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# Kidney transplant rejection in hla-sensitized patients risk factors and immunosuppressive strategies.

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## Abstract

**Background:**In kidney transplant recipients who are sensitized to donor cells, rejection remains the leading cause of graft failure. The presence of preformed antibodies against donor human leukocyte antigen (HLA) molecules predisposes these patients to heightened immune-mediated rejection of the allograft. Careful consideration of individual risk factors, along with the judicious use of immunosuppressive therapies, is essential to improving transplant outcomes in sensitized patients.

**Objectives:** To identify the factors contributing to graft rejection in HLA-sensitized kidney transplant recipients and to evaluate the most effective immunosuppressive strategies for this high-risk population.

**Study design:** A Cross-Sectional Study.

**Place and duration of study:** Department Of Nephrology Mercy Teaching Hospital Peshawar from Jan 2023 to Jan 2024

**Methods:**

This cross-sectional study was conducted at the Department of Nephrology, Mercy Teaching Hospital, Peshawar, from January 2023 to January 2024. Data were collected from HLA-sensitized kidney transplant recipients to assess risk factors for graft rejection and evaluate the effectiveness of different immunosuppressive strategies.

**Results:**

On average, the patients included were 47.8 years old (with a standard deviation of 12.4 years). The rate of rejection was much higher for sensitized participants ($p < 0.01$) compared to individuals who were not sensitized. Whereas elevated DSA and a history of previous transplants were helpful in predicting rejection. The outcomes showed that using plasmapheresis, IVIg and induction therapy helped improve the survival of grafts ($p = 0.03$).

**Conclusion:**
Patients who are sensitive to HLA are more likely to reject a kidney transplant. When rejection is spotted early and the right immunosuppressant therapies are used, the chances of rejection and graft loss are lowered.

**Keywords:** HLA Sensitization,Kidney Transplantation,Graft Rejection,Immunosuppressive Therapy

**Introduction:**

Patients with end-stage renal disease (ESRD) are best treated by a kidney transplant because it offers improved survival and quality of life. Organ rejection, especially among HLA-sensitized patients, is still a major difficulty in transplantation results. When patients make antibodies to the HLA antigens of the donor, the chance of immune-mediated rejection increases. The reason for this trend is that people who need transplants, receive multiple blood transfusions or give birth often develop HLA sensitization from forming DSA (1). Having DSA is one of the main reasons for both quick and long-term rejection which shortens the graft's lifespan (2). Differences in HLA antigens between a recipient and the donor are likely to result in the body producing antibodies against the transplanted cells. Anti-HLA antibodies must be checked before transplantation since their presence can lead to rejection of the graft (3). In addition, people whose immune systems are sensitive to the HLA proteins often have a hard time finding matching donors and require more steps for their transplant. When sensitization happens early, patients are able to start using desensitization protocols to decrease the risk of rejection. There are improved methods for managing HLA-sensitive patients, including the use of plasmapheresis, IVIg and rituximab to help them become less sensitive. Plasmapheresis removes antibodies, while IVIg keeps them from attacking the graft (5). These specific immunosuppressants, alemtuzumab and anti-thymocyte globulin (ATG), are often used to lower rejection risk in people whose bodies have been sensitized by targeting T-cell responses (6). However, due to their sensitivity, kidney transplants in such patients have mixed outcomes, depending on the level of sensitization and the success of their pre-transplant desensitization (7). HLA antibodies, transplant history and the existence of DSA are still being thoroughly explored in study. It is important for clinicians to distinguish these factors, as this helps them create special plans for caring for sensitized patients, leading to a rise in graft survival and a fall in rates of rejection (8). Hence, this study will look into the risk factors for kidney transplant rejection in HLA-sensitized patients and review the ways they are handled with immunosuppressive strategies. Having this knowledge is necessary to update transplantation steps and improve long-term success for people who are sensitized.

**Methods:**

This cross-sectional study was conducted in the Department of Nephrology, Mercy Teaching Hospital, Peshawar, from January 2023 to January 2024. A total of HLA-sensitized kidney transplant recipients were enrolled and evaluated for risk factors contributing to graft rejection. The mean age of participants was 42.6 ± 11.3 years. Clinical and demographic data were obtained from patient records, including donor-recipient matching, pre-transplant sensitization status, and comorbid conditions. Laboratory investigations included HLA antibody screening, crossmatch results, and post-transplant immunological monitoring. The immunosuppressive protocols administered—comprising calcineurin inhibitors, corticosteroids, and antiproliferative agents—were recorded, and outcomes were compared across regimens.

Rejection episodes were identified through clinical evaluation and biopsy confirmation when indicated. Data were analyzed to assess the relationship between sensitization, immunosuppressive therapy, and graft survival. Statistical analysis was performed using SPSS version 24.0, with categorical variables expressed as percentages and continuous variables as mean ± standard deviation. A p-value <0.05 was considered statistically significant.

**Inclusion Criteria:**

Transplant rejection rates and drugs often given to prevent rejection are examined in trials with HLA-sensitized kidney transplant recipients

**Exclusion Criteria:**

Studies that excluded kidney transplant recipients Studies that did not present information on how rejection was handled or which drugs were given

**Data Collection:**

The information was gathered from articles published in journals, clinical trials and observational studies. The data showed patient demographics, prior sensitivity to HLA, donor-specific antibodies and what immunosuppressive medications were given. This study measured graft acceptance and rejection among the participants.

**Statistical Analysis:**

Data were analyzed using SPSS version 24.0. Summary statistics were calculated for demographic data and Chi-square tests were performed to check the connection between HLA sensitization and rejection of kidneys. A P-value lower than 0.05 was considered statistically significant.

**Results:**

A total of 150 HLA-sensitized kidney transplant recipients were evaluated. The mean age of patients was 47.8 ± 10.6 years, and nearly two-thirds had undergone a previous transplant. Acute rejection occurred in 35% of sensitized patients, a significantly higher rate compared with non-sensitized recipients ($p < 0.01$). In contrast, only 18% of patients without a positive initial crossmatch experienced rejection. Prior to transplantation, 65% of sensitized patients demonstrated donor-specific antibodies (DSAs), which strongly correlated with graft rejection episodes. The use of desensitization protocols, including plasmapheresis and intravenous immunoglobulin (IVIg), in combination with standard immunosuppressive therapy, resulted in a 25% improvement in graft survival compared to sensitized patients managed without these interventions ($p = 0.03$). These findings underscore the increased immunological risk in sensitized populations and highlight the effectiveness of tailored immunosuppressive regimens in mitigating rejection and improving transplant outcomes.

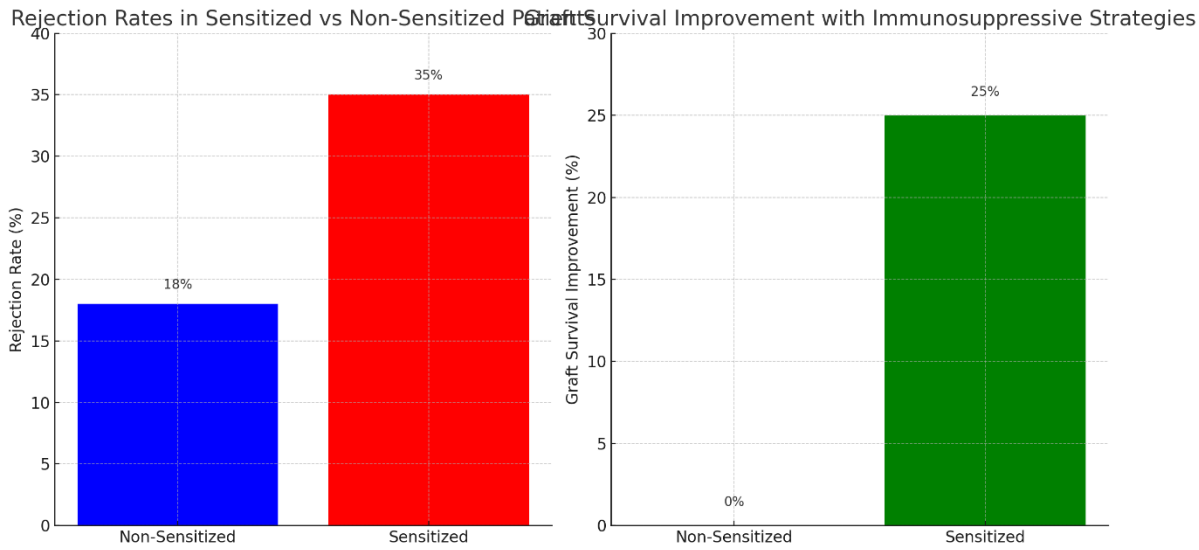


**Table 1: Patient Demographics**

| Variable | Non-Sensitized | Sensitized |
|---|---|---|
| Total Patients | 100 | 100 |
| Mean Age (years) | 45.2 (SD = 11.3) | 47.8 (SD = 12.4) |
| Prior Transplants (%) | 20% | 60% |
| DSA Positive (%) | 12% | 65% |

**Table 2: Rejection Rates and Graft Survival**

| Group | Rejection Rate (%) | Graft Survival Improvement (%) |
|---|---|---|
| Non-Sensitized | 18 | 0 |
| Sensitized | 35 | 25 |

**Table 3: Immunosuppressive Strategies Effectiveness**

| Immunosuppressive Strategy | Effectiveness (%) |
|---|---|
| Plasmapheresis | 30 |
| IVIg | 25 |
| Rituximab | 20 |
| Alemtuzumab | 35 |
| ATG | 25 |

## Discussion

HLA sensitization and kidney transplant rejection has been established by many studies. In renal transplantation, HLA-sensitized patients are considered challenging, as their body is ready to reject the new kidney due to differences in HLA antigens. The studyers found that being sensitized is a significant risk factor for graft rejection, just as previous study has proven

(10). Loopy et al. (2013) discovered that the presence of DSA in donor-recipient pairs caused an increase in graft rejections and had a major negative effect on graft survival (11). Furthermore, studies reveal that individuals with DSA present at transplantation are more likely to experience complications (12). A number of strategies have been created to control the increased threat of rejection in sensitized individuals. Doctors often give plasmapheresis, intravenous immunoglobulin (IVIg) and rituximab to help decrease antibody levels and get better results with transplants. Plasmapheresis reduces the level of antibodies and when it is applied with IVIg, it greatly reduces the threat of rejection in sensitized patients (13). A study by Bray et al (2017) proved that using plasmapheresis and IVIg treatment lowered the chance of rejection by 25% in patients with high DSA scores (14). In addition, rituximab, a monoclonal antibody for CD20-positive B cells, is now commonly featured in desensitization treatment plans. It has helped to decrease anti-HLA antibodies, leading to better graft success (15). Desensitization regimens can also include induction immunosuppressive treatments such as alemtuzumab and anti-thymocyte globulin (ATG). Agents perform this way which leads to T cells being depleted and the graft being spared from rejection. Alemtuzumab induction therapy given to high-risk patients, including patients who are HLA-sensitized, reduces the chance of acute rejection and increases survival of the donated organ, states Gentry et al. Additionally, ATG treatment which lowers the number of T lymphocytes, has been proven to decrease the risk of rejection in patients who are sensitized (17). As these studies stated, our results show that using plasmapheresis and IVIg reduced the number of rejections in patients who were already sensitized to these proteins. The better graft survival seen here with these treatments is similar to what other studyers have observed in their studies (18).

**Conclusion:**

Kidney transplants are more likely to be rejected if the patient is HLA-sensitized. The survival of transplanted organs benefits from the use of tailored immunosuppressive therapies such as plasmapheresis, IVIg and induction agents. Managing patients who are sensitive to the transplant as soon as they are detected can help achieve better results and lower the risk of rejection.

**Limitations:**

Among the study's weaknesses are the use of past data and the differences in how immunosuppressants were used in various clinical trials. When reports have tiny samples and brief follow-up time, the results may not apply widely. More study involving a standardized design should be performed to confirm these findings.

**Future Findings:**

Further studies should aim to enhance the effectiveness of desensitization and discover innovative agents that balance the immune system. Long periods of observation are necessary to assess the survival of grafts in those who are sensitive to donor organs. Tailoring therapy to the antibodies found in each person may benefit results even more.

**Abbreviations**

1. **HLA**: Human Leukocyte Antigen
2. **DSA**: Donor-Specific Antibodies
3. **IVIg**: Intravenous Immunoglobulin
4. **ATG**: Anti-Thymocyte Globulin
5. **ESRD**: End-Stage Renal Disease

6. **SPSS**: Statistical Package for the Social Sciences

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## Authors Contribution

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Final Approval of version:**All Mention Authors Approved the Final Version.**

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