Presenting Features and Short-Term Outcome According to Pathologic Variant in Childhood Primary Focal Segmental Glomerulosclerosis

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This was a retrospective analysis of children in one center who had primary (idiopathic) FSGS. There were 41 patients: 34.1% female, 65.9% male, 80.5% black, and 19.5% white. At presentation, the mean age was 10.9 ± 0.9 yr. The mean time of follow-up was 3.9 ± 0.5 yr. During the observation period, the systolic BP (SBP) and diastolic BP (DBP) remained stable, serum albumin rose slightly, and the GFR was stable. Among those who received corticosteroids at presentation, 21.2% were steroid sensitive. At last follow-up among all patients, 71% were in remission, 78% had stage 1 or 2 chronic kidney disease, and 4.9% had reached ESRD. At last follow-up, the GFR was significantly higher (P = 0.01) in patients who were initially steroid sensitive. Ethnicity had no effect on clinical data or response to therapy. The pathologic variants were as follows: Cellular, 32%; collapsing, 24%; and not otherwise specified (NOS), 44%. The chronicity scores were as follows: Cellular, 4.3; collapsing 6.4; and NOS, 4.0 (significantly higher, P = 0.02, in collapsing versus NOS). At presentation, SBP (P = 0.03) and DBP (P = 0.03) were significantly higher and GFR was lower (P = 0.03) in patients with the collapsing compared with NOS variant. Remission after the initial course of corticosteroids was less common with the collapsing variant. At last follow-up, SBP (P = 0.02) and DBP (P = 0.04) were significantly higher in patients with the collapsing versus NOS variant. It is concluded that the short-term outcome in pediatric primary FSGS is generally favorable, but a more guarded prognosis exists for patients with collapsing FSGS.


The term FSGS refers to a group of histologic entities that are characterized by the onset of proteinuria or nephrotic syndrome (NS). Patients with FSGS exhibit a variable degree of renal insufficiency depending on the stage of the disease and the cause (1). Primary (idiopathic) FSGS is defined by the absence of antecedent cause. Secondary FSGS, which is often clinically similar to primary FSGS, is seen mainly in adults and may be due to chronic hypertension, reflux nephropathy, HIV, morbid obesity, or heroin nephropathy (2,3). Although adults may develop either primary or secondary FSGS, the vast majority of pediatric FSGS is classified as primary FSGS (4–8).

Histologic variants of primary FSGS have been described in the past several years (9–13). However, there is some dispute regarding the predictive value of these variants. Schwartz et al. (12) demonstrated that the pathologic variant had no predictive value for long-term outcome. Similarly, the Southwest Pediatric Nephrology Study group (5) showed that the pathologic variant had no definitive predictive value for renal function. In contrast, recent studies showed that the type of histologic variant may have a significant impact on the clinical outcome. For example, the so-called tip lesion predicts a more benign course (14), whereas the collapsing variant may portend a more aggressive course (9).

Efforts have been directed to clarify the characteristics of the different variants and develop a hierarchy of classification. To this end, the Columbia classification of primary FSGS was recently defined and prioritized into a hierarchy of five distinct pathologic variants: (1) Collapsing, (2) tip lesion, (3) cellular, (4) hilar, and (5) not otherwise specified (NOS) (9,10). Clinical heterogeneity of FSGS may be explained, in part, by the presence of these pathologic variants (1,2,11–13).

Pediatric FSGS is a disease of increasing incidence and represents a major cause of chronic kidney disease (CKD) (6,7,15,16). One recent study in pediatric FSGS showed that there was no difference in renal survival on the basis of histologic variants, although the outcome of the patients in the study was significantly more favorable than in previous studies. Despite the valuable information provided in their study, there were some limitations. First, approximately 16% of their patients did not have the classical segmental scar that many consider to be essential for the diagnosis of FSGS. Second, the age of onset of disease (5 yr) in their study population was significantly younger than that in other studies of pediatric FSGS (13). Another recent pediatric study showed that the majority (72%) of children with FSGS had the NOS variant, and there were no clinical indicators that differentiated the variants (17).

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Systematic study of the clinicopathologic variants according to the Columbia classification, features at presentation, and the clinical course of each variant may improve our understanding of this disease and aid in tailoring therapies to improve the outcome. We assessed the presenting features and clinical course in all children in our center who met the histologic and clinical criteria of primary FSGS.

Materials and Methods

Patients

Inclusion Criteria. This was a retrospective study of patients who were aged 1 to 18 yr at diagnosis, presented to our institution from 1995 to 2004, and underwent renal biopsy for one or more of the following: (1) Fixed proteinuria, (2) unexplained hematuria, and (3) NS that was unresponsive to 1 mo of corticosteroid therapy. Inclusion criteria were histologic diagnosis of primary FSGS as defined by the Columbia FSGS classification system (9,10) and follow-up for at least 1 yr after biopsy.

Exclusion Criteria. Patients in whom complete data at presentation or last follow-up were not available, those who received previous dialysis or renal transplant, those whose renal biopsy contained inadequate sample (fewer than five glomeruli), and those with secondary FSGS (e.g., chronic hypertension, reflux nephropathy, HIV, morbid obesity, heroin nephropathy, unilateral renal agenesis or renal atrophy, or genetic disease with predisposition to FSGS) or other glomerular disease with sclerotic lesions were excluded.

Follow-Up Data

Data were collected on disease presentation on each outpatient visit. On each patient encounter, we obtained a history, vital signs, casual BP, urinalysis, and information regarding immunosuppression treatment. Serum electrolytes and albumin and random urine protein and creatinine were measured intermittently according to the clinical circumstance. GFR was calculated by the Schwartz formula. NS was defined as the extracellular accumulation or condensation of matrix that impinged on or obliterated capillary lumens. We used the Columbia classification system in which the following variants are described (9,10): (1) Cellular, (2) hiliar, (3) collapsing, (4) tip lesion, and (5) NOS.

Treatment of NS

Patients who presented with NS were treated according to ISKDC guidelines (4) with oral corticosteroids (60 mg/m² per d, up to a maximum of 80 mg/d), in either two or three divided doses for 1 mo, after which they were treated with oral corticosteroids (40 mg/m² every other day) for an additional month. All relapses of NS were treated with oral corticosteroids (60 mg/m² per d, up to a maximum of 80 mg/d, in either two or three divided doses) until the urinalysis dipstick was negative or trace for 3 consecutive days. Thereafter, they were treated with oral corticosteroids (40 mg/m² every other day) for an additional month.

Patients who were steroid resistant (SR) were treated with calcineurin inhibitors (CNI; tacrolimus or cyclosporine) according to the individual physician’s preference. Tacrolimus was started at a dosage of 0.1 mg/kg per d, with target trough level of 5 to 9 ng/dl, and titrated to achieve partial or complete remission of NS. Cyclosporine was started at a dosage of 4 mg/kg per d, with the target trough level of 150 to 250 ng/dl, and titrated to achieve partial or complete remission of NS.

Patients who presented with proteinuria but without NS were treated with an angiotensin-converting enzyme inhibitor (ACEI), angiotensin-receptor blocker (ARB), or a combination of these agents. A majority of patients who were treated with either corticosteroids or CNI were simultaneously treated with ACEI and/or ARB.

Assessment of BP

Casual BP was measured by oscillometry on validated devices. Use of proper size cuff on the right arm and in a calm atmosphere in the presence of a nurse was performed in our clinic. All patients were instructed to reduce salt intake. BP was defined according to the Fourth Report of Blood Pressure in Children (18). BP percentiles were determined by STAT-Growth BP (Austin Physician Productivity LLC, Austin, TX), which uses CDC Growth Charts and National High Blood Pressure Education Program (NHBPEP) BP tables.

Kidney Biopsy Methods

Kidney biopsy specimens were evaluated by (1) light microscopy on B-5-fixed, paraffin-embedded tissue using hematoxylin and eosin, Jones, periodic acid Schiff, and Masson trichrome staining; 2.5% glutaraldehyde fixed tissue; embedded with Spur (EMS, Hatfield PA); and stained with toluidine blue and epoxy tissue stain (EMS); (2) immunofluorescence microscopy on frozen tissue using fluoresceinated antibodies to IgG, IgA, IgM, C3, and C1q (Ventana, Tucson, AZ) and fibrin; and (3) transmission electron microscopy on tissue fixed in 2.5% glutaraldehyde and spurr-embedded. Patients with any of the structural expressions of FSGS were entered into the registry. Pathologic findings in the vascular, glomerular, and interstitial compartments, including arteriosclerosis, glomerular sclerosis, interstitial fibrosis, interstitial leukocyte infiltrate, and tubular injury or atrophy, were scored using a semiquantitative scale of 0 = normal, 1 = mild, 2 = moderate, 3 = moderately severe, and 4 = severe. A global chronicity score was calculated by the sum of the individual scores for arteriosclerosis, glomerular sclerosis, interstitial fibrosis, interstitial leukocyte infiltrate, and tubular atrophy with a maximum score of 16 (11). The renal biopsy materials were categorized according to the Columbia FSGS classification system (9,10) and retrospectively reviewed without the clinical data other than the previous diagnosis of FSGS by the study pathologist (RC).

Classification of FSGS

All variants had segmental consolidation of at least one glomerulus that was either predominantly sclerotic or cellular. Glomerular sclerosis was defined as the extracellular accumulation or condensation of matrix that impinged on or obliterated capillary lumens. We used the Columbia classification system in which the following variants are described (9,10): (1) Cellular, (2) hiliar, (3) collapsing, (4) tip lesion, and (5) NOS.

Statistical Analyses

Comparison between two groups was achieved by the t test. Correlation among more than two groups was achieved by ANOVA with Bonferroni post hoc test. Correlation between groups was determined by linear regression analysis.

Results

General Demographics

Forty-one patients were included in the study; 14 (34.1%) were female, 27 (65.9%) were male, 33 (80.5%) were black, and eight (19.5%) were white. At presentation, the mean age was 10.9 ± 0.9 yr. The time of follow-up was 3.9 ± 0.5 yr (range 1 to 17 yr).
Clinical Features and Prescribed Therapy at Presentation

The most common initial presenting symptom was NS (63.4%). A minority (31.7%) of patients presented with fixed proteinuria, one (2.4%) patient with hematuria alone, and one (2.4%) with ESRD. The majority (67.6%) had blood on the initial urinalysis. A total of 80.4% received oral corticosteroids alone as initial therapy, one (2.4%) received high-dosage intravenous corticosteroids, 12.2% were treated with an ACEI alone, and one (2.4%) received a CNI alone.

Clinical Data at Presentation and Last Follow-up

At first presentation, approximately one half had elevated systolic BP (SBP), approximately one quarter had elevated diastolic BP (DBP), serum albumin (Alb) was low, and the GFR was slightly low. At the end of the observation period, the SBP and DBP remained stable, the serum albumin was significantly higher, and the GFR had declined slightly. The minority of patients achieved clinical remission after the initial treatment; however, the majority were in remission at last follow-up (Table 1). Among those who received corticosteroids, 21.2 achieved an initial remission with corticosteroid therapy.

Clinical Features and Therapy at Last Follow-Up

At last follow-up, 29.3% were receiving corticosteroids, 63.4% were receiving an ACEI and/or an ARB, 31.7% were being treated with a CNI, and two (4.9%) were receiving mycophenolate mofetil; 14.6% were not receiving any therapy. On last follow-up, 29 (70.7%) of 41 were in remission. At last observation, the distribution according to CKD stage (19) was as follows: Stage 1, 25 (60.9%) of 41; stage 2, seven (17.1%) of 41; stage 3, four (9.8%) of 41; stage 4, three (7.3%) of 41; stage 5, two (4.9%) of 41.

Outcome in Patients Observed for at Least 3 Yr

Among these patients, the mean follow-up period was 6.6 yr. In these patients, we observed no significant change in SBP (120.0 ± 3.5 [initial] versus 124.4 ± 4.1 [end] mmHg; P = 0.4), SBP percentile (87.7 ± 4.0 [initial] versus 83.6 ± 4.7 [end]; P = 0.5), DBP (69.2 ± 2.1 [initial] versus 73.3 ± 2.4 [end] mmHg; P = 0.2), or DBP percentile (80.1 ± 3.9 [initial] versus 75.7 ± 4.4 [end]; P = 0.5); a similar percentage of patients had SBP or DBP >95th percentile at presentation and last observation. GFR (114.3 ± 5.8 [initial] versus 106.0 ± 8.9 [end] ml/min per 1.73 m²; P = 0.5) was stable over the entire observation period. A higher percentage of patients achieved remission at the end of the study: 38.9% [initial] versus 55.6 [end].

Table 1. Clinical features and laboratory data at presentation and last follow-up

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Initial Presentation (n = 41)</th>
<th>Last Follow-Up (n = 41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>10.9 ± 0.9</td>
<td>14.8 ± 0.7</td>
<td>NA</td>
</tr>
<tr>
<td>SBP (mmHg; mean percentile)</td>
<td>122.9 ± 2.6 (85.2 ± 2.9)</td>
<td>126.0 ± 2.9 (85.2 ± 2.9)</td>
<td>0.4 (0.9)</td>
</tr>
<tr>
<td>Percentage SBP &gt;95th percentile</td>
<td>58.5</td>
<td>60.9</td>
<td>NA</td>
</tr>
<tr>
<td>DBP (mmHg; mean percentile)</td>
<td>72.5 ± 1.9 (78.1 ± 2.9)</td>
<td>75.9 ± 1.7 (78.6 ± 3.0)</td>
<td>0.2 (0.9)</td>
</tr>
<tr>
<td>Percentage DBP &gt;95th percentile</td>
<td>29.3</td>
<td>34.1</td>
<td>NA</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>2.5 ± 0.2</td>
<td>3.3 ± 0.2b</td>
<td>0.002</td>
</tr>
<tr>
<td>Random urine protein/creatinine (mg/mg)</td>
<td>NA</td>
<td>3.8 ± 1.1</td>
<td>NA</td>
</tr>
<tr>
<td>GFR (ml/min per 1.73 m²)</td>
<td>105.4 ± 4.6</td>
<td>92.2 ± 6.4</td>
<td>0.1</td>
</tr>
<tr>
<td>No. (%) who achieved clinical remission</td>
<td>24.2</td>
<td>70.7</td>
<td>NA</td>
</tr>
<tr>
<td>after initial treatment or at last follow-up</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Systolic BP (SBP), SBP percentile, diastolic BP (DBP), and DBP percentile were similar at both time points studied. An almost identical percentage of patients had SBP or DBP >95th percentile at both time points. The serum albumin was significantly higher at last follow-up, and the GFR remained stable during the observation period. A higher proportion of patients were in clinical remission at last follow-up compared with those who achieved remission after initial therapy. NA, not applicable.

bP < 0.05 versus initial presentation.
proteinuria, and 5.6% hematuria alone. The chronicity scores were similar in patients with the cellular (4.3) and NOS (4.0) variants but significantly ($P = 0.02$) higher in those with the collapsing (6.4) variant compared with the NOS variant.

As shown in Table 3, at presentation, the SBP and DBP were significantly higher in patients with the collapsing versus the NOS variant. The serum albumin was similar in all groups at presentation. The GFR was significantly lower at presentation in patients with the collapsing versus NOS variant, whereas that of patients with the cellular variant fell in between. Finally, a higher percentage of patients with the cellular or NOS variant achieved initial remission compared with those with the collapsing variant.

At last follow-up, the SBP, SBP percentile, DBP, and DBP percentile were significantly higher in patients with the collapsing versus NOS variant. The GFR trended lower in patients with the collapsing versus NOS variant, but this did not reach statistical significance.

When we assessed the GFR according to Kidney Disease Outcomes Quality Initiative (K/DOQI) CKD stage, we observed diverse distribution patterns among the three variant subtypes. At the end of the observation period, the majority of patients with either the cellular or the NOS variant had stage 1 (GFR >90 ml/min per 1.73 m²) CKD compared with only 36.4% of the patients with the collapsing variant (Table 4). A higher percentage of patients with the collapsing variant reached stages 3 to 5 CKD (46%) compared with the cellular (16.7%) or NOS (11.1%) variants. In addition, compared with the response to initial therapy, a higher percentage of patients with all variants were in remission at last observation. Finally, as shown in

### Table 2. Clinical features and laboratory data at presentation according to the response to corticosteroids: SS and SR

<table>
<thead>
<tr>
<th>Clinical Features</th>
<th>Initial Presentation</th>
<th>Last Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SS (n = 7; 21%)</td>
<td>SR (n = 26; 79%)</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>9.0 ± 2.1</td>
<td>10.4 ± 1.1</td>
</tr>
<tr>
<td>SBP (mmHg; mean percentile)</td>
<td>111.3 ± 4.4 (74.1 ± 7.3)</td>
<td>123.6 ± 3.0 (87.9 ± 3.6)</td>
</tr>
<tr>
<td>Percentage SBP &gt;95th percentile</td>
<td>28.6</td>
<td>68.0</td>
</tr>
<tr>
<td>DBP (mmHg; mean percentile)</td>
<td>67.3 ± 32.2 (77.9 ± 5.4)</td>
<td>73.5 ± 2.6 (78.2 ± 4.0)</td>
</tr>
<tr>
<td>Percentage DBP &gt;95th percentile</td>
<td>0.0</td>
<td>36.0</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>2.1 ± 0.4</td>
<td>2.3 ± 0.2</td>
</tr>
<tr>
<td>Urine protein/creatinine (mg/mg)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>% of patients in clinical remission after initial treatment or at last observation</td>
<td>122.4 ± 79</td>
<td>103.5 ± 5.1</td>
</tr>
<tr>
<td>GFR (ml/min per 1.73 m²)</td>
<td>107.6 ± 7.2</td>
<td>88.2 ± 10.7</td>
</tr>
<tr>
<td>No. (%) in clinical remission after initial treatment or at last observation</td>
<td>4/12 (33.3)</td>
<td>0/11 (0.0)</td>
</tr>
</tbody>
</table>

*All clinical features were statistically similar at presentation in patients depending on initial steroid sensitivity. SBP, SBP percentile, DBP, and DBP percentile were similar at last follow-up, but the serum albumin was significantly lower and GFR significantly higher in patients who were initially steroid sensitive (SS). ND, not done; SR, steroid resistant.

$p < 0.05$ versus initially SS.

### Table 3. Clinical features and laboratory data at presentation according to histology

<table>
<thead>
<tr>
<th>Clinical and Histologic Features</th>
<th>Initial Presentation</th>
<th>Last Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cellular (12/41; 29.3%)</td>
<td>Collapsing (11/41; 26.8%)</td>
</tr>
<tr>
<td>Chronicity score</td>
<td>4.3 ± 0.7</td>
<td>6.4 ± 0.6$^b$</td>
</tr>
<tr>
<td>SBP (mmHg; mean percentile)</td>
<td>121.5 ± 5.0</td>
<td>133.4 ± 4.4$^b$</td>
</tr>
<tr>
<td>DBP (mmHg; mean percentile)</td>
<td>75.1 ± 5.0</td>
<td>78.6 ± 2.8$^b$</td>
</tr>
<tr>
<td>Serum albumin (g/dl)</td>
<td>2.2 ± 0.3</td>
<td>2.5 ± 0.3</td>
</tr>
<tr>
<td>Random urine protein/creatinine (mg/mg)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>GFR (ml/min per 1.73 m²)</td>
<td>107.6 ± 7.2</td>
<td>88.2 ± 10.7$^b$</td>
</tr>
<tr>
<td>No. (%) in clinical remission after initial treatment or at last observation</td>
<td>4/12 (33.3)</td>
<td>0/11 (0.0)</td>
</tr>
</tbody>
</table>

*At presentation, ANOVA shows that the chronicity score was significantly higher in patients with collapsing versus either cellular or not otherwise specified (NOS) variant. SBP and DBP were significantly higher and GFR was lower in patients with the collapsing versus the NOS variant. A higher percentage of patients with the cellular or NOS variant achieved remission after initial therapy compared with those with the collapsing variant. At last observation, SBP, SBP percentile, DBP, and DBP percentile were significantly higher in patients with the collapsing versus the NOS variant. Compared with the response at presentation, a higher percentage of patients with each variant were in clinical remission at last follow-up.

$p < 0.05$ versus NOS.
Figure 1, the chronicity score correlated with GFR at presentation ($r = 0.36$, $P = 0.03$). GFR trended lower in patients with a higher chronicity score at last follow-up ($r = 0.26$, $P = 0.1$), but this did not reach statistical significance.

Clinical Data on Presentation and Last Follow-Up According to Ethnicity

The distribution of histologic variant was as follows: Cellular: black, nine (27.3%) of 33, white, three (37.5%) of eight; collapsing: black, 10 (30.3%) of 33, white, one (12.5%) of eight; NOS: black, 14 (42.2%) of 33, white, four (50.0%) of eight. In summary, the distribution among the variants was equal for black patients, whereas white patients tended to exhibit either the cellular or the NOS variant.

At presentation, BP and BP percentile were almost identical in the two groups. At last follow-up, BP and BP percentile trended higher in black patients, but the differences were not statistically significant. Serum albumin was the same in the two groups at both time points. The random urine protein/creatinine was twice as high in black compared with white patients at last observation, but this was not statistically significant. Finally, the GFR trended lower in black patients at both time periods, but these differences were not statistically significant.

In summary, ethnicity had no effect on the clinical data at first presentation and final observation (Table 5).

Discussion

FSGS is a disease that usually is characterized at onset by fixed proteinuria or NS. There has been a rising incidence of FSGS in children and adults in the past two decades (6,7,15,16,20,21). A major factor prompting the heightened interest in FSGS is the aggressive nature of the disease. Indeed, approximately 30 to 40% of adult patients who develop FSGS will experience significant renal insufficiency within the first decade after diagnosis (7), although there is evidence that the prognosis may be less ominous in childhood primary FSGS. For example, Abrantes et al. (13) showed that the probability of severe renal impairment in childhood FSGS is 8% at 5 yr, 17% at 10 yr, and 32% at 15 yr, which confirmed the data in another study of childhood FSGS (21). However, other studies in pediatric FSGS suggest a grimmer prognosis. Sorof et al. (8) showed high rates of significant renal dysfunction in pediatric FSGS, particularly in black patients.

There are five variants of FSGS: (1) Collapsing, (2) tip lesion, (3) cellular, (4) hilar, and (5) NOS (9,10). Two earlier studies showed that the glomerular variant was not a predictive factor for clinical outcome in adult FSGS (5,12). However, one recent study showed that the outcome for adults with the collapsing variant of FSGS is dismal (11).

Because of the controversy regarding the overall prognosis and impact of the histologic variant on renal survival, we studied the presenting features, short-term outcome, and impact of pathologic variant on outcome in childhood primary (idiopathic) FSGS. The most common presenting features among our patients were NS and fixed proteinuria. Our studies also show that the short-term outcome in pediatric primary FSGS is generally favorable, with more than three quarters showing no or mild change in GFR over several years. In a subgroup in which the mean follow-up period was almost 7 yr, the clinical features remained generally favorable during the entire observation period. These results are consistent with those of Abrantes et al. (13) and Paik et al. (17), who showed higher rates of renal survival in children with FSGS compared with previous studies in children and adults. The improved short-term outcome among the three recent pediatric studies is

<table>
<thead>
<tr>
<th>CKD Stage (GFR, in ml/min per 1.73 m^2)</th>
<th>Cellular 12/41 (29.3%)</th>
<th>Collapsing 11/41 (26.8%)</th>
<th>NOS 18/41 (43.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (&gt;90)</td>
<td>7/12 (58.3%)</td>
<td>4/11 (36.4%)</td>
<td>14/18 (77.8%)</td>
</tr>
<tr>
<td>2 (60 to 89)</td>
<td>3/12 (25.0%)</td>
<td>2/11 (18.2%)</td>
<td>2/18 (11.1%)</td>
</tr>
<tr>
<td>3 (30 to 59)</td>
<td>0/12 (0.0%)</td>
<td>2/11 (18.2%)</td>
<td>2/18 (11.1%)</td>
</tr>
<tr>
<td>4 (15 to 29)</td>
<td>2/12 (16.7%)</td>
<td>1/11 (9.1%)</td>
<td>0/18 (0.0%)</td>
</tr>
<tr>
<td>5 (&lt;15)</td>
<td>0/12 (0.0%)</td>
<td>2/11 (18.2%)</td>
<td>0/18 (0.0%)</td>
</tr>
</tbody>
</table>

aThe majority of patients with the cellular or NOS variants had stage 1 CKD; in contrast, only 36.4% of patients with the collapsing variant had stage 1 CKD.
likely due to several factors, including earlier recognition of disease and more available treatment options.

We assessed the effect of the response to therapy on remission rates and renal survival. Similar to most studies of pediatric FSGS (reviewed in reference [22,23]), approximately 20% of our patients were initially SS. However, this percentage was lower than that reported by Abrantes et al. (13), in which 39% were initially SS. One plausible reason for this discrepancy may be the older age at onset of disease in our patients. Regarding our patient cohort, the slope of GFR over time was more favorable in SS versus SR patients (1.0 [SS] versus −4.5 [SR]), confirming the prognostic significance of initial steroid sensitivity. Indeed, our data show that GFR remains stable (and normal) in patients who are initially SS, whereas it declines in those who are initially SR. Owing to our frequent use of ACEI, ARB, and CNI in SR patients, a relatively high proportion of these patients were in remission at last observation. These results are consistent with recent studies showing that there are higher rates of clinical remission in childhood SR FSGS with the use of either alkylating agents (24–26) or CNI compared with corticosteroids (27–30).

One major aim of our study was to assess the impact of the FSGS variant on presenting features and renal survival. Three variants were observed among our patients: Cellular, collapsing, and NOS. Similar to recent studies in adult FSGS (11,12), the NOS variant was more commonly observed than either the cellular or the collapsing variant. However, the overall distribution of pathologic variants among our cohort is different than in adult FSGS (11). Specifically, the cellular and collapsing variants were more frequently observed in children compared with adults. Another difference between ours and the adult data is the absence of either the tip or perihilar lesions in our population. There are several potential reasons for this. First, the lack of tip lesions may be due to either the age or the predominance of black patients in our population, in which tip lesions reportedly are unusual. Furthermore, the collapsing variant reportedly is more frequent in black and in younger patients (7,11–13), and this may explain the prevalence in our study.

The distribution of pathologic variants was also different between ours and other recent pediatric studies. The most common pathologic variant that we observed was the NOS variant, with the remainder equally divided between the cellular and collapsing variants. The proportion of patients with the collapsing variant was higher in our cohort compared with that reported by Abrantes et al. (13) (27 versus 16%). Similar to our report, Paik et al. (17) reported that the most common pathologic variant in their Asian pediatric population was the NOS variant. However, the overall proportion of our patients with the NOS variant (44%) was significantly lower than in their (72%) cohort. In summary, the discrepant results among the three pediatric FSGS studies (including ours) described herein highlight, in part, the impact of demographics on outcome.

Our results show that the type of variant affects clinical and laboratory features at presentation and during the course of the disease. Compared with patients with the collapsing or NOS variant, patients with the cellular variant more commonly presented with NS. In addition, the collapsing variant was heralded by higher SBP and DBP and lower GFR. The NOS variant carried the most favorable prognosis, the cellular variant portended a generally favorable prognosis, and those with the collapsing variant carried the most guarded prognosis. Unlike the results reported by Abrantes et al. (13) and Paik et al. (17) but similar to adult patients with FSGS (11), we observed differences in renal survival on the basis of histologic variant, with a much higher percentage of patients with the collapsing variant reaching stages 3 to 5 CKD (46%) compared with the cellular (16.7%) or NOS (11.1%) variants.

Finally, we studied the impact of ethnicity on outcome in primary FSGS, prompted by reports showing that renal survival is shorter in pediatric black versus white patients with FSGS (8). Despite the relatively higher number of black (30.3%) versus white (12.5%) patients with the collapsing variant, we did not observe any short-term differences in the outcome according to ethnicity.

Our study has several limitations. First, this was a retrospective study in which the patients were cared for by a group of physicians. Although bias was not inherent in the study design,
individual patient outcome may have been affected by each physician’s treatment preference. Second, we did not perform ambulatory BP monitoring, which may minimize conclusions regarding the prevalence (and impact) of hypertension. Finally, the average time of observation was only approximately 4 yr, a relatively short time span for a disease that may take up to 10 yr to show significant progression.

Conclusion

Our results show, first, that, overall, the short-term outcome of pediatric primary FSGS is generally promising but more guarded for patients with the collapsing variant. Second, the distribution of pathologic FSGS variants is different in children compared with adults. Finally, although our study did not focus on treatment outcomes, our impression is that more aggressive treatment with CNI, in combination with ACEI/ARB or with mycophenolate mofetil, may provide more favorable prognosis for renal survival in pediatric FSGS.

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Disclosures

None.

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