



# An Aggressive Management Strategies for Acute Kidney Transplant Rejection: An Indonesian Tertiary Center Experience

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<p><b>Track Record Article</b></p> <p>Revised: 27 January 2026 Accepted: 10 March 2026 Published: 31 March 2026</p> <p><b>How to cite:</b> Annas, Y., Utomo, T., &amp; Ghinorawa, T. (2026). An Aggressive Management Strategies for Acute Kidney Transplant Rejection: An Indonesian Tertiary Center Experience. <i>Contagion: Scientific Periodical Journal of Public Health and Coastal Health</i>, 8(1), 328–336.</p>	<p style="text-align: center;"><b>Abstract</b></p> <p><i>Acute kidney transplant rejection remains a major cause of early graft malfunction worldwide especially in low- and middle-income countries where diagnostic and treatment resources are limited. Global data indicate that 10–20% of recipients experience acute rejection within the first year, with higher rates reported in developing regions. This study examined the clinical attributes and outcomes of intensive therapy approaches for acute graft malfunction at Dr. Sardjito General Hospital in Yogyakarta, Indonesia. A retrospective case series included four adult kidney transplant recipients who developed acute graft malfunction within 30 days of transplantation (2024 - 2025), defined as a &gt;25% rise in serum creatinine and/or oliguria. Demographic data, Doppler ultrasound resistive index (RI), immunosuppressive therapy, therapeutic plasma exchange (TPE), and short-term outcomes were analyzed descriptively. The study comprised three males and one female (aged 23 – 54 years old). All patients showed elevated RI (&gt;0.75). TPE was performed in three cases (75%), resulting in two full recoveries, one partial recovery, and one persistent dysfunction due to combined immunological and surgical complications. Higher RI values were associated with more intensive treatment. These findings suggest that personalized aggressive therapies, such as TPE and intravenous immunoglobulin, may serve as viable salvage options for severe early graft malfunction. In resource-limited settings, Doppler ultrasound provides valuable non-invasive support when biopsy is unavailable. Larger multicenter studies are needed to confirm long-term efficacy and generalizability.</i></p> <p><b>Keywords:</b> <i>Kidney Transplantation, Acute Rejection, Therapeutic Plasma Exchange, Doppler Ultrasound, Immunosuppression.</i></p>
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## INTRODUCTION

Kidney transplantation is widely regarded as the most effective renal replacement therapy for end-stage renal failure, offering better survival and quality of life compared to dialysis. (Mudiayi et al., 2022). However, acute rejection remains a major cause of graft malfunction and long-term transplant failure worldwide (Cooper, 2020). In high-income countries, the incidence of biopsy-confirmed acute rejection has declined to approximately 10–15% in the first year, largely due to advancements in immunosuppressive therapy (Chandran & Mannon, 2022). In contrast, developing nations continue to report higher early rejection rates, often linked to delayed diagnosis, greater infection prevalence, and limited healthcare resources (Prabu et al., 2022).

Globally, antibody-mediated rejection and T cell-mediated rejection remain key immunological drivers to graft deterioration, each requiring distinct therapeutic strategies (Cornell, 2021; Tamargo & Kant, 2023). International guidelines identify biopsy confirmation

as the diagnostic gold standard (Stevens et al., 2024). However, in many low-resource settings, limited access to timely biopsies necessitates reliance on clinical assessment and imaging markers for diagnosis.

Doppler ultrasonography resistive index (RI) is widely used as a non-invasive marker of intrarenal vascular resistance and early transplant dysfunction. Although elevated RI values ( $>0.70$ – $0.75$ ) are not specific to rejection, they have been consistently associated with poor graft outcomes (Moein et al., 2023). In cases of severe or refractory rejection, particularly antibody-mediated rejection, therapeutic plasma exchange (TPE) and intravenous immunoglobulin are increasingly employed as adjunctive treatments (Alasfar et al., 2023; Alkan et al., 2020).

Indonesia, as a developing country with a high burden of infectious diseases and limited transplant facilities, faces distinct challenges in managing acute rejection (Mudiayi et al., 2022). Despite these difficulties, there is little local data on the use of aggressive management strategies. This study therefore aims to describe the clinical spectrum, Doppler ultrasound findings, and outcomes of intensive treatment for acute graft failure at a tertiary care center in Indonesia.

## **METHODS**

### **Study Design and Setting**

This retrospective case study was performed in the Kidney Transplantation Unit of Dr. Sardjito General Hospital, Yogyakarta, Indonesia, a tertiary referral facility. The trial duration spanned from January 2024 until December 2025.

### **Study Subjects and Sample Size**

Four adult kidney transplant recipients met the inclusion criteria and were incorporated into this study ( $n = 4$ ). Eligible patients were those who developed acute graft malfunction within 30 days of transplantation, defined as a  $> 25\%$  increase in serum creatinine from baseline and/or oliguria. Inclusion was limited to patients with comprehensive clinical, laboratory, and Doppler ultrasound data. Exclusion criteria included pediatric recipients ( $<18$  years), insufficient medical records, isolated surgical complications without immunological involvement, and patients lost to follow-up during the early postoperative period.

### **Data Collection and Variables**

Data collected included demographic attributes, main renal pathology, sequential laboratory metrics, tacrolimus trough concentrations, Doppler ultrasound resistance index values, modifications in immunosuppressive therapy, administration of high-dose

corticosteroids, basiliximab, intravenous immunoglobulin, and therapeutic plasma exchange. Short-term graft results during hospitalization were documented.

### **Ethical Approval**

The study was approved by the Institutional Review Board of Dr. Sardjito General Hospital–Faculty of Medicine, Universitas Gadjah Mada. Due to its retrospective design using anonymized data, informed consent was waived.

### **RESULTS**

Four kidney transplant recipients (three males, one female; aged 23 to 54 years) experienced acute graft malfunction within the initial 17 days following transplantation. All patients exhibited an elevated intrarenal resistance index ( $RI > 0.75$ ) on Doppler ultrasonography at presentation. Therapeutic Plasma Exchange (TPE) was conducted in three out of four instances (75%) as an element of a tailored salvage approach. Two patients exhibited enhancement in graft function, one shown partial recovery, and one encountered enduring graft failure despite intensive care.

#### **Case 1: Severe Acute Rejection with TPE and Nephrotic Syndrome Aftermath**

A 31-year-old male with type 1 diabetes initially received a successful kidney transplant. On the third day, his creatinine level escalated to 2.14 mg/dL. Doppler ultrasonography revealed renal tissue edema with a resistance score of 0.85. Foreseeing significant rejection, potentially attributable to antibodies, the researchers initiated an extensive therapy regimen: high-dose methylprednisolone for three days, followed by therapeutic plasma exchange on day four, intravenous immunoglobulin, and basiliximab injections. Subsequent to TPE, his tacrolimus levels significantly dropped, requiring immediate dosage adjustment. His renal function improved, as indicated by a decrease in creatinine levels to 1.15 mg/dL on the seventh day. On day 12, he exhibited significant edema in his scrotum. Tests revealed increased protein levels in his urine, indicating potential irreversible damage to the kidney's filtration system due to rejection.

#### **Case 2: Acute Vascular Crisis (RI 1.0) from Drug Toxicity**

A 54-year-old woman with hypertension demonstrated considerable diuresis promptly following surgery. On the initial day, her Tacrolimus level rose markedly to 38.3 ng/mL. During the second and third days, her urine output diminished, and her blood pressure elevated. A Doppler scan indicated a troubling finding: a RI of 1.0, signifying total cessation of blood flow during the cardiac relaxation phase as a result of substantial artery constriction. To

maintain renal function, she received salvage plasma exchange therapy on day 4 to eliminate surplus medicine and inflammation, in conjunction with steroid treatment. Subsequently, her urine output progressively resumed, and the Doppler resistance index diminished to 0.93 on day 9, therefore safeguarding the kidney graft.

### **Case 3: "Double Hit" of Sepsis and Rejection**

A 45-year-old guy exhibited a delayed initiation of graft function and necessitated dialysis following surgery. On day 6, he had signs of severe sepsis, indicated by increased infection markers, and symptoms of rejection (enlarged kidney, RI 0.86). Faced with the intricate problem of immunosuppression vs disease care, the team chose a balanced strategy: delivering a moderate dose of Methylprednisolone in conjunction with broad-spectrum antibiotics, while forgoing therapeutic plasma exchange (TPE). The sepsis cleared; however, his renal function did not fully recuperate throughout our surveillance.

### **Case 4: Tricky Diagnosis of Stubborn Rejection and Urine Leak**

A 23-year-old guy demonstrated inadequate graft function, shown by consistently elevated creatinine levels. He was initially diagnosed with acute rejection and underwent comprehensive treatment, including high-dose steroids, two sessions of therapeutic plasma exchange (TPE), intravenous immunoglobulin (IVIG), and basiliximab, but showed negligible improvement. A follow-up assessment on day 9 confirmed urinary incontinence. He underwent surgical reconstruction of the ureter. Despite improved drainage, his renal function and hemodynamic parameters (RI 0.82-0.85) remained abnormal. This signifies a convergence of problems: simultaneous damage to renal tissue and surgical complications.

In general, elevated RI values correlated with enhanced treatment intensity, especially the application of TPE, whereas clinical outcomes differed based on underlying etiology and the existence of concurrent comorbidities.

## **DISCUSSION**

This case series highlights the considerable challenges of managing early acute graft failure at a high-volume tertiary transplant center in Indonesia. The most notable finding was the frequent use of therapeutic plasma exchange (TPE), applied in 75% of cases. This pattern reflects an institutional tendency toward prompt, aggressive intervention in urgent clinical situations, rather than definitive evidence of treatment efficacy. Global studies identify TPE as a cornerstone in the management of antibody-mediated rejection, particularly in severe or refractory cases (Alasfar et al., 2023; Naesens et al., 2024). In practice, however, escalation of

therapy often requires individualization based on hemodynamic instability, vascular impairment, and resistance to corticosteroids (Pittappilly et al., 2025).

In Case 2, therapeutic plasma exchange (TPE) appeared to serve a dual role. Beyond its established function in antibody removal, TPE facilitated a rapid reduction in markedly elevated tacrolimus levels, consistent with principles of therapeutic monitoring and toxicity management in the early post-transplant phase (Naesens et al., 2024; Shabunin et al., 2023). An RI of 1.0 indicated severe intrarenal vascular resistance and potential transplant ischemia. A subsequent decline in RI following intervention suggested partial restoration of microvascular perfusion, despite persistence abnormal Doppler findings. Although a causal relationship cannot be confirmed, these observations align with prior studies reporting hemodynamic improvement after intensive treatment of severe rejection or drug-induced vasoconstriction (Alkan et al., 2020; Naik et al., 2025).

Case 3 exemplifies the intricate equilibrium between rejection care and infection control, a vital concern in regions with a significant prevalence of infectious illnesses. Global guidelines emphasize the necessity for prompt high-dose corticosteroid therapy in cases of acute rejection (Stevens et al., 2024). However, excessive immunosuppression in the presence of severe sepsis may increase mortality risk (Naik et al., 2025). The calculated application of medium-dose steroids alongside broad-spectrum antibiotics illustrates a planned adjustment to local epidemiological circumstances. Contextual decision-making is gaining recognition in transplant practices globally, especially in low- and middle-income nations where infectious complications are prevalent (Clayton et al., 2019; Mudiayi et al., 2022).

Case 4 highlights the significance of iterative diagnostic reevaluation. Ongoing graft malfunction despite intensive immunosuppression necessitated an assessment for surgical consequences, which ultimately identified ureteral leaking. Contemporary transplant pathology literature extensively documents the mixed etiologies of graft malfunction, including rejection, acute tubular necrosis, and mechanical problems (Cornell, 2021; Naesens et al., 2024). The persistence of high RI values post-surgical correction reinforces the notion that Doppler ultrasound identifies global intrarenal hemodynamic disturbances but lacks specificity in differentiating between immunological and non-immunological etiologies (Moein et al., 2023).

In every instance, the RI value surpassed 0.75 at presentation, highlighting the significance of Doppler ultrasound as an early, non-invasive method for evaluating graft failure. Biopsy is the conclusive standard for diagnosis Mudiayi et al., (2022), access may be impeded in resource-limited environments. In many circumstances, imaging biomarkers facilitate early risk assessment and prompt response (Moein et al., 2023; Mudiayi et al., 2022).

Nonetheless, RI must be interpreted with caution, as it indicates intrarenal vascular resistance rather than particular histological damage.

This research highlights the significance of systematic pharmacological monitoring. Timely detection of suprathreshold tacrolimus concentrations indicates compliance with contemporary immunosuppressive optimization strategies aimed at minimizing nephrotoxicity while preserving graft viability (Naesens et al., 2024; Shabunin et al., 2023). Innovative therapeutic strategies, like as antibody-targeted therapies and personalized immunosuppressive modulation, are continually transforming contemporary rejection therapy (Chandran & Mannon, 2022; Connolly et al., 2025).

Numerous constraints must be recognized. The retrospective case study methodology and absence of a control group impede causal inferences on the efficacy of TPE or alternative therapy. Secondly, the absence of histologic confirmation in certain instances may restrict diagnostic precision. The little follow-up period constrains the evaluation of long-term graft survival, which is considerably influenced by the occurrence of early rejection (Zhang, 2018). The limited sample size ( $n = 4$ ) and single-center design restrict external validity. Consequently, our results should be regarded as descriptive and hypothesis-generating, necessitating larger multicenter investigations to elucidate the role of aggressive personalized methods in comparable resource-limited settings.

## CONCLUSIONS

The management of acute rejection at Dr. Sardjito General Hospital illustrates that a systematic, assertive, and personalized multimodal strategy, which includes therapeutic plasma exchange and intravenous immunoglobulin, can be safely executed and effectively aid in graft preservation in specific severe cases within this institution. Doppler ultrasonography with resistive index assessment is a useful and dependable diagnostic instrument for facilitating prompt clinical decision-making.

These findings must be considered within the context of many limitations, including the single-center design, limited sample size, and lack of a comparison control group, which restrict external validity and hinder application to other centers or healthcare systems. Thus, the findings predominantly represent local practices and institutional experiences rather than outcomes indicative of developing countries in their entirety. Additional multicenter studies with bigger cohorts are necessary to confirm these findings and to more accurately delineate the applicability of this technique across various resource environments.

## REFERENCES

- Alasfar, S., Kodali, L., & Schinstock, C. A. (2023). Current Therapies in Kidney Transplant Rejection. *Journal of Clinical Medicine*, 12(15), 4927. <https://doi.org/10.3390/jcm12154927>
- Alkan, F. T., Tatar, E., Karatas, M., Simsek, C., Tercan, I. C., Aykas, A., & Uslu, A. (2020). Response to treatment in kidney transplant recipients with acute antibody-mediated rejection: A follow-up biopsy study. *Clinical Nephrology*, 93(2), 85–90. <https://doi.org/10.5414/CN109819>
- Anesi, J. (2022). Commentary: Effectiveness of two-dose vaccination with mRNA COVID-19 vaccines against COVID-19-associated hospitalizations among immunocompromised adults—nine states, January–September 2021. *American Journal of Transplantation*, 22(1), 304–305. <https://doi.org/10.1111/ajt.16910>
- Chandran, S., & Mannon, R. B. (2022). T cell-mediated rejection in kidney transplant recipients: The end(point) is also the beginning. *American Journal of Transplantation*, 22(3), 683–684. <https://doi.org/10.1111/ajt.16964>
- Clayton, P. A., McDonald, S. P., Russ, G. R., & Chadban, S. J. (2019). Long-Term Outcomes after Acute Rejection in Kidney Transplant Recipients: An ANZDATA Analysis. *Journal of the American Society of Nephrology*, 30(9), 1697. <https://doi.org/10.1681/ASN.2018111101>
- Coemans, M., Süsal, C., Döhler, B., Anglicheau, D., Giral, M., Bestard, O., Legendre, C., Emonds, M.-P., Kuypers, D., Molenberghs, G., Verbeke, G., & Naesens, M. (2018). Analyses of the short- and long-term graft survival after kidney transplantation in Europe between 1986 and 2015. *Kidney International*, 94(5), 964–973. <https://doi.org/10.1016/j.kint.2018.05.018>
- Connolly, H., Watson, A., Wynd, M., Lieberman, K., Chaung, M., Goldstein, M. J., Hidalgo, G., Batal, I., Amoroso, M., & Jain, N. G. (2025). Daratumumab for Treatment of Acute Antibody-Mediated Rejection in a Pediatric Kidney Transplant Recipient. *Pediatric Transplantation*, 29(5), e70116. <https://doi.org/10.1111/petr.70116>
- Cooper, J. E. (2020). Evaluation and Treatment of Acute Rejection in Kidney Allografts. *Clinical Journal of the American Society of Nephrology: CJASN*, 15(3), 430–438. <https://doi.org/10.2215/CJN.11991019>
- Cornell, L. D. (2021). Histopathologic Features of Antibody Mediated Rejection: The Banff Classification and Beyond. *Frontiers in Immunology*, 12. <https://doi.org/10.3389/fimmu.2021.718122>
- Doganci, M., Izdes, S., Cirik, M. O., Doganci, M., Izdes, S., & Cirik, M. O. (2023). The Evaluation of Risk Factors for Vancomycin-Resistant Enterococcus Colonization and Infection Among Mixed Adult Intensive Care Unit Patients. *Cureus*, 15(1). <https://doi.org/10.7759/cureus.33210>
- Hariharan, S., Israni, A. K., & Danovitch, G. (2021). Long-Term Survival after Kidney Transplantation. *New England Journal of Medicine*, 385(8), 729–743. <https://doi.org/10.1056/NEJMra2014530>
- Khudari, R. A., Doba, D., Esmandar, A., & Kheder, M. (2024). Treatment outcome at the pediatric stem cell transplantation center in Syria: A single-center experience. *Pediatric Transplantation*, 28(5), e14789. <https://doi.org/10.1111/petr.14789>
- Koshy, P., Furian, L., Nickerson, P., Zaza, G., Haller, M., de Vries, A. P. J., & Naesens, M. (2024). European Survey on Clinical Practice of Detecting and Treating T-Cell Mediated Kidney Transplant Rejection. *Transplant International: Official Journal of the European Society for Organ Transplantation*, 37, 12283. <https://doi.org/10.3389/ti.2024.12283>

- Leung, K. C., Ng, W. W. S., Ciofani, J., & Kwok, W. (2025). Survival of kidney transplantation in people living with HIV/AIDS: A systematic review and meta-analysis. *BMC Infectious Diseases*, 25(1), 1160. <https://doi.org/10.1186/s12879-025-11480-7>
- Marbun, M. B. H., Susalit, E., Susilowati, U., & Andina, T. (2022). Long-term outcomes and prognostic factors in kidney transplant recipients in Jakarta, Indonesia: A cohort study. *BMJ Open*, 12(5), e059631. <https://doi.org/10.1136/bmjopen-2021-059631>
- Moein, M., Papa, S., Ortiz, N., Saidi, R., Moein, M., Papa, S., Ortiz, N., & Saidi, R. (2023). Protocol Biopsy After Kidney Transplant: Clinical Application and Efficacy to Detect Allograft Rejection. *Cureus*, 15(2). <https://doi.org/10.7759/cureus.34505>
- Mudiayi, D., Shojai, S., Okpechi, I., Christie, E. A., Wen, K., Kamaleldin, M., Elsadig Osman, M., Lunney, M., Prasad, B., Osman, M. A., Ye, F., Khan, M., Htay, H., Caskey, F., Jindal, K. K., Klarenback, S., Jha, V., Rondeau, E., Turan Kazancioglu, R., ... Bello, A. K. (2022). Global Estimates of Capacity for Kidney Transplantation in World Countries and Regions. *Transplantation*, 106(6), 1113–1122. <https://doi.org/10.1097/TP.0000000000003943>
- Naesens, M., Kuypers, D. R. J., & Sarwal, M. (2009). Calcineurin inhibitor nephrotoxicity. *Clinical Journal of the American Society of Nephrology: CJASN*, 4(2), 481–508. <https://doi.org/10.2215/CJN.04800908>
- Naesens, M., Roufousse, C., Haas, M., Lefaucheur, C., Mannon, R. B., Adam, B. A., Aubert, O., Böhmig, G. A., Callemeyn, J., Groningen, M. C., Cornell, L. D., Demetris, A. J., Drachenberg, C. B., Einecke, G., Fogo, A. B., Gibson, I. W., Halloran, P., Hidalgo, L. G., Horsfield, C., ... Mengel, M. (2024). The Banff 2022 Kidney Meeting Report: Reappraisal of microvascular inflammation and the role of biopsy-based transcript diagnostics. *American Journal of Transplantation*, 24(3), 338–349. <https://doi.org/10.1016/j.ajt.2023.10.016>
- Naik, R. H., Hassanein, M., & Shawar, S. H. (2025). Acute Renal Transplantation Rejection. In *StatPearls*. StatPearls Publishing. <http://www.ncbi.nlm.nih.gov/books/NBK553074/>
- Pittappilly, M., Sharshir, M., & Paramesh, A. (2025). Chronic Allograft Nephropathy—A Narrative Review of Its Pathogenesis, Diagnosis, and Evolving Management Strategies. *Biomedicine*, 13(4), 929. <https://doi.org/10.3390/biomedicine13040929>
- Prabu, O. G., Hustrini, N. M., Marbun, M. B. H., Septianto, T., Indriani, A., Septiar, D., Lydia, A., Nugroho, P., & Susalit, E. (2022). Acute rejection associated with short-term and long-term survival in kidney transplantation: A single center study in Indonesia. *Korean Journal of Transplantation*, 36(1), 200–200. <https://doi.org/10.4285/ATW2022.F-3342>
- Shabunin, A. V., Drozdov, P. A., Makeev, D. A., Nesterenko, I. V., Zhuravel, O. S., Karapetyan, L. R., Astapovich, S. A., & Lidzhieva, E. A. (2023). Personalized dosing protocol for extended-release tacrolimus in kidney transplant recipients in the early postoperative period. *Russian Journal of Transplantology and Artificial Organs*, 25(1), 52–61. <https://doi.org/10.15825/1995-1191-2023-1-52-61>
- Stevens, P. E., Ahmed, S. B., Carrero, J. J., Foster, B., Francis, A., Hall, R. K., Herrington, W. G., Hill, G., Inker, L. A., Kazancıoğlu, R., Lamb, E., Lin, P., Madero, M., McIntyre, N., Morrow, K., Roberts, G., Sabanayagam, D., Schaeffner, E., Shlipak, M., ... Levin, A. (2024). KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney International*, 105(4), S117–S314. <https://doi.org/10.1016/j.kint.2023.10.018>
- Surdi, L. M., Dagher, M., Merhej, T., Choi, J., & Azzi, J. R. (2025). Antibody-Mediated Rejection in Kidney Transplantation: Immunopathogenesis, Innate–Adaptive Crosstalk, and Therapeutic Advances. *OBM Transplantation*, 9(3), 1–44. <https://doi.org/10.21926/obm.transplant.2503258>
- Tamargo, C. L., & Kant, S. (2023). Pathophysiology of Rejection in Kidney Transplantation. *Journal of Clinical Medicine*, 12(12), 4130. <https://doi.org/10.3390/jcm12124130>

- Yeow, M., Soh, S., Wong, J., Tan, E., & Ganpathi Iyer, S. (2022). Gender Diversity in Transplantation Leadership Positions in Transplantation Journals and Organizations. *Transplantation*, 106(7), e352. <https://doi.org/10.1097/TP.0000000000004123>
- Zhang, R. (2018). Donor-Specific Antibodies in Kidney Transplant Recipients. *Clinical Journal of the American Society of Nephrology: CJASN*, 13(1), 182–192. <https://doi.org/10.2215/CJN.00700117>