

ORIGINAL ARTICLE

Short term treatment outcomes of primary focal segmental glomerulosclerosis: A single center experience from a tertiary care hospital of South Punjab, Pakistan.

Raheel Khan¹, Javaria Karamat², Syed Saad Gardezi³, Qazi Masroor Ali⁴, Suhail Iqbal Malik⁵, Urwah Rasool⁶, Junaid Sarwar⁷

ABSTRACT... Objective: To determine the short-term treatment outcomes of biopsy-proven focal segmental glomerulosclerosis (FSGS). **Study Design:** Retrospective, Cohort study. **Setting:** Department of Nephrology, Kidney Center, Bahawal Victoria Hospital, Bahawalpur, Pakistan. **Period:** January 2019 to June 2025. **Methods:** A total of 66 patients with biopsy-proven FSGS, aged 12–60 years, with a minimum follow-up duration of 6 months were analyzed. Information was extracted from registry and hospital records. Baseline demographic, clinical, laboratory and treatment related information were recorded. At six months, outcomes were measured by proteinuria and serum creatinine changes. Statistical analysis was done using SPSS v26, with chi-square, or Fisher's exact test and statistical significance at $p < 0.05$. **Results:** In a total of 66 patients, the median age was 22.0 years (IQR 16.0–33.5), and 34 (51.5%) were male. Steroid monotherapy was used in 46 (69.7%), and steroids with cyclosporine in 10 (15.2%) patients. At six months, 44 (66.7%) achieved complete proteinuria remission, 12 (18.2%) partial, 8 (12.1%) had persistent, and 2 (3.0%) had massive proteinuria. Renal function remained normal in 58 (87.9%), improved in 4 (6.1%), and worsened in 4 (6.1%) patients. Proteinuria remission correlated with gender ($p = 0.006$) and baseline renal dysfunction ($p = 0.019$). Treatment modality was significantly associated with post-treatment renal dysfunction ($p < 0.001$). No mortality was reported during the study period. **Conclusion:** Short-term analysis of biopsy-proven FSGS demonstrated that two-thirds of patients achieved complete remission of proteinuria and the majority maintained stable renal function after six months of therapy.

Key words: Focal Segmental Glomerulosclerosis, Mortality, Proteinuria, Serum Albumin, Serum Creatinine.

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INTRODUCTION

Focal segmental glomerulosclerosis (FSGS) is a histopathologic lesion marked by focal and segmental sclerosis, and represents a common cause of the nephrotic syndrome and progressive glomerular disease worldwide.¹ Large epidemiological data describes the incidence of FSGS ranging between 1.4-21 cases per million population per year.² FSGS pathogenesis is centered on podocyte injury, decline in filtration barrier integrity, and progressive scarring, which may be triggered by genetic, adaptive, viral, or idiopathic mechanisms.³ Clinically, FSGS frequently manifests with heavy proteinuria (50-60% adults), hypoalbuminemia, edema, and variable degrees of renal dysfunction.⁴ Despite decades of study, much remains uncertain about the short-term course of FSGS, particularly in resource-constrained settings. A systematic review of immunosuppressive therapy

in primary FSGS noted significant proteinuria reductions but emphasized uncertainties regarding effects on long-term kidney survival.⁵

In Pakistan and the South Asian region, data about FSGS outcomes remain scarce. A Pakistani cohort from a single center reported clinicopathologic features and medium-term outcomes of FSGS variants, but did not focus on very early treatment responses.⁶ Among children in Pakistan, one study found that 54.8% achieved complete remission, 17.7% partial remission, while 8.9% progressed to end-stage kidney disease.⁷ Another retrospective adult FSGS cohort in Karachi ($n = 401$) found that about 24.4% had renal insufficiency at presentation and, in that subgroup, complete remission was achieved in about 24.6% and partial remission in 11.1%.⁸

1. MBBS, FCPS (Medicine), Assistant Professor Medicine, Quaid e Azam Medical College, Bahawalpur, Pakistan.

2. MBBS, FCPS (Nephrology), Assistant Professor Nephrology, Quaid e Azam Medical College, Bahawalpur, Pakistan.

3. MBBS, FCPS (Histopathology), Assistant Professor Pathology, Quaid e Azam Medical College, Bahawalpur, Pakistan.

4. MBBS, FCPS (Medicine), MCPS-HPE, Medical Specialist Medicine, Aleena Hospital, Bahawalpur, Pakistan.

5. MBBS, FCPS (Medicine), FCPS (Nephrology), Associate Professor Nephrology, Nishtar Medical University, Multan, Pakistan.

6. MBBS, Postgraduate Resident Nephrology, Quaid-e-Azam Medical College, Bahawalpur, Pakistan.

7. MBBS, Postgraduate Resident Nephrology, Quaid-e-Azam Medical College, Bahawalpur, Pakistan.

Correspondence Address:

Dr. Raheel Khan
Department of Medicine, Quaid e Azam Medical College, Bahawalpur, Pakistan.
x_raheel@yahoo.com

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Evaluating short-term outcomes of FSGS remains valuable as early remission of proteinuria or improvement in renal function often portends better long-term prognosis.⁹ In Pakistan's context, socioeconomic, health system, and adherence factors may influence early treatment response differently than in Western cohorts. Therefore, in this study, the short-term outcomes among biopsy-proven FSGS patients with particular attention to associations of demographic, clinical and therapeutic factors were explored. This analysis may provide insight into local prognostic factors and guide early therapeutic decision making in our patient population. The aim of this study was to determine the short-term treatment outcomes of biopsy-proven FSGS.

METHODS

This retrospective cohort was carried out in the Nephrology Department at the Kidney Center, Bahawal Victoria Hospital, Bahawalpur, Pakistan. The study period spanned from January 2019 through June 2025. Ethical clearance was obtained from the Institutional Review Board of Bahawal Victoria Hospital (letter number: 466/DME/QAMC Bahawalpur, dated: 26-09-2018), and the study adhered to the Declaration of Helsinki. Sample size was determined by total case availability. As this was a single-centre retrospective cohort of biopsy-proven FSGS with mandatory 6-month follow-up, all consecutive eligible patients from January 2019 to June 2025 were included. After record screening, 66 cases met inclusion criteria and formed the final sample. Inclusion criteria were renal biopsy confirmed FSGS patients of any gender, and aged 12-60 years. Only those who had continued follow-up and completed at least six months of treatment were eligible. Exclusion criteria included patients with incomplete record, or those with secondary FSGS causes (e.g., obesity-associated glomerulopathy, reflux nephropathy, HIV infection, illicit drug exposure, or use of established nephrotoxins), and patients with concomitant systemic diseases including diabetes mellitus, systemic lupus erythematosus, amyloidosis, or other glomerular diseases.

All patient information was de-identified prior to analysis, confidentiality ensured. Retrospective

data were obtained from renal biopsy reports, hospital medical records, and the departmental nephrology registry on a standardized data extraction form for completeness and uniformity. Baseline demographic parameters consisted of age, gender, and domicile, and clinical information included symptom duration before diagnosis and pertinent laboratory parameters. Laboratory data obtained at the moment of diagnosis were 24-hour proteinuria or spot urine protein-to-creatinine ratio (uPCR), albumin level, and creatinine. Estimated glomerular filtration rate (eGFR) was determined by the CKD-EPI formula, and renal impairment at baseline was a cut-off value of eGFR < 60 mL/min/1.73 m².¹¹ Information on treatment regimens such as corticosteroid monotherapy or combination immune-suppressive regimens with drugs like cyclosporine, tacrolimus, mycophenolate mofetil, cyclophosphamide, or supportive care with ACE inhibitors/ARBs, were systematically documented. At the follow-up at six months, response to treatment was assessed in terms of decrease in proteinuria and alteration in serum creatinine, which indicates improvement or worsening in renal function. The response to treatment was subsequently compared with baseline demographic and clinical variables to elucidate potential prognostic correlations. Quality of data was confirmed by double verification of extracted records by two independent reviewers to reduce errors of transcription and ensure dataset reliability.

All collected data were entered and analyzed in IBM-SPSS Statistics, version 26.0. Continuous variables such as age, symptom duration, albumin, proteinuria, and creatinine were assessed for normality using the Shapiro–Wilk test, and summarized as mean ± standard deviation (SD) or median with interquartile range (IQR), depending on distribution. Categorical variables like gender, baseline renal dysfunction, and remission categories were expressed as counts and percentages. Associations between baseline categorical or dichotomous predictors and 6-month outcomes were evaluated using chi-square or Fisher's exact test as appropriate. A two-tailed p-value < 0.05 was considered statistically significant.

RESULTS

A total of 66 patients with biopsy-proven FSGS were included in the study. The median age of the cohort was 22.0 years (IQR: 16.0–33.5), with an age range of 12 to 48 years. There were 34 (51.5%) males and 32 (48.5%) females. The age distribution showed that 28 (42.4%) patients were between 12 and 18 years, 28 (42.4%) were aged >18 to 40 years, and 10 (15.2%) were aged >40 to 60 years. The duration of symptoms prior to diagnosis was ≤6 months in 46 (69.7%) patients and >6 months in 20 (30.3%). At presentation, proteinuria ≥3.5 g/day was recorded in 52 (78.8%) patients, while 12 (21.2%) had sub-nephrotic proteinuria <3.5 g/day. Baseline serum albumin <2.0 g/dL was noted in 48 (72.7%), 14 (21.2%) had levels between 2.0 and 3.5 g/dL, and 4 (6.1%) had levels >3.5 g/dL. Renal dysfunction at diagnosis, defined as eGFR <60 mL/min/1.73 m², was identified in 20 (30.3%), whereas 46 (69.7%) had preserved renal function (Table-I).

TABLE-I

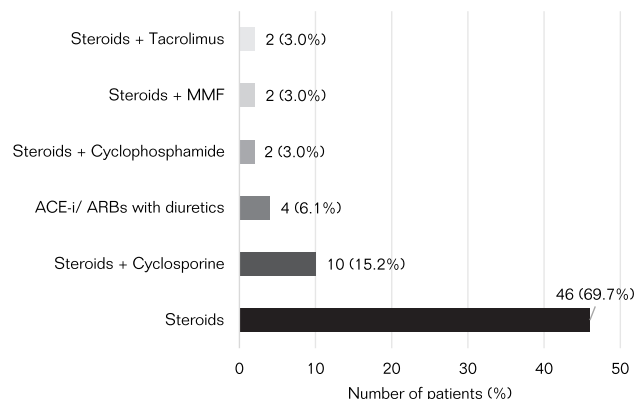
Baseline characteristics of focal segmental glomerulosclerosis patients (N=66)

Characteristics		Frequency (%)
Gender	Male	34 (51.5%)
	Female	32 (48.5%)
Age (years)	12-18	28 (42.4%)
	>18 to 40	28 (42.4%)
	>40-60	10 (15.2%)
Duration of symptoms (months)	≤6 months	46 (69.7%)
	>6 months	20 (30.3%)
Proteinuria at diagnosis	<3.5	12 (21.2%)
	≥3.5	52 (78.8%)
	<2.0	48 (72.7%)
Serum albumin (g/dl)	2.0-3.5	14 (21.2%)
	>3.5	4 (6.1%)
	Yes	20 (30.3%)
Renal dysfunction	No	46 (69.7%)

A total of 46 (69.7%) patients were treated with corticosteroids alone, while 10 (15.2%) received a combination of steroids and cyclosporine. Figure-1 is showing details about the distribution of treatment regimens in FSGS patients.

FIGURE-1

Distribution of treatment regimens among patients with focal segmental glomerulosclerosis (N=60)



ACE-i: Angiotensin-Converting Enzyme Inhibitors; ARBs: Angiotensin II Receptor Blockers; MMF: Mycophenolate Mofetil

At the 6-month follow-up, treatment response was evaluated based on proteinuria evaluation. No proteinuria was observed in 44 (66.7%) patients, <3.5 g/day in 12 (18.2%), persistent nephrotic-range proteinuria (3.5–10 g/day) in 8 (12.1%), and massive proteinuria (>10 g/day) in 2 (3.0%) patients. No mortality was reported during the study period. Gender showed a statistically significant association with respect to post-treatment proteinuria evaluation ($p=0.006$), where no proteinuria occurred in 28 (63.6%) males, and 16 (36.4%) females, while higher residual proteinuria levels were more frequent among females. The age distribution did not demonstrate a statistically significant association with proteinuria response ($p=0.340$), although no proteinuria occurred in 20 (45.5%) patients aged 12–18 years, 16 (36.4%) aged >18–40 years, and 8 (18.2%) aged >40–60 years. Duration of symptoms did not seem to significantly influence treatment response ($p=0.424$). Baseline proteinuria ($p=0.283$), and serum albumin ($p=0.293$) were not significantly associated with post-treatment proteinuria evaluation. Renal dysfunction at diagnosis demonstrated a significant association with proteinuria response ($p=0.019$) as post-treatment no proteinuria was achieved in 16 (36.4%) patients with baseline renal dysfunction, and 28 (63.6%) without renal dysfunction. When stratified by treatment regimen, no significant association between post-treatment proteinuria and treatment

regimen were noted ($p=0.205$), and the details are shown in TABLE-II.

Assessment of renal function response at six months showed that 58 (87.9%) patients had serum creatinine <1.1 mg/dL, 4 (6.1%) had serum creatinine >1.1 mg/dL but improved from baseline, and 4 (6.1%) exhibited worsening of renal function based upon serum creatinine evaluation. Age showed a significant association ($p=0.024$) with post-treatment serum creatinine evaluation as all 4 (100%) patients with worsening post-treatment serum creatinine were aged >18 –40 years, whereas all patients with normal renal function were aged 12–18 years. Baseline proteinuria demonstrated a significant association with post-treatment serum creatinine response ($p<0.001$), as all 4 (100%) patients who improved despite elevated baseline creatinine had proteinuria <3.5 g/day, while all 4 (100%) with worsening renal function had proteinuria ≥ 3.5 g/day. Baseline serum albumin showed a significant relationship with post-treatment serum creatinine evaluation ($p=0.001$) as patients with baseline albumin <2.0 g/dL had higher rates of renal deterioration compared with those with higher albumin levels. Baseline renal dysfunction was significantly associated with treatment-related renal outcomes ($p<0.001$) as none of the patients with normal renal function at diagnosis demonstrated post-treatment serum creatinine worsening. Treatment modality was significantly associated with post-treatment renal dysfunction ($p<0.001$) as patients treated with ACE inhibitors or ARBs with diuretics showed improvement in 2 (50.0%), steroid therapy alone maintained renal stability in 42 (72.4%), while regimens including steroids plus MMF were associated with deterioration in 2 (50.0%), and those receiving steroids with cyclosporine, cyclophosphamide, or tacrolimus had stable serum creatinine levels (Table-III).

DISCUSSION

The present study investigated the short-term treatment outcomes of biopsy-proven FSGS at a tertiary nephrology center in South Punjab, Pakistan. Treatment response was evaluated after six months, focusing on remission of proteinuria and renal function improvement. At six months, 66.7% achieved complete remission of proteinuria, 18.2%

had partial remission, and 15.1% showed persistent nephrotic-range or massive proteinuria. Renal function was stable or better in 93.9% of patients, and 6.1% had deterioration. Jafry et al.⁸, working at the Sindh Institute of Urology and Transplantation reported complete remission in 24.6% and partial remission in 11.1% of adults with diminished renal function, totaling 35.7% response following steroid therapy. Contrarily, this study showed a greater combined rate of remission of 84.9% that could be due to variations in baseline renal function, severity of disease, and shorter follow-up period restricted to six months. Safdar et al.⁷, documented complete remission in 54.8% and partial remission in 17.7% of children with primary FSGS. The observed remission rate here was higher to some extent, probably due to earlier detection of the disease, enrollment of both adults and adolescents, and compliance with organized corticosteroid-based regimens.

The gender and treatment response association were significant ($p=0.006$), with 63.6% males showing complete remission versus 36.4% females. Gipson et al.¹¹, in a US and Canada multicenter analysis, identified male patients as having a more benign short-term course, possibly secondary to variation in pharmacogenomic response to corticosteroids and cyclosporine. Jafry et al.⁸, noted a predominance of males in the FSGS population without a gender-specific difference in response reported.

No statistically significant correlation between remission of proteinuria and age was observed ($p=0.340$). Conversely, Turkish data indicated that FSGS in younger children showed improved steroid responsiveness and later development of chronic kidney disease.¹² The failure to find association in this study may be accounted for by a wider age range and the dominance of adolescents and young adults that might present with variable chronicity of the disease and variability of response to steroids. Chan et al.¹³, observed older age to be linked with increased chronicity indices and interstitial fibrosis, parameters that confine reversibility of proteinuria.

These observations indicate age not to have a significant effect on early remission rates in populations with early clinical presentation and little chronic alteration.

TABLE-II

Association between baseline characteristics, treatment regimen, and treatment response based on proteinuria evaluation at six months among patients with focal segmental glomerulosclerosis (N=60)

Characteristics No Proteinuria (n=44)		Treatment Response (Proteinuria)			P-Value	
		<3.5 g/dl (n=12)	3.5-10.0 g/dl (n=8)	>10.0 g/dl (n=2)		
Gender	Male	28 (63.6%)	2 (16.7%)	2 (25.0%)	2 (100%)	0.006
	Female	16 (36.4%)	10 (83.3%)	6 (75.0%)	-	
Age (years)	12-18	20 (45.5%)	6 (50.0%)	2 (25.0%)	-	0.340
	>18 to 40	16 (36.4%)	6 (50.0%)	4 (50.0%)	2 (100%)	
	>40-60	8 (18.2%)	-	2 (25.0%)	-	
Duration of symptoms (months)	≤6 months	28 (63.6%)	10 (83.3%)	6 (75.0%)	2 (100%)	0.424
	>6 months	16 (36.4%)	2 (16.7%)	2 (25.0%)	-	
Proteinuria at diagnosis	<3.5	10 (22.7%)	4 (33.3%)	-	-	0.283
	≥3.5	34 (77.3%)	8 (66.7%)	8 (100%)	2 (100%)	
Serum albumin (g/dl)	<2.0	30 (68.2%)	10 (83.3%)	6 (75.0%)	2 (100%)	0.293
	2.0-3.5	12 (27.3%)	-	2 (25.0%)	-	
	>3.5	2 (4.5%)	2 (16.7%)	-	-	
Renal dysfunction	Yes	16 (36.4%)	2 (16.7%)	-	2 (100%)	0.019
	No	28 (63.6%)	10 (83.3%)	8 (100%)	-	
Treatment	ACE-i/ ARBs with diuretics	4 (9.1%)	-	-	-	0.205
	Steroids	30 (68.2%)	6 (50.0%)	8 (100%)	2 (100%)	
	Steroids + Cyclophosphamide	2 (4.5%)	-	-	-	
	Steroids + Cyclosporine	6 (13.6%)	4 (33.3%)	-	-	
	Steroids + MMF	-	2 (16.7%)	-	-	
	Steroids + Tacrolimus	2 (4.5%)	-	-	-	

ACE-i: Angiotensin-Converting Enzyme Inhibitors; ARBs: Angiotensin II Receptor Blockers; MMF: Mycophenolate Mofetil

Symptoms duration prior to diagnosis had no significant correlation with response to treatment ($p=0.424$). On the other hand, it has been reported by Kitajima et al.¹⁴, that patients with longer symptomatic periods prior to treatment had lower remission rates as a result of delayed therapeutic intervention and irreversible histologic damage. The shorter symptomatic period in the present study in two-thirds of patients may have contributed towards increased remission rates, indicating the significance of early diagnosis and treatment.

Baseline proteinuria ($p=0.283$), and levels of serum albumin ($p=0.293$) were not significantly correlated with 6-month remission. These results

differ from those of Stamellou et al., in the German Chronic Kidney Disease (GCKD) cohort, where increased urinary albumin-to-creatinine ratio was an independent predictor of progression of kidney disease and composite kidney events.¹⁵ The discrepancy might be because of the short follow-up period of this study, recording early response to treatment as opposed to prolonged renal loss.

More patients with nephrotic-range proteinuria at baseline received corticosteroids, which could have resulted in faster recovery of albumin and masking of early trends in prognosis.¹⁶ Kidney impairment at diagnosis was associated with post-treatment outcomes of proteinuria ($p=0.019$).

TABLE-III

Association between baseline characteristics, treatment regimens, and treatment response based on renal function (serum creatinine) at six months among patients with focal segmental glomerulosclerosis (N=66)

Characteristics <1.1 mg/dl (n=58)	Treatment response (serum creatinine)			P-value	
	>1.1 but improved with treatment (n=4)	Worsening serum creatinine (n=4)			
Gender	Male	28 (48.3%)	4 (100%)	2 (50.0%)	
	Female	30 (51.7%)	-	2 (50.0%)	
Age (years)	12-18	28 (48.3%)	-	-	0.024
	>18 to 40	22 (37.9%)	2 (50.0%)	4 (100%)	
	>40-60	8 (13.8%)	2 (50.0%)	-	
Duration of symptoms (months)	≤6 months	38 (65.5%)	4 (100%)	4 (100%)	0.138
	>6 months	20 (34.5%)	-	-	
Proteinuria at diagnosis	<3.5	10 (17.2%)	4 (100%)	-	<0.001
	≥3.5	48 (82.8%)	-	4 (100%)	
Serum albumin (g/ dl)	<2.0	44 (75.9%)	-	4 (100%)	0.001
	2.0-3.5	12 (20.7%)	2 (50.0%)	-	
	>3.5	2 (3.4%)	2 (50.0%)	-	
Renal dysfunction	Yes	12 (20.7%)	4 (100%)	4 (100%)	<0.001
	No	46 (79.3%)	-	-	
Treatment	ACE-i/ ARBs with diuretics	2 (3.4%)	2 (50.0%)	-	<0.001
	Steroids	42 (72.4%)	2 (50.0%)	2 (50.0%)	
	Steroids + Cyclophosphamide	2 (3.4%)	-	-	
	Steroids + Cyclosporine	10 (17.2%)	-	-	
	Steroids + MMF	-	-	2 (50.0%)	
	Steroids + Tacrolimus	2 (3.4%)	-	-	

ACE-i: Angiotensin-Converting Enzyme Inhibitors; ARBs: Angiotensin II Receptor Blockers; MMF: Mycophenolate Mofetil

Patients with intact renal function attained improved remission rates, in agreement with Jafry et al.,⁸ who showed that baseline eGFR was a strong predictor of steroid responsiveness ($p=0.006$). Likewise, Stamellou et al.¹⁵, noted that elevated baseline eGFR was protective against kidney failure and severe cardiovascular events in FSGS. The current results reaffirm that early disease and intact renal function increase the probability of proteinuria remission, highlighting the prognostic significance of timely diagnosis.^{6,17}

Renal function evaluation at six months showed that 87.9% had serum creatinine levels less than

1.1 mg/dL, 6.1% improved, and 6.1% worsened renal function. Baseline renal dysfunction strongly correlated with follow-up creatinine results ($p<0.001$). This trend follows that of the GCKD study, in which lower eGFR at baseline was an indicator of worse kidney outcomes.¹⁵ The protective effect of early preservation of the kidneys highlights that treatments implemented before extensive nephron loss have the potential to alter the course of the disease.¹⁸

Age was significantly correlated with post-treatment renal function ($p=0.024$). All worsening creatinine patients were 18–40 years old, suggesting that

adults can have quicker progression once renal impairment has occurred. Yadav et al.¹⁹, reported similar observations in an Indian population, where adult FSGS patients with nephrotic syndrome had variable response to steroids but increased risk of early progression in comparison to children. This highlights the fact that disease pattern could vary between pediatric and adult patients, most probably because of histologic heterogeneity and variance in immune modulation.

Treatment regimen had significant clinical implications. Patients treated with corticosteroids alone achieved stable renal function in 72.4% of cases and remission in 68.2%. Combination therapy with steroids and cyclosporine resulted in partial remission in 33.3%, while regimens containing MMF were associated with renal deterioration in half of the treated patients. Sozeri et al., reported that cytotoxic therapy or calcineurin inhibitors along with steroids enhanced long-term renal preservation.¹² Safdar et al.⁷, also noted increased rates of remission with calcineurin inhibitors over steroids alone in children with primary FSGS. Variability between studies can reflect differences in histologic subtype, compliance with treatment, and socioeconomic limitations on drug choice in local clinical practice. By contrast, Canaud et al.²⁰, illustrated significantly higher remission rates of almost 90% in adult transplant recipients who received aggressive plasma exchange and cyclosporine, emphasizing that remission can be induced rapidly by intense immunomodulation in severe disease. These interventions are still limited in developing countries, which could be the reason for the use of standard steroid-based regimens in this study.

The clinical significance of these results is significant. Early remission of proteinuria and stabilization of renal function continue to be the strongest predictors of long-term renal survival in FSGS.^{21,22} The high remission rate in this study points out the efficacy of corticosteroid treatment as the cornerstone of management when initiated early.^{23,24} The correlation between maintained baseline renal function and successful outcome supports the imperative of early detection programs and periodic monitoring of high-risk patients. In view of the heterogeneity in response between adults and younger patients,

treatment plans individualized according to age, renal status, and baseline biochemical parameters must be incorporated into clinical algorithms.²⁵

There are known limitations. Retrospective design has potentially caused information bias, as data were subject to completeness and accuracy of medical records. Single-center setting, and moderate sample size constrained external generalizability. The six-month follow-up period made evaluation of late relapse rates, histologic transformation, or renal survival impossible. Quantitative data on adherence, genetic markers, or FSGS subvariants were lacking, which may have impacted response patterns. Multicenter prospective studies in the future with genetic profiling, uniform treatment protocols, and longer follow-up beyond two years would yield stronger evidence on prognostic determinants and therapeutic optimization in FSGS.

CONCLUSION

Short-term analysis of biopsy-proven FSGS demonstrated that two-thirds of patients achieved complete remission of proteinuria and the majority maintained stable renal function after six months of therapy. Male gender and preserved renal function at baseline were associated with better outcomes. Timely diagnosis, close monitoring, and judicious use of immunosuppressive agents remain essential for improving renal outcomes in FSGS patients, particularly in low-resource healthcare settings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

1	Raheel Khan: Conception of idea, data collection, drafting.
2	Javaria Karamat: Critical revision.
3	Syed Saad Gardezi: Data collection.
4	Qazi Masroor Ali: Proof reading.
5	Suhail Iqbal Malik: Study design.
6	Urwah Rasool: Responsible for data's integrity.
7	Junaid Sarwar: Drafting.