

# INCIDENCE AND MANAGEMENT OF RECURRENT FSGS IN POST RENAL TRANSPLANT PATIENTS IN SOUTH ASIAN POPULATION: A SINGLE CENTER EXPERIENCE IN A RESOURCE LIMITED COUNTRY

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## ABSTRACT

**Objective:** To determine the frequency of recurrent focal segmental glomerulosclerosis after renal transplantation, identify associated factors, and compare graft-related outcomes across recorded management strategies.

**Materials and Methods:** This retrospective, record-based observational study was conducted at the Pakistan Kidney and Liver Institute, Lahore. We reviewed records of recipients transplanted between 22 November 2024 and 31 October 2025 under an Institutional Review Board exemption. We included 100 recipients aged 18 to 60 years with biopsy-proven primary focal segmental glomerulosclerosis, using consecutive sampling. Recurrence was defined by allograft biopsy. Recorded management approaches were plasmapheresis plus rituximab plus renin-angiotensin-aldosterone system blockade, plasmapheresis plus renin-angiotensin-aldosterone system blockade, and renin-angiotensin-aldosterone system blockade alone.

**Results:** Recurrent focal segmental glomerulosclerosis was identified in 27/100 recipients (27.0%). The median time from transplantation to recurrence was 42 days. Proteinuria was present in all 27 recurrent cases (100.0%). Hematuria was documented in 3/27 cases (11.1%), and dialysis was required in 7/27 cases (25.9%). Mean recent serum creatinine was  $5.07 \pm 2.38$  mg/dL, and mean urinary protein-to-creatinine ratio was  $7.57 \pm 2.63$  mg/mg. Living-related donor transplantation was more frequent in the recurrent group than in the non-recurrent group (24/27, 88.9% versus 47/73, 64.4%;  $p=0.039$ ). No statistically significant differences were observed across management groups for creatinine, urinary protein-to-creatinine ratio, dialysis requirement, graft dysfunction, or graft loss.

**Conclusion:** Recurrent focal segmental glomerulosclerosis occurred early in more than one-quarter of this cohort. Outcome comparisons across management approaches were descriptive and showed no statistically significant differences.

**Keywords:** Allograft dysfunction; Focal segmental glomerulosclerosis; Kidney transplantation; Proteinuria; Recurrence

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## INTRODUCTION

Focal segmental glomerulosclerosis (FSGS) is an important glomerular disease that can progress to end-stage renal disease (ESRD). Kidney transplantation is the preferred treatment for many patients with ESRD. However, primary FSGS can recur after renal transplantation and may lead to proteinuria, graft dysfunction, and graft loss. <sup>1</sup>

The burden of ESRD in Pakistan is difficult to esti-

mate accurately because national renal registries are limited. Many patients present late, and the original cause of kidney failure is often not confirmed by biopsy. These problems are more important in resource-limited settings, where delayed diagnosis and limited follow-up can affect transplant outcomes. <sup>2</sup>

Post-transplant recurrence of FSGS has been reported at variable rates across populations. A recent meta-analysis found a pooled recurrence rate of 38% after kidney transplantation. Younger age at transplantation, younger age at disease onset, rapid progression to kidney failure, and higher pre-transplant proteinuria were associated with recurrence, whereas human leukocyte antigen (HLA) mismatches were not consistently associated with recurrence. <sup>3</sup>

Early recurrence is clinically important because it may occur soon after transplantation and can present with

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heavy proteinuria. A recent study also found that pre-transplant plasmapheresis was associated with a lower rate of immediate postoperative recurrence in patients with biopsy-proven primary FSGS.<sup>4</sup> These findings suggest that timely risk assessment may help plan surveillance and management after renal transplantation.

Management of recurrent FSGS remains challenging. Plasma exchange, rituximab, and supportive antiproteinuric therapy are commonly used, but responses are variable. A recent review reported that plasma exchange and rituximab are the main treatment options, but strong evidence from large randomized trials is still lacking.<sup>5</sup> A recent systematic review also found that adding rituximab to plasma exchange did not confer a clear additional benefit in all patients.<sup>6</sup>

The scientific gap is more pronounced in South Asian and resource-limited settings. Published local data on biopsy-proven recurrent FSGS after renal transplantation are scarce. Treatment decisions are also influenced by cost, availability of plasmapheresis, access to rituximab, biopsy facilities, and the regularity of follow-up. A recent transplant outcome study found that recurrent FSGS has worse graft survival than de novo FSGS, underscoring the need for more center-based outcome data.<sup>7</sup>

The working hypothesis of the present study was that recurrent FSGS is a clinically significant cause of graft morbidity after renal transplantation and that renal outcomes may vary by treatment strategy. This single-center study aims to determine the frequency of recurrent FSGS after renal transplantation, identify factors associated with recurrence, and compare renal outcomes across treatment strategies.

## MATERIALS AND METHODS

This retrospective, record-based observational study was conducted at the Department of Nephrology, Pakistan Kidney and Liver Institute and Research Center, Lahore, Pakistan. An Institutional Review Board exemption was obtained from the Pakistan Kidney and Liver Institute and Research Center, Lahore, under reference number PKLI-IRB/AP/00492024, dated 18 November 2024. Data extraction was performed after the exemption was granted and within the approved exemption period. The investigators conducted no prospective patient enrollment, follow-up, or intervention.

The hospital records screened for this study included renal transplant recipients who underwent transplantation between 22 November 2024 and 31 October 2025. Eligible records were selected consecutively.

The study included recipients aged 18 to 60 years, of either gender, with biopsy-proven primary FSGS as the cause of renal failure before transplantation. We excluded recipients with renal failure due to causes other than

FSGS. We included patients without recurrence in the non-recurrent group only if post-transplant follow-up information was available in the medical record.

We estimated the sample size using the single-population-proportion formula. The expected frequency of recurrent FSGS was set at 21%, based on the recurrence rate reported by Kwon et al. among kidney transplant recipients with primary FSGS. At a 95% confidence level and 8% absolute precision, the required sample size was 99.58. Therefore, 100 recipients were included.

We collected data from patient files and the hospital's electronic medical record system using a structured pro forma. The recorded variables included demographic characteristics, body mass index (BMI), transplant date, pre-transplant dialysis status, donor relationship, transplant type, HLA mismatches, pre-transplant plasmapheresis, serum creatinine, urinary protein-to-creatinine ratio (UPCR), hematuria, proteinuria, recurrence status, biopsy findings, management approach, dialysis requirement, graft dysfunction, graft loss, follow-up regularity, and medication non-adherence.

Recurrent FSGS was defined as biopsy-proven recurrence in the renal allograft after transplantation. Protocol biopsies were not performed in all transplant recipients. We performed allograft biopsies in recipients with clinical suspicion of recurrence, primarily new-onset or worsening post-transplant proteinuria with or without graft dysfunction. We classified only patients with biopsy findings consistent with recurrent FSGS as having recurrence. We calculated the recurrence proportion as the number of biopsy-proven recurrent cases divided by the total number of eligible recipients with primary FSGS.

For recurrent cases, we reviewed post-transplant records to document the time from transplantation to recurrence, clinical presentation, management approach, and graft-related outcomes. Graft-related outcomes included serum creatinine at follow-up, UPCR, dialysis requirement, graft dysfunction, and graft loss. Recorded management approaches included plasmapheresis plus rituximab plus renin-angiotensin-aldosterone system (RAAS) blockade, plasmapheresis plus RAAS blockade, and RAAS blockade alone. Treatment assignment was not randomized.

The treating nephrology team selected management based on routine clinical practice, disease severity, clinical condition, treatment availability, and patient-related factors. Therefore, treatment comparisons were descriptive and were not intended to establish causal superiority of one approach over another. The primary objective was to determine the frequency of recurrent FSGS after renal transplantation and to compare graft-related outcomes across recorded management approaches. The secondary objectives were to identify factors associated with

recurrence and to describe the post-transplant course of recurrent cases.

All data were entered and analyzed using IBM SPSS version 27. Quantitative variables were summarized as mean  $\pm$  standard deviation (SD) or as median with interquartile range (IQR), as appropriate. Categorical variables were presented as frequencies and percentages. Continuous variables were compared using the independent-samples t-test or one-way analysis of variance, as appropriate. Categorical variables were compared using the chi-square test or Fisher's exact test, as appropriate. A p-value of 0.05 or less was considered statistically significant.

## RESULTS

Baseline recipient and transplant characteristics were compared by recurrence status. Age, gender, BMI, pre-transplant dialysis status, HLA mismatches, and pre-transplant plasmapheresis were comparable between patients with and without recurrence.

Transplant type differed significantly between the groups. Living-related donor transplantation was more common in the recurrent group, whereas living-unrelated donor transplantation was more common in the non-recurrent group, as shown in Table 1.

Values are presented as mean  $\pm$  SD or n (%). Percentages were calculated within each column. FSGS: focal segmental glomerulosclerosis; BMI: body mass index; HLA: human leukocyte antigen; SD: standard deviation. Among 27 patients with biopsy-proven recurrent focal segmental glomerulosclerosis, the median time from transplantation to recurrence was 42 days.

Proteinuria was present in all recurrent cases, and all had biopsy findings consistent with recurrent focal segmental glomerulosclerosis. Hematuria was documented in 3/27 patients (11.1%), and dialysis was required in 7/27 patients (25.9%). The most frequently recorded management approach was plasmapheresis plus rituximab plus RAAS blockade, followed by RAAS blockade alone and plasmapheresis plus RAAS blockade, as shown in Table 2.

Values are presented as mean  $\pm$  SD, median (IQR), or n (%). Percentages were calculated using 27 recurrent cases as the denominator. FSGS: focal segmental glomerulosclerosis; IQR: interquartile range; SD: standard deviation; UPCR: urinary protein-to-creatinine ratio.

Graft-related outcomes across the recorded management approaches are presented descriptively. Recent serum creatinine and UPCR were numerically highest in the plasmapheresis plus rituximab plus RAAS blockade group, but the differences across groups were not statistically significant.

Dialysis requirement, graft dysfunction, and graft loss were observed across the three management groups, with no statistically significant differences. These comparisons should be interpreted cautiously because treatment was not randomized, subgroup sizes were small, and management was based on routine clinical practice rather than study allocation, as shown in Table 3.

Values are presented as mean  $\pm$  SD or n (%). Percentages were calculated within each management group. Comparisons are descriptive because treatment allocation was not randomized and subgroup sizes were small. SD: standard deviation; UPCR: urinary protein-to-creatinine ratio.

**Table No 1: Baseline recipient and transplant characteristics according to recurrence status (n=100)**

| Characteristic                         | Overall (n=100) | Recurrent FSGS (n=27) | No recurrence (n=73) |
|----------------------------------------|-----------------|-----------------------|----------------------|
| Age, years, mean $\pm$ SD              | 33.6 $\pm$ 7.8  | 33.0 $\pm$ 7.6        | 33.8 $\pm$ 7.9       |
| Gender, n (%)                          |                 |                       |                      |
| Male                                   | 80 (80.0%)      | 20 (74.1%)            | 60 (82.2%)           |
| Female                                 | 20 (20.0%)      | 7 (25.9%)             | 13 (17.8%)           |
| BMI, kg/m <sup>2</sup> , mean $\pm$ SD | 24.2 $\pm$ 3.7  | 23.6 $\pm$ 4.1        | 24.4 $\pm$ 3.6       |
| Pre-transplant status, n (%)           |                 |                       |                      |
| Dialysis dependent                     | 82 (82.0%)      | 22 (81.5%)            | 60 (82.2%)           |
| Pre-emptive                            | 18 (18.0%)      | 5 (18.5%)             | 13 (17.8%)           |
| Transplant type, n (%)                 |                 |                       |                      |
| Living related donor                   | 71 (71.0%)      | 24 (88.9%)            | 47 (64.4%)           |
| Living unrelated donor                 | 19 (19.0%)      | 1 (3.7%)              | 18 (24.7%)           |
| Deceased donor                         | 10 (10.0%)      | 2 (7.4%)              | 8 (11.0%)            |
| HLA mismatches, mean $\pm$ SD          | 3.3 $\pm$ 1.5   | 3.3 $\pm$ 1.4         | 3.3 $\pm$ 1.5        |
| Pre-transplant plasmapheresis, n (%)   |                 |                       |                      |
| Yes                                    | 19 (19.0%)      | 4 (14.8%)             | 15 (20.5%)           |
| No                                     | 81 (81.0%)      | 23 (85.2%)            | 58 (79.5%)           |

Values are presented as mean  $\pm$  SD or n (%). Percentages were calculated within each column. FSGS: focal segmental glomerulosclerosis; BMI: body mass index; HLA: human leukocyte antigen; SD: standard deviation.

**Table No 2: Clinical profile and management distribution of recurrent focal segmental glomerulosclerosis episodes (n=27)**

| Variable                                                                            | Recurrent cases (n=27) |
|-------------------------------------------------------------------------------------|------------------------|
| Time to recurrence                                                                  |                        |
| Time from transplant to recurrence, days, median (IQR)                              | 42 (30–67)             |
| Renal function and proteinuria                                                      |                        |
| Nadir serum creatinine, mg/dL, mean $\pm$ SD                                        | 1.16 $\pm$ 0.24        |
| Recent serum creatinine, mg/dL, mean $\pm$ SD                                       | 5.07 $\pm$ 2.38        |
| Urinary protein-to-creatinine ratio, mg/mg, mean $\pm$ SD                           | 7.57 $\pm$ 2.63        |
| Clinical and biopsy findings                                                        |                        |
| Proteinuria, n (%)                                                                  | 27 (100.0%)            |
| Hematuria, n (%)                                                                    | 3 (11.1%)              |
| Biopsy findings consistent with recurrent focal segmental glomerulosclerosis, n (%) | 27 (100.0%)            |
| Required dialysis after recurrence, n (%)                                           | 7 (25.9%)              |
| Recorded management approach                                                        |                        |
| Plasmapheresis + rituximab + RAAS blockade, n (%)                                   | 14 (51.9%)             |
| Plasmapheresis + RAAS blockade, n (%)                                               | 3 (11.1%)              |
| RAAS blockade alone, n (%)                                                          | 10 (37.0%)             |

Values are presented as mean  $\pm$  SD, median (IQR), or n (%). Percentages were calculated using 27 recurrent cases as the denominator. FSGS: focal segmental glomerulosclerosis; IQR: interquartile range; SD: standard deviation; UPCR: urinary protein-to-creatinine ratio.

**Table No 3: Descriptive comparison of graft-related outcomes according to recorded management approach among recurrent cases (n=27)**

| Outcome                                       | Plasmapheresis + rituximab + RAAS blockade (n=14) | Plasmapheresis + RAAS blockade (n=3) | RAAS blockade alone (n=10) | p-value |
|-----------------------------------------------|---------------------------------------------------|--------------------------------------|----------------------------|---------|
| Recent serum creatinine, mg/dL, mean $\pm$ SD | 5.98 $\pm$ 2.25                                   | 4.97 $\pm$ 1.62                      | 3.83 $\pm$ 2.36            | 0.107   |
| UPCR, mg/mg, mean $\pm$ SD                    | 8.11 $\pm$ 2.51                                   | 6.91 $\pm$ 3.82                      | 7.00 $\pm$ 2.60            | 0.620   |
| Required dialysis, n (%)                      | 3 (21.4%)                                         | 1 (33.3%)                            | 3 (30.0%)                  | 0.852   |
| Graft dysfunction, n (%)                      | 6 (42.9%)                                         | 1 (33.3%)                            | 4 (40.0%)                  | 0.953   |
| Graft loss, n (%)                             | 2 (14.3%)                                         | 1 (33.3%)                            | 1 (10.0%)                  | 0.606   |

Values are presented as mean  $\pm$  SD or n (%). Percentages were calculated within each management group. Comparisons are descriptive because treatment allocation was not randomized and subgroup sizes were small. SD: standard deviation; UPCR: urinary protein-to-creatinine ratio.

## DISCUSSION

Recurrent FSGS was observed in 27.0% of renal transplant recipients in this single-center cohort. Recurrence occurred early, with a median time of 42 days after transplantation, and proteinuria was present in all recurrent cases. This pattern is consistent with the recognized clinical behavior of recurrent FSGS, which often appears soon after transplantation and may present with heavy proteinuria. The observed recurrence proportion was lower than the 38% pooled rate reported in an adult meta-analysis, but it remained within the broad range reported in published studies.<sup>3</sup> A systematic review in children with steroid-resistant nephrotic syndrome also showed that post-transplant recurrence remains common, especially in non-genetic disease.<sup>8</sup> Recent reviews suggest that early recurrence may be linked to circulating permeability factors, which supports the early post-transplant presentation observed in this cohort.<sup>9</sup> Most baseline recipient and transplant characteristics were not significantly associated with recurrence. Age, sex, BMI, HLA mis-

matches, pre-transplant dialysis status, and pre-transplant plasmapheresis were comparable between patients with and without recurrence. Transplant type was the only variable that differed significantly between the groups, with living-related donor transplantation more frequent in the recurrent group. This association should be interpreted cautiously. A recent pediatric meta-analysis did not identify living-related donation as a consistent risk factor for recurrence.<sup>10</sup> Other studies suggest that disease phenotype, initial steroid response, serum albumin, and selected immunological factors may also influence recurrence risk.<sup>11, 12</sup> These findings indicate that recurrence likely involves multiple clinical and biological factors rather than donor relationship alone.<sup>13</sup>

Outcome comparisons across management approaches were descriptive in this study. The recorded approaches included plasmapheresis plus rituximab plus RAAS blockade, plasmapheresis plus RAAS blockade, and RAAS blockade alone. No statistically significant dif-

ferences were observed across these groups in recent serum creatinine, UPCR, dialysis requirement, graft dysfunction, or graft loss. These findings should not be interpreted as evidence of equal efficacy among treatments. Treatment was not randomized, subgroup sizes were small, and patients with more severe disease may have been more likely to receive intensive therapy.

Published evidence also supports a cautious interpretation of treatment outcomes. Plasmapheresis with adjustment of immunosuppression may induce remission in selected recurrent cases.<sup>14</sup> Long-term apheresis may help some patients who remain dependent on extracorporeal therapy.<sup>15</sup> Early plasmapheresis followed by rituximab has also been associated with favorable outcomes in selected pediatric cohorts.<sup>16</sup> However, treatment response is variable, and targeted therapy such as abatacept appears relevant only in selected subgroups.<sup>17</sup> These data explain why treatment comparisons in small observational cohorts should remain descriptive rather than causal.

Local data on biopsy-proven recurrent FSGS after renal transplantation remain scarce in Pakistan. A recent study from a developing-country setting highlighted guarded renal outcomes in primary glomerular disease and the impact of resource limitations on renal care.<sup>18</sup> Regionally, a Korean study reported recurrent FSGS in 26.3% of patients with primary FSGS and found poorer graft survival in recurrent disease than in de novo disease.<sup>7</sup> Registry data from Australia and New Zealand also showed that FSGS is associated with a higher risk of disease recurrence and allograft loss after transplantation.<sup>19</sup> The present study adds single-center data from Pakistan and describes the early recurrence pattern, management approaches, and graft-related outcomes of biopsy-proven recurrent FSGS in a resource-limited transplant setting.

This study has some limitations. It was a retrospective record-based observational study conducted at a single center, so the findings may not be generalizable to all transplant centers. The number of patients with recurrent FSGS was small, and the management subgroups were also small, which may have limited the precision of outcome comparisons.<sup>20</sup> Treatment was not randomized and was selected according to routine clinical practice. Therefore, comparisons among management approaches may have been affected by confounding by indication, as patients with more severe disease may have been more likely to receive intensive therapy.<sup>21</sup> These findings should be interpreted as descriptive rather than causal.

## CONCLUSION

Recurrent focal segmental glomerulosclerosis was observed in more than one-quarter of this cohort and typically occurred early after renal transplantation. The three recorded management approaches did not differ significantly in graft-related outcomes. These findings are descriptive and should be interpreted in light of the retrospective design, single-center setting, small recurrent group, and non-randomized treatment assignment.

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#### Authors Contribution:

Following authors have made substantial contributions to the manuscript as under

| Authors   | Conceived & designed the analysis | Collected the data | Contributed data or analysis tools | Performed the analysis | Wrote the paper | Other contribution |
|-----------|-----------------------------------|--------------------|------------------------------------|------------------------|-----------------|--------------------|
| Imran U   | ✓                                 | ✓                  | ✓                                  | ✓                      | ✓               | ✓                  |
| Manzoor A | ✓                                 | ✗                  | ✓                                  | ✓                      | ✓               | ✗                  |
| Sarwar A  | ✓                                 | ✓                  | ✗                                  | ✗                      | ✗               | ✓                  |
| Zahra M   | ✓                                 | ✗                  | ✓                                  | ✓                      | ✓               | ✗                  |
| Fatima Z  | ✓                                 | ✗                  | ✓                                  | ✓                      | ✓               | ✗                  |
| Baig S    | ✓                                 | ✓                  | ✗                                  | ✗                      | ✗               | ✓                  |

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

#### Ethical Approval:

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