Clinicopathological Study of Primary Focal Segmental Glomerulosclerosis: A New Vision of all Variants

Sakhi Anand¹, Aminder Singh¹* and Mary Mathew²

¹Department of Pathology, Dayanand Medical College & Hospital, Ludhiana, India
²Department of Pathology, Kasturba Medical College, Manipal, Karnataka, India

Keywords: Primary Focal Segmental Glomerulosclerosis, Immunofluorescence, Nephrotic Syndrome, Variant.

ABSTRACT

Background: This study is a detailed clinical and histomorphological analysis of Primary Focal Segmental Glomerulosclerosis diagnosed by combined approach of histopathology and direct immunofluorescence. The aim was to identify the morphologic variants with histopathological prognostic features of primary focal segmental glomerulosclerosis and to establish the clinical, laboratory & pathologic findings in nephrotic syndrome & renal insufficiency associated with primary focal segmental glomerulosclerosis.

Methods: It was a prospective & retrospective analysis of 41 cases of primary Focal Segmental Glomerulosclerosis. Routine & special stains were done all renal biopsies. Immunofluorescence studies were performed. Multiple comparisons among the groups were performed using ANOVA. Mean comparison of two groups was performed using independent sample t-test. A categorical variable was tested using Chi-square test and fishers exact test.

Results: Out of 718, all the 41 renal biopsies of primary FSGS classified into morphologic variants. Primary Focal segmental glomerulosclerosis constituted 5.7% of total kidney biopsies. Mean age was 35.93 years having male preponderance. Proteinuria was highest in Perihilar variant while hematuria was more in the cellular variant. Nephrotic syndrome was most commonly associated with the cellular and perihilar variant. It was only histological parameter whose distribution among the different variants was statistically significant. A statistically significant correlation (p<0.05) was noted between the percentage of globally sclerosed glomeruli with hypertension & serum creatinine. A significant correlation was found between serum creatinine and mesangial hypercellularity, serum albumin, podocyte hyperplasia, arteriolar hyalinosis, intimal sclerosis and medial hypertrophy.

Conclusions: This comprehensive study of primary FSGS reiterates that different histological variants of FSGS have substantial differences in clinical and histological features.

*Corresponding author:
Dr. Aminder Singh, Assistant Professor, Department of Pathology, Dayanand Medical College & Hospital, Tagore Nagar, Ludhiana
Phone: +91 8968966550
Email: dramisingh@gmail.com
Introduction

Focal and segmental glomerulosclerosis (FSGS) is a clinicopathological entity that affects both adults and children and manifests clinically by persistent nephrotic syndrome, non-selective proteinuria, microscopic haematuria, hypertension and commonly, renal insufficiency at presentation. The clinical course of patients with FSGS is one of progressive deterioration of renal function leading to end-stage renal disease (ESRD) over 5-10 years. Some patients with FSGS respond to steroids, others do not. FSGS can be primary or secondary to other primary processes. At present, there is no agreement on histological feature or constellation of features that separates patients with primary FSGS into prognostically distinct groups. A new classification scheme has been proposed by D’Agati et al in 2004 which subcategorizes FSGS into distinct histomorphologic categories, which have distinct aetiopathogenetic factors. The morphologic variants based on specific diagnostic inclusion/exclusion criteria are an attempt to separate lesions with different clinical outcomes. This study was planned to identify morphologic variants and other histo-morphologic prognostic features of FSGS and correlate with clinical parameters at the time of renal biopsy. In addition, this study also correlates the clinical, laboratory and pathologic findings in renal insufficiency associated with primary FSGS.

Material and Methods

This is a prospective and retrospective study of 4 years duration. A total of forty-one patients diagnosed with primary Focal Segmental Glomerulosclerosis (FSGS) were included in this study. Diseases associated with secondary FSGS: morbid obesity, chronic hypertension, renal dysplasia, solitary kidney, reflux nephropathy, infections (HIV, parvovirus B19), medication (pamidronate, lithium, interferon-α) or intravenous drug abuse, family history of genetic diseases with predisposition to FSGS, history of sickle cell anaemia, history of infections present or absence of haematuria, hypertension, nephrotic syndrome and renal insufficiency were studied. The presence or absence of hematuria, hypertension, nephrotic syndrome and renal insufficiency were studied. The mean age of presentation in adult patients with primary FSGS was 35.9±15.53 years whereas in children it was 10.8±3.25 years. A male preponderance was seen in the adult population with M: F ratio of 1:2.8 whereas in children female predilection was noted with M: F ratio of 0.8:1. Clinical parameters at the time of biopsy i.e. duration of onset of illness, hypertension, and the degree of proteinuria, presence or absence of haematuria, serum albumin levels and creatinine levels at the time of renal biopsy. Glomerular filtration rate was calculated as GFR (ml/min) = 186 x serum creatinine (mg/dl)-1.154 x age-0.203 x 0.742 (for female). Morphologic variants, various histomorphologic parameters and immunofluorescence were correlated with clinical and laboratory parameters at the time of presentation. Statistical comparisons were carried out with the aid of SPSS statistical software. Multiple comparisons among the groups were performed using ANOVA. Mean comparison of two groups was performed using independent sample t-test. Categorical variable was tested using Chi-square test and fishers exact test. Pearsons correlation was performed among continuous variables. A p-value of <0.05 was set to be statistically significant.

Results

A total of 718 kidney biopsies were examined. Presence of minimum 10 glomeruli taken as adequacy criteria for a renal biopsy to be included in the study. Out of these 106 cases (14.76%) were diagnosed as Focal Segmental Glomerulosclerosis. Only 41 cases (5.7%) were diagnosed as primary FSGS and selected for further histomorphological analysis. The mean age of presentation in adult patients with primary FSGS was 35.9±15.53 years whereas in children it was 10.8±3.25 years. A male preponderance was seen in the adult population with M: F ratio of 1.28:1 whereas in children female predilection was noted with M: F ratio of 0.8:1. Clinical parameters at the time of biopsy i.e. duration of onset of illness, presence or absence of hematuria, hypertension, nephrotic syndrome and renal insufficiency were studied. The mean duration of onset of illness in months in primary FSGS was 13.44±28.48 months. The most common presenting symptom was nephrotic syndrome followed by hypertension. More than half of the total patients presented with hypertension. Haematuria and renal insufficiency were less frequently observed.

The mean serum creatinine, serum albumin, urine protein and GFR values 1.32±0.70 mg%, 2.18±0.99 gm, 4.16±2.12 g/day, 7.59±41.95 ml/min/m2 respectively. No significant difference was noted in the mean age of presentation of patients with and without renal insufficiency (p=0.848). Significantly higher urea levels and serum creatinine levels in patients with renal insufficiency. (p=0.03, 0.00 respectively). Mean GFR values were significantly lower in patients with renal insufficiency (p=0.00). Patients manifesting with nephrotic syndrome had a higher mean urinary protein excretion (5.12±1.76 g/day) compared to cases with non-nephrotic proteinuria (1.79±1.59 g/day). This difference was highly statistically significant.
Immunofluorescence was done in 35 cases, of which 4 biopsies were inadequate. In 7 cases (22.58%) both IgM & C3 were positive. Six cases showed IgM and 2 with C3 positivity (19.35% and 6.45% respectively). Immunofluorescence was negative in 16 cases. The frequency of the morphologic variants in the present study was, Not otherwise specified (NOS) 51.2%, perihilar 24.4%, tip 19.55 and cellular 4.9%. NOS was the commonest variant and cellular the least common. Collapsing variant of FSGS was not identified in this study. The majority of the cases of primary FSGS (31.7%) were between 17-25 years at the time of biopsy. 60% of the cases of perihilar variant were less than 25 years, whereas the majority of the cases of the tip variant were older and ranged between 26-50 years. There was no statistical significance between the age group of different morphologic variants [Table 1].

The cellular variant presented the earliest (0.83±0.24 months). The perihilar variant had a longer duration of onset of illness (20.10±52.07 months). This difference was however statistically not significant. (p=0.078). On an average 36.6% cases of FSGS presented with hematuria. The cellular variant was most often associated with haematuria (50%) and the lowest association was seen with the perihilar variant and the difference was statistically not significant (p value=0.947). The majority of the cases were hypertensive. Among the hypertensive cases, the maximum patients had mild hypertension (26.8%) followed by moderate hypertension (22%). All the cases of cellular variant and 80% of cases of perihilar variant presented with nephrotic syndrome. The NOS and tip variant were less frequently associated with nephrotic syndrome [Figure 1-3].

Table 1: Age distribution among the morphologic variants.

<table>
<thead>
<tr>
<th>Variant</th>
<th>Age group</th>
<th></th>
<th></th>
<th></th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 17 Years</td>
<td>17-25 Years</td>
<td>26-50 Years</td>
<td>&gt; 50 years</td>
<td>Total</td>
</tr>
<tr>
<td>NOS</td>
<td>5(23.8%)</td>
<td>7(33.3%)</td>
<td>5(23.8%)</td>
<td>4(19%)</td>
<td>21</td>
</tr>
<tr>
<td>Tip</td>
<td>1(12.5%)</td>
<td>2(25%)</td>
<td>4(50%)</td>
<td>1(12.5%)</td>
<td>8</td>
</tr>
<tr>
<td>Cellular</td>
<td>0(0%)</td>
<td>1(50%)</td>
<td>0(0%)</td>
<td>1(50%)</td>
<td>2</td>
</tr>
<tr>
<td>Perihilar</td>
<td>3(30%)</td>
<td>3(30%)</td>
<td>2(20%)</td>
<td>2(20%)</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>9(22%)</td>
<td>13(31.7%)</td>
<td>11(26.8%)</td>
<td>8(19.5%)</td>
<td>41</td>
</tr>
</tbody>
</table>

Fig. 1: A) NOS Variant (H & E x 200) B) NOS variant (Jones Methenamine silver x200) C) Tip variant (H & E X200) D) Tip variant (PASM X200) E) Perihilar variant (H & E x200) F) Perihilar variant (Jones Methenamine silver x200) G) Cellular variant with intraglomerular foam cells (H & E X200) H) Cellular variant with podocyte hyperplasia (Jones Methenamine silver x200).
Overall renal insufficiency was seen in 36.5% of the cases. In the tip and the cellular variants about half of the cases presented with renal insufficiency whereas 30% of cases of the perihilar variant were associated with renal insufficiency. The difference was however statistically not significant (p=0.787). The average serum creatinine level in 41 cases of primary FSGS was 1.32±0.70mg/dL. Different morphologic variants presented with different creatinine levels, which were highest in the cellular variant (1.80±0.84) and lowest in perihilar variant (1.13±0.419), but the comparison was statistically not significant (p=0.394). The average urine protein excretion rate was 4.16±2.12g/day. The degree of proteinuria did not vary significantly (p=0.916) among the different variants and ranged from 4.59±2.5g/day in the perihilar variant to 4.03±2.26 g/day in the tip variant. The mean serum albumin levels were 2.18±0.944gm. Serum albumin levels were significantly higher in the tip (2.31±1.29) and the perihilar variants (2.72±0.88) than NOS (1.92±0.8) and cellular variants (1.8±0.28). However, this difference was statistically significant between NOS and perihilar variant (p=0.025).
Correlation Between Percentage of Glomerular Sclerosis with Clinical & Histological Parameters

**Table 2**: Hypertensive patients have a higher degree of glomerular sclerosis (total), global and segmental sclerosis. A statistically significant difference was observed between globally sclerosed glomeruli with presence or absence of hypertension at the time of biopsy. (p=0.03). No significant association was observed between the percentage of totally sclerosed, globally sclerosed and segmentally sclerosed with presence of hematuria at the time of biopsy. (p>0.05). The interstitial fibrosis became more severe with an increase in the percentage of glomerular sclerosis. There is statistically significant difference in the degree of interstitial fibrosis in the biopsies with different percentages of segmentally sclerosed glomeruli. (p=0.02).

There was statistically significant difference in the degree of tubular atrophy in the biopsies with different percentages of glomeruli sclerosed (total), global and segmental sclerosis (p=0.002, 0.002, 0.038 respectively). Tubular atrophy was absent when the percentages of totally sclerosed, globally and segmentally sclerosed glomeruli were 22.66±10.17%, 3.0±6.7% and 19.66±9.67% respectively and were severe when the same were, 69.09±37.55%, 23.08±18.92%, 46.01±25.47% respectively. Thus, the tubular atrophy became more severe with an increase in the percentage of glomerular sclerosis.

The histological parameters (intraglomerular hyalinosis, glomerulomegaly, podocyte hyperplasia, mesangial hypercellularity, intraglomerular foam cells, adhesion, tubular atrophy, interstitial fibrosis and inflammation, arteriolar hyalinosis, intimal sclerosis, medial hypertrophy) were correlated with clinical and laboratory parameters at presentation i.e. blood pressure, hematuria, serum creatinine, serum albumin, proteinuria, GFR and urea in forty-one cases of primary FSGS. A statistically significant correlation was found between serum creatinine and mesangial hypercellularity, serum albumin and podocyte hyperplasia, arteriolar hyalinosis, intimal sclerosis and medial hypertrophy of vessels. Similarly, there was statistically significant correlation between urine protein, adhesion and intimal sclerosis, between haematuria and intraglomerular foam cells and interstitial fibrosis and between blood pressure, chronic interstitial inflammation and medial hypertrophy of vessels. A higher percentage of segmentally sclerosed and globally sclerosed glomeruli were involved in patients with renal insufficiency. This difference was statistically significant (p=0.004, 0.05 respectively).

The association of podocyte hyperplasia, adhesion, mesangial hypercellularity and interstitial fibrosis with renal insufficiency was not statistically significant. Chronic interstitial inflammation was observed in 86.7% cases with renal insufficiency and in only 53.8% of cases without renal insufficiency. This difference was again statistically significant (p=0.04). The percentage of segmental sclerosis and global sclerosis was higher in patients not presenting with nephrotic syndrome, 37.43±24.84% and 11.11±13.33% respectively. However, the difference was not statistically significant. (p=0.296 & 0.587).

**Discussion**

It is important to realize that FSGS is a histological diagnosis and not a single disease entity. FSGS is responsible for 2% to 41% of primary glomerulopathies as reported from different countries. This study was undertaken with the main aim of identifying the various morphologic variants and other histo-morphologic prognostic features of FSGS and their correlation with clinical parameters at the time of renal biopsy. Banfi et al and Shiki et al suggesting that hypertension at presentation is induced

<table>
<thead>
<tr>
<th>Variant</th>
<th>Foam cells</th>
<th>Adhesion</th>
<th>Podocyte hyperplasia</th>
<th>Mesangial hypercellularity</th>
<th>Glomerulomegaly</th>
<th>Hyalinosis</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOS</td>
<td>8 (38.1%)</td>
<td>20 (95.2%)</td>
<td>5 (23.8%)</td>
<td>17 (81%)</td>
<td>20 (95.2%)</td>
<td>10 (47.6%)</td>
<td>21</td>
</tr>
<tr>
<td>Tip</td>
<td>4 (50%)</td>
<td>7 (87.5%)</td>
<td>0 (0%)</td>
<td>3 (37.5%)</td>
<td>8 (100%)</td>
<td>5 (62.5%)</td>
<td>8</td>
</tr>
<tr>
<td>Cellular</td>
<td>1 (50%)</td>
<td>2 (100%)</td>
<td>0 (0%)</td>
<td>2 (100%)</td>
<td>2 (100%)</td>
<td>1 (50%)</td>
<td>2</td>
</tr>
<tr>
<td>Perihilar</td>
<td>4 (40%)</td>
<td>10 (100%)</td>
<td>2 (20%)</td>
<td>10 (100%)</td>
<td>10 (100%)</td>
<td>7 (70%)</td>
<td>10</td>
</tr>
<tr>
<td>All Cases</td>
<td>17 (41.5%)</td>
<td>39 (95.1%)</td>
<td>7 (17.1%)</td>
<td>32 (78%)</td>
<td>40 (97.6%)</td>
<td>23 (56.1%)</td>
<td>41</td>
</tr>
<tr>
<td>P value</td>
<td>0.939</td>
<td>0.655</td>
<td>0.425</td>
<td>0.011</td>
<td>0.807</td>
<td>0.668</td>
<td></td>
</tr>
</tbody>
</table>

Annals of Pathology and Laboratory Medicine, Vol. 03, No. 04, October - December 2016
by hemodynamic changes, not by permanent histological changes. Comparisons of histopathological features were performed with different studies.[16-20,23] [Table 3].

Association of Nephrotic Syndrome with The Morphologic Variants: In our study, all cases of cellular variant and 80% of cases of perihilar variant presented with nephrotic syndrome. Least association of nephrotic syndrome was seen in the tip variant. This finding is in discordance with the studies of Thomas et al.[20], Stokes et al[21], Chun et al[22] and Deegens et al[23] where the tip variant was associated with highest percentage of nephrotic cases (97%, 94.8%, 88% and 91% respectively). In a study by Alexopoulous et al[24] patients manifesting with nephrotic syndrome had a significantly higher mean urinary protein excretion as seen in our study.

Association of Renal Insufficiency with The Morphologic Variants: The incidence of renal insufficiency among the morphologic variants as reported in two North American and one west European studies[20,21,23] has shown that renal function is usually preserved in patients with the tip variant at presentation and collapsing and cellular FSGS present with maximum renal insufficiency. In our study, no association was found between interstitial fibrosis and renal insufficiency as opposed to the findings of Taheri et al[25] where a statistically significant association was established between interstitial fibrosis and renal insufficiency. Another study in Iranian adults[26] with primary FSGS was unable to establish a significant association between interstitial fibrosis and renal insufficiency.

Association Between Sclerosed Glomeruli with The Morphologic Variants: Laura et al & Chun et al[27,22] demonstrated the percentage of glomeruli involved was maximum in the classic lesion (43±23%) and least in tip lesion (24±17%) (p<0.05). Similarly, the percentage of glomeruli sclerosed (total) was also maximum in perihilar variant (39.55±18.82%) and least in tip variant (17.87±12.26%) (p=0.015).

However Few studies, showed that the number of glomeruli involved was maximum in perihilar variant and least in the tip variant whereas segmentally sclerosed glomeruli was maximum in perihilar but lowest in the cellular variant. [27,18] Thomas et al[20] found maximum glomerular sclerosis/consolidation in collapsing and least in tip variant.

Table 3: Comparative clinical and laboratory parameters of variants of FSGS in different series:

<table>
<thead>
<tr>
<th>Variant</th>
<th>Various studies</th>
<th>Age</th>
<th>Duration (months)</th>
<th>Serum creatinine (mg/dL)</th>
<th>Proteinuria gm/24 hrs</th>
<th>Hypertension %</th>
<th>Haematuria %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Collapsing</td>
<td>Thomas et al[20]</td>
<td>38±12</td>
<td>NA</td>
<td>3.1±3.8</td>
<td>10.0±5.3</td>
<td>67</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Nada et al[18]</td>
<td>46±10</td>
<td>10.75±16.88</td>
<td>2.75±1.3</td>
<td>6.1±4.6</td>
<td>0</td>
<td>33.3</td>
</tr>
<tr>
<td></td>
<td>Deegens et al[23]</td>
<td>63±18</td>
<td>1.9(1.5-2.2)</td>
<td>2.3±1.6</td>
<td>10.4±6.7</td>
<td>71</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Present study</td>
<td>NF</td>
<td>NF</td>
<td>NF</td>
<td>NF</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Cellular</td>
<td>Thomas et al[20]</td>
<td>45±13</td>
<td>NA</td>
<td>2.5±1.7</td>
<td>16±15</td>
<td>75</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Nada et al[18]</td>
<td>30±13</td>
<td>4.38±5.57</td>
<td>1.49±0.7</td>
<td>4.6±2.8</td>
<td>59</td>
<td>61.5</td>
</tr>
<tr>
<td></td>
<td>Deegens et al[23]</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Present study</td>
<td>36±22.62</td>
<td>0.83±0.24</td>
<td>1.8±0.84</td>
<td>4.3±2.1</td>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>Tip</td>
<td>Thomas et al[20]</td>
<td>54±13</td>
<td>NA</td>
<td>1.5±0.9</td>
<td>9.7±7.0</td>
<td>54</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Nada et al[18]</td>
<td>30±14</td>
<td>20.39±1.07</td>
<td>1.84±1.02</td>
<td>3.3±1.3</td>
<td>61</td>
<td>20.83</td>
</tr>
<tr>
<td></td>
<td>Deegens et al[23]</td>
<td>44±16</td>
<td>2.3(2-10.6)</td>
<td>1.3±0.9</td>
<td>10.0±5.7</td>
<td>68</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Present study</td>
<td>33.8±19.79</td>
<td>14.69±13.5</td>
<td>1.6±0.9</td>
<td>2.7±2.8</td>
<td>75</td>
<td>37.5</td>
</tr>
<tr>
<td>Perihilar</td>
<td>Thomas et al[20]</td>
<td>50±16</td>
<td>NA</td>
<td>2.0±1.4</td>
<td>4.4±3.3</td>
<td>80</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Nada et al[18]</td>
<td>27±17</td>
<td>6.53±99.3</td>
<td>0.93±1.53</td>
<td>1.9±9</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Deegens et al[23]</td>
<td>50±12</td>
<td>49(0.7-303)</td>
<td>1.6±0.9</td>
<td>5.2±2.6</td>
<td>80</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Present study</td>
<td>28.5±16.26</td>
<td>20.10±52.07</td>
<td>1.13±0.41</td>
<td>4.59±2.5</td>
<td>60</td>
<td>30</td>
</tr>
<tr>
<td>NOS</td>
<td>Thomas et al[20]</td>
<td>50±15</td>
<td>NA</td>
<td>2.1±1.8</td>
<td>5.5±4.6</td>
<td>80</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Nada et al[18]</td>
<td>32±14</td>
<td>20.25±36.09</td>
<td>2.29±2.49</td>
<td>3.3±1.8</td>
<td>70</td>
<td>24.8</td>
</tr>
<tr>
<td></td>
<td>Deegens et al[23]</td>
<td>51±17</td>
<td>4.3 (0.15-10)</td>
<td>2.0±1.3</td>
<td>6.9±4.9</td>
<td>66</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>Present study</td>
<td>29.6±17.6</td>
<td>10.39±16.02</td>
<td>1.243±0.72</td>
<td>4.1±2.05</td>
<td>47.6</td>
<td>38.1</td>
</tr>
</tbody>
</table>

*NA= Not available, NF= Not found, NOS= Not otherwise specified
The Frequency of Tubulointerstitial Changes in The Morphologic Variants: Nada et al\(^{18}\) found mild inflammatory infiltrate in all the cases of perihilar variant and severe inflammation was seen in only NOS variant. Thomas et al\(^{20}\) showed that interstitial inflammation was maximum in collapsing and least in tip variant (p<0.001). However, cases of collapsing variant were not identified in our study. Our findings are similar to the two studies by where the difference in the degree of interstitial fibrosis between different variants was statistically not significant.\(^{12,18}\) They also showed that interstitial fibrosis was absent or of a mild degree in the majority of cases (41% and 38.5% respectively) and was severe in only 5% of total FSGS cases. Severe degree of interstitial fibrosis was observed only in variant (6.6%).

Association of Vascular Changes with the Morphologic Variants: In the present study, arteriolar hyalinosis and intimal sclerosis were absent in the cellular variant. Arteriolar hyalinosis was maximum in the tip variant (60%) and intimal sclerosis was maximum in the perihilar variant. Varying degree of medial hypertrophy was seen among the variants (37.5% to 50%). No statistical significance could be established. Many studies\(^{28-32}\) particularly Nada et al\(^{18}\) showed the absence of arteriolar hyalinosis and intimal sclerosis in all of the cases of collapsing variant.

Frequency of The Morphologic Variants: Overall, cellular variant was less frequent in most series, comprising only 3–4.5% of cases in multiethnic cohorts\(^{20,21}\) except the Chinese series in which only one-quarter showed the cellular variant, and the Indian cohort in which one-tenth of the cases belonged to the cellular variant.\(^{13,18}\) Regarding tip lesions, these are just morphologic abnormalities in glomeruli that otherwise appear normal on light microscopy and it would considered as a part of minimal change disease which clinically like only. The prognosis in tip lesion may be more benign than other morphologic variants so that’s the reason some studies\(^{27}\) thought that tip lesion is an intermediate form between Minimal change disease and FSGS but according to latest study done by Luis F et al\(^{34}\) it should not to be considered as benign disease. They found that tip lesions presents with less chronic histologic alterations, but the prognostic implications were not favourable as chronic kidney disease developed in 30.8% and end stage in 19.2% of patients. So their study suggested that the tip variant should not be considered a prognostically favourable disease rather it could be a more early stage of a severe glomerular disease. Another study with predominant African Americans documents 32% of cases as cellular variant in the paediatric age group.\(^{35}\)

Limitations of The Study: The study included only 41 cases so the sample size is a limiting factor in analyzing all the clinicopathological variables. Few morphological variants like cellular variant was seen only in a couple of biopsies thus, might not represent the actual prevalence. The study comprised of all age groups and not specifically related to children. Electron microscopy & genetic testing were not done because of financial constrains.

Conclusion
To conclude, this comprehensive study of primary FSGS reiterates that different histological variants of FSGS have substantial differences in clinical and histological features. Although histological appearance does not permit to know the cause of FSGS and it is not a perfect indicator of outcome but a statistically significant correlation (p<0.05) was noted between the percentage of globally sclerosed glomeruli with hypertension & serum creatinine. A significant correlation was found between serum creatinine and mesangial hypercellularity, serum albumin, podocyte hyperplasia, arteriolar hyalinosis, intimal sclerosis and medial hypertrophy.

Acknowledgements
No Financial and material support and conflict of interests

Funding
None

Competing Interests
None Declared

References


