3	SGF	ABMR	Plasma Exchange with IVIG	Nil	1.08	Alive
4	DGF	TCMR	MP Pulse with ATG	Nil	1.14	Alive
5	DGF	ATN	Conservative	Nil	1.16	Alive
6	DGF	ATN	Conservative	Graft Pyelonephritis	1.23	Alive
7	NA	NA	NA	NA	NA	Alive
8	NA	NA	NA	NA	NA	Alive
9	NA	NA	NA	NA	NA	NA
10	NA	NA	NA	NA	NA	NA
11	NA	NA	NA	NA	NA	NA
12	IGF	ND	NA	Nil	0.95	Alive
13	IGF	ND	NA	Nil	1.12	Alive

TABLE 5: Graft and patient outcome

NA: not available; ND: not done, DGF: delayed graft function; SGF: slow graft function; IGF: immediate graft function; ATN: acute tubular necrosis; TCMR: T-cell-mediated rejection; ABMR: antibody-mediated rejection; IVIG: intravenous immunoglobulin; MP: methyl prednisolone

Discussion

This prospective observational study suggests that desensitization with plasmapheresis, IVIG, and rituximab is feasible and is associated with antibody reduction and transplantation in selected sensitized patients, with favorable short-term outcomes.

In our study group, the mean age of patients is 38.5 ± 9.6 years, ranging from 20 to 55 years, with the majority clustered between 26 and 40 years. A significant male predominance was observed, with 70% of the patients being male and only 30% female. In contrast to our observation, Maisarah Jalalonmuhali et al. [7] reported a predominance of female recipients, which may reflect differences in patient populations and referral patterns, although small numbers preclude firm conclusions. Unlike the predominantly Western data reported by Montgomery et al. [8], where sensitized recipients were generally older at transplantation, patients in our study underwent transplantation at a younger age, reflecting differences in ESRD demographics and referral pathways.

The study population shows a moderate dialysis vintage, with 60% of patients on dialysis for >24 months, and the remaining 40% had a vintage of <24 months. Vijay Kumar Sinha et al. [9] similarly showed a range of two to 96 months, including one patient each on dialysis for 42 and 96 months, indicating prolonged sensitization.

In our study, the most common etiology for ESRD was CKD of unknown etiology (CKD-UE), observed in 46% of patients. The next most prevalent causes were DKD, CGN, and post-transplant CKD, each accounting for 15%, followed by chronic tubulointerstitial nephritis (CTIN) (8%). In contrast, Maisarah Jalalonmuhali et al. [7] reported three patients with unknown etiology, which aligns with the global issue of underdiagnosis or under-documentation of primary kidney disease, particularly in small cohorts. Notably, the current study uniquely reports post-transplant CKD, reflecting a population undergoing repeat transplantation, a complex group typically with high sensitization.

In our study, the distribution of PRA Class I revealed that 46% of patients had high sensitization levels (61-

90%), and 15% had moderate levels (31-60%). Similarly, for PRA Class II, 46% had a low level (1-30%), 38% had a moderate level (31-60%), and 15% had a high level (61-90%), with no patients exceeding 90%. In contrast to our observation, Vijay Kumar Sinha et al. [9] described uniformly high PRA Class I and Class II positivity (>60%), suggesting a more severe sensitization burden in their study population. Unlike Western series such as that of Montgomery et al. [8], which reported mean PRA levels exceeding 80%, our cohort demonstrated a broader range of sensitization.

A paired analysis of patients demonstrated a statistically significant reduction in Class I DSA strength. The mean Class I MFI decreased from 10,327 ± 4,429 before treatment to 3,115 ± 1,490 after desensitization (paired t-test, $p = 0.0002$). Paired analysis also demonstrated a significant reduction in Class II DSA levels in the patient. Mean Class II MFI decreased from 5,048 ± 5,128 before treatment to 3,239 ± 5,093 after desensitization (paired t-test, $p = 0.0036$). Although statistically reduced, Class II antibodies showed incomplete suppression and frequently remained at clinically relevant levels. In contrast to our cohort, Constantino Fernández et al. [10] reported higher baseline MFI (>5000) values without detailed post-desensitization trends, limiting direct assessment of immunologic response to therapy. Protocols differ between centers in the antibody level accepted at transplantation, which limits direct comparison. Vijay Kumar Sinha et al. [9] presented a population with much higher sensitization; Class I MFI values ranged from 1147 to 23,440, with multiple values well above 10,000. Class II values also exceeded 10,000.

In the DDKT group, four patients (50%) had transplanted recipients with biopsy-proven acute tubular necrosis (ATN); one (12.5%) had ABMR, and one (12.5%) had T cell-mediated rejection (TCMR); donor ischemic and immunological factors cannot be separated in this design. In contrast, no rejection episodes were noted in the living donor group. When compared to existing literature, the findings from Constantino Fernández et al. [10] show an acute rejection rate of 17.4% over a median follow-up of 30 months, including one case of ABMR, two TCMR, and one mixed rejection. Similarly, Jeong-Hoon Lim et al. [11] reported biopsy-proven acute rejection (BPAR) rates of 6.0% in the HLAi group, while graft failure was observed in 2.0% of HLAi patients.

The overall one-year patient and graft survival of 100% among transplanted recipients in our cohort highlights the feasibility of desensitization in this cohort, although with only eight recipients the 95% CI for one-year graft survival is wide (63-100%). Our findings are comparable to published Indian data; Kute et al. [12] from IKDRC reported successful outcomes in deceased donor and HLA-incompatible living donor transplants, with one-year graft survival exceeding 90% and acceptable rates of ABMR. In a meta-analysis of patients treated with IVIG, plasmapheresis, and rituximab, Chandramohan et al. [13] evaluated desensitization in highly sensitized patients and demonstrated improved access to transplantation, although DGF and early rejection rates were higher compared to non-sensitized recipients.

Strengths and limitations

Strengths

This study used prospective enrollment from the start of desensitization, predefined desensitization pathways, and patient-level immunological and clinical data, with complete 12-month follow-up of all transplanted recipients. It contributes real-world data from an Indian deceased-donor allocation system, which is under-represented in the literature.

Limitations

First, the sample is very small (13 enrolled, eight transplanted, two living donors), so estimates are imprecise, and the study was not powered for hypothesis testing; no adjusted analyses were possible. Second, there was no control group of sensitized patients who did not receive desensitization. We therefore cannot determine whether transplantation rates or antibody changes differ from what would have occurred without treatment, including natural fluctuation in MFI or the effect of new organ offers. Third, selection bias is likely, because desensitization was offered only to waitlisted candidates with an allocation score > 10 and to clinically suitable patients. Fourth, outcome data were missing for three of 13 patients (two withdrawn because of infection, one lost to follow-up), and their exclusion from the antibody and outcome analyses may make our estimates optimistic. Fifth, all recipients received the same r-ATG induction, so the contributions of desensitization, induction, and donor factors to outcomes cannot be separated. Sixth, Class II antibodies were incompletely suppressed. Seventh, follow-up was limited to 12 months, which precludes assessment of chronic ABMR, de novo DSA, and long-term graft survival. Eighth, protocol biopsies and systematic post-transplant DSA surveillance were not performed, and routine BK virus and parvovirus B19 screening was not available. Subclinical rejection, de novo DSA formation, and viral infections may therefore have been missed, and the 12-month results cannot exclude chronic antibody-mediated injury. Ninth, because waitlisted deceased-donor candidates had no identified donor during desensitization, a pre-desensitization crossmatch was not possible, and response was judged by MFI alone, which is semi-quantitative.

Conclusions

In this small, single-center, uncontrolled cohort, protocol-based desensitization was feasible and was associated with promising short-term outcomes in carefully selected sensitized patients. Class I anti-HLA antibody levels fell substantially, Class II antibodies responded less, and eight of 13 enrolled patients underwent transplantation, with 100% patient and graft survival at 12 months among the recipients. DGF was frequent after DDKT, and serious infections occurred during desensitization. Because the study lacked a control group, protocol biopsies, and long-term DSA surveillance, these findings are preliminary and hypothesis-generating. Larger multicenter studies with comparison groups and longer follow-up are needed to establish effectiveness, safety, and generalizability.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institute Ethics Committee of Institute of Kidney Diseases and Research Centre-Institute of Transplantation Sciences (IKDRC-ITS) and Gujarat University of Transplantation Sciences (GUTS) issued approval Guts/Ec-06/Nephro-06. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Evans RW, Manninen DL, Garrison LP Jr, et al.: The quality of life of patients with end-stage renal disease . N Engl J Med. 1985, 312:553-9. 10.1056/NEJM198502283120905
2. Josephson MA: Monitoring and managing graft health in the kidney transplant recipient . Clin J Am Soc Nephrol. 2011, 6:1774-80. 10.2215/CJN.01230211
3. Loupy A, Hill GS, Jordan SC: The impact of donor-specific anti-HLA antibodies on late kidney allograft failure. Nat Rev Nephrol. 2012, 8:348-57. 10.1038/nrneph.2012.81
4. Kazatchkine MD, Kaveri SV: Immunomodulation of autoimmune and inflammatory diseases with intravenous immune globulin. N Engl J Med. 2001, 345:747-55. 10.1056/NEJMra993360
5. Jackson AM, Kraus ES, Orandi BJ, Segev DL, Montgomery RA, Zachary AA: A closer look at rituximab induction on HLA antibody rebound following HLA-incompatible kidney transplantation. Kidney Int. 2015, 87:409-16. 10.1038/ki.2014.261
6. SOTTO Gujarat, G-DOT Guideline . (2019). https://sotto.nic.in/DownloadForms/SOTTO.pdf.
7. Jalalonmuhali M, Ng KP, Lim SJ, Ong CS, Wong CM, Lim SK: Kidney transplant in sensitized patients: a case series from a premier teaching hospital in Malaysia. Transplantation Reports. 2018, 3:1-4. 10.1016/j.tpr.2018.03.001
8. Montgomery RA, Lonze BE, King KE, et al.: Desensitization in HLA-incompatible kidney recipients and survival. N Engl J Med. 2011, 365:318-26. 10.1056/NEJMoa1012376
9. Sinha VK, Singh RK, Devra AK, Choudhary LP, Singh K, Pandey P, Pande A: Desensitization therapy in kidney transplantation cases with positive baseline complement-dependent cytotoxicity Crossmatch and high donor-specific antibodies: a retrospective study. Indian J Transplant. 2021, 15:332-7. 10.4103/ijot.ijot_38_21
10. Fernández C, Calvo M, Leite N, et al.: Kidney transplantation from HLA-incompatible live donors: efficiency and outcome of 32 patients after desensitisation. Nefrologia. 2017, 37:638-45. 10.1016/j.nefro.2017.06.006

11. Lim JH, Cho JH, Jung HY, et al.: Excellent outcome after desensitization in high immunologic risk kidney transplantation. PLoS One. 2019, 14:e0222537. 10.1371/journal.pone.0222537
12. Kute VB, Vanikar AV, Trivedi HL, et al.: Desensitization protocol for highly sensitized renal transplant patients: a single-center experience. Saudi J Kidney Dis Transpl. 2011, 22:662-9.
13. Chandramohan D, Adisa O, Patel D, Ware E, Eleti N, Agarwal G: Outcomes of kidney transplantation in highly HLA-sensitized patients treated with intravenous immuno-globulin, plasmapheresis and rituximab: a meta-analysis. Life (Basel). 2024, 14: 10.3390/life14080998