International Journal of Research in Medical Sciences
Wani AS et al. Int J Res Med Sci. 2022 Feb;10(2):360-363
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20220067

Original Research Article

Histological pattern of focal segmental glomerulosclerosis and its clinical correlation

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Received: 26 December 2021
Revised: 09 January 2022
Accepted: 10 January 2022

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ABSTRACT

Background: Focal segmental glomerulosclerosis (FSGS) is a pattern of injury and it has five histological subtypes with varying prognosis and therapeutic response. Our aim was to study the pattern of primary FSGS in our population along with their clinicopathological characteristics.
Methods: This is a 2-year retrospective, single centre cohort, observational study. All adult patients with primary FSGS were identified.
Results: There were 51 patients of primary FSGS. The mean age of patients was 37.2±15.3 years with overall male dominance. The clinical presentations were nephrotic syndrome (88.2%), proteinuria with hematuria (11.7%), hypertension (47.05%) and renal insufficiency (60%). FSGS-NOS were seen in 26 patients, tip variant in 11, perihilar in 6, cellular variant in 6 and collapsing variant in 2 patients. The mean age of collapsing variant was significantly less than others (20.5±9.1 years vs 37.2±15.3 years). Massive proteinuria was seen in collapsing and tip variant significantly higher than rest of the variants and tip variant had the least degree of interstitial fibrosis and tubular atrophy.
Conclusions: FSGS is a pattern of injury which shows histological variations. Although it most commonly affects males, tip and cellular variants show female preponderance. Massive proteinuria was mostly seen in collapsing and tip variants and the features of chronicity were mostly seen in tip variant. Larger studies are required for the differences in treatment protocols and prognosis of different variants.

Keywords: FSGS, Histological pattern, Renal biopsy

INTRODUCTION

Focal segmental glomerulosclerosis (FSGS) is a pattern of injury on histology rather than a single disease and is characterized by scarring of a part of glomerulus (segmental) in some glomeruli (focal) along with foam-cell infiltration, and podocyte precursor proliferation.[1] Only on exclusion all the causes of this pattern of injury, can we label the rest as primary FSGS.[2,3]

The last two decades has seen further histological subtyping of this entity, most notable ones being cellular, tip and collapsing lesions. It is important to recognize these variants due to the supposed varying prognosis and therapeutic response of these lesions. However, these variations still remain controversial.[4] Apart from the histological subtype differences racial/ genetic factors as well as treatment protocol may be responsible for variations in outcomes between different studies.[5] There have been numerous studies which report notable differences in the clinical features as well as outcomes of

patients between variants of FSGS, according to the Columbia classification.[6] Our aim was to study the histological pattern of primary FSGS in our population along with their clinic-pathological characteristics.

METHODS

Study design, setting and participants

This is a 2-year observational study (October 2019 to October 2021) conducted at government medical college, Srinagar, India. All adult patients with primary FSGS in their native kidney biopsies were included. The diagnosis of primary FSGS was established when there was no evidence of any other primary glomerular disease or any systemic disease associated with segmental sclerosis in the glomeruli or when there was no evidence of morbid obesity, malignant hypertension, reflux nephropathy, single kidney, human immunodeficiency virus infection, intravenous drug abuse, or any family history of kidney disease.

Exclusion criteria

We excluded patients with FSGS in renal transplant biopsies, patients with inadequate biopsies (less than five glomeruli per level of section), repeat biopsies, as well as pediatric patients.

Renal biopsy evaluation

Three core biopsies were taken under ultrasound guidance, one for light microscopy, immunofluorescence and electron microscopy. Standard processing techniques were followed in all the biopsies. The pathologic diagnosis of FSGS was established when at least one glomerulus with a segmental lesion was present along with remaining glomeruli being relatively normal. Pathologic findings in the vascular, glomerular, and interstitial compartments were noted. The interstitial fibrosis and tubular atrophy (IFTA) were classified as none- 0%, mild- <25%, moderate –25-50%, severe- >50%.

Definitions

Patients >18 years of age were regarded as adults.

Microscopic hematuria was defined as at least 5 red cells per high-power field on microscopic examination or positive blood by urine dipstick. Nephrotic syndrome was defined as nephrotic range proteinuria >3.5 gm per 24 hours per 1.73 m^2 (in children >40 mg/m^2 /hour or PCR>2000 mg/g [>200 mg/mmol]) along with hypoalbuminemia and edema.[7]

Hypertension was defined when systolic blood pressure was >140 mmHg and diastolic blood pressure was >90 mmHg.[8]

Data source and variables

Clinical data, laboratory data and follow up records of the patients were retrieved from the hospital information system. The treatment received by the patients was noted from the treatment charts.

ESRD was defined as a decrement in the patient's kidney function to a level at which either long-term dialysis or kidney transplantation is required to the sustain life.[9] eGFR was calculated using the updated Schwartz equation.[10]

The level of proteinuria was divided into two groups-nephrotic-range when proteinuria was>3.5 gm/d and massive proteinuria when proteinuria was>10 gm/d in accordance to previous studies.[8]

The renal biopsy materials were categorized according to the Columbia FSGS classification system. Each case was classified as one of the five histological variants-Collapsing, Tip, cellular, perihilar, or not otherwise specified (NOS). In the collapsing variant, the increased cellularity is caused by extra-capillary hypercellularity by epithelial hypertrophy and hyperplasia outside the basement membrane. The tip lesion variant of FSGS usually has segmental increased cellularity caused by a combination of endocapillary foam cells and hypertrophied epithelial cells that are in segments adjacent to the proximal tubular epithelial cells. Perihilar FSGS is characterized by hyalinosis and sclerosis in the perihilar region.[11]

Follow-up

The follow-up period was considered to be the time interval between renal biopsy as well as the last outpatient visit, death, or kidney failure, whichever happened earlier.

Statistical analysis

The statistical analysis was done using SPSS Version 23.0 (IBM Corp., Armonk, NY, USA). Categorical variables expressed as numbers or percentages were compared using Chi Square and Fisher's exact test (as applicable). Continuous variables reported as mean or median (depending on the normality of data), were compared using Wilcoxon rank-sum methods.

Ethics approval and consent

This was not sought as it was a retrospective study and did not involve any active participation of the patients. The patients whose data was analysed could also not be contacted further. Many patients were de-identified and waiver of their consent did not adversely affect the rights and welfare of the participants.

RESULTS

There were fifty-one patients of primary Focal segmental glomerulosclerosis. The demographic profile, laboratory findings and histopathological features of patients with primary focal glomerulosclerosis is shown in Table 1. Most of the patients were adult males. The variants included tip variant, perihilar variant, cellular variant, collapsing variant and Focal segmental glomerulosclerosis-Not otherwise specified (NOS) as shown in the Figure 1. The mean age of collapsing variant was significantly less than others (20.5±9.1 years versus 37.2±15.3 years) and higher in perihilar variant (46.5±16.9 years versus 37.2±15.3 years). Although males outnumbered females overall, females were higher in number in tip and cellular variant (Male: Female ratio 2.6:1 and 2:1 respectively). Massive proteinuria was seen in collapsing and tip variant in significantly higher numbers than rest of the variants and tip variant had the least degree of interstitial fibrosis and tubular atrophy. Perihilar variant had significantly higher cases of hypertension than the rest subtypes.

Table 1: Demographic profile, laboratory findings and histopathological features of patients with primary focal glomerulosclerosis, (n=51).

Variables		Number (%)
Mean age at diagnosis (years)		37.2±15.3
Male: female		1.8:1
Clinical presentation	Nephrotic syndrome	45(88.2)
	Hematuria and proteinuria	6 (11.7)
Massive proteinuria (>10 mg/24 hours)		13 (25.4)
Hypertension		24 (47.05)
Renal insufficiency		31 (60)
Light microscopic pattern*	Fsgs-nos	26 (50.9)
	Tip variant	11(21.6)
	Perihiar variant	6 (11.8)
	Collapsing variant	2 (3.9)
	Cellular variant	6 (11.8)
Interstitial fibrosis and tubular atrophy	None	10 (19.6)
	Mild	25 (49.01)
	Moderate	11 (21.5)
	Severe	5 (9.8)
Vascular changes	None	27 (52.9)
	Hypertensive changes	24 (47.05)
Follow up time (months)		6.7±2.6
Outcome**	Cr	19 (37.2)
	Pr	12 (23.5)
	Esrd	14 (27.4)
	Ltf	6 (11.7)

*fsgs- focal segmental glomerulosclerosis, nos- not otherwise specified.
**cr; complete remission, pr; partial remission, esrd; end stage renal disease, ltf; lost to follow-up.

The mean follow-up time was 6.7±2.6 months. Follow-up of patients is shown in Table 1.

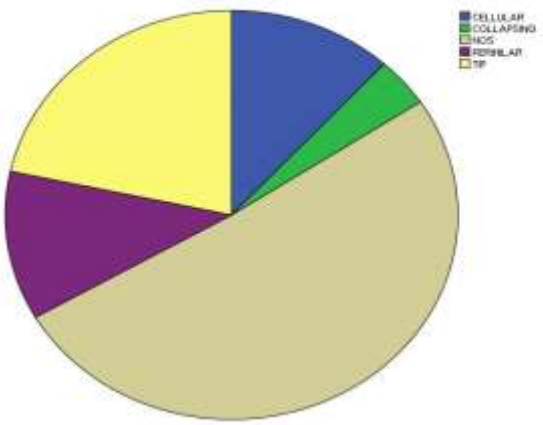

Figure 1: Histological variants in primary FSGS in our study.

DISCUSSION

Idiopathic FSGS includes a pathologically diverse group which has wide range of demographic characteristics, clinical presentations and disease outcome.[5] The aim of this study was to see the heterogeneity of this disease in a homogenous population in North India.

The mean age of our patients was 37.2±15.3 years. In a study conducted by Rydel et al it was 40±17 years whereas that conducted by Taneda et al showed it to be 39.4±1.7 years.[6,12] Although this disease entity has a wide age range, the patients with collapsing variant were comparatively younger and perihilar variant were relatively older than other variants. This observation was supported by other studies as well. The most common subtype was classical variant (NOS). It was also the most common variant in other studies as well.[5]

Although most of our patients were males, the comparison of different subtypes of FSGS showed female preponderance in cellular and tip variants. The bias towards females in tip variant was studied by others as well.[6,13]

Most of our patients presented with nephrotic syndrome with proteinuria >10 gm/24 hours in 13 (25.4%) patients. Hypertension was seen in 24 (47.05%) patients and renal insufficiency in 31 (60%) patients. Massive proteinuria was most commonly seen in collapsing and tip variants in our study.

Nephrotic syndrome, hypertension, and renal insufficiency were the commonest symptoms and were seen in all the histological variants of FSGS. Thomas et al also found that collapsing and tip lesions in FSGS had severe nephrotic syndrome with mean 24 hours protein excretions of 10.0 and 9.7 gm/day, respectively.[5]

The features of chronicity on biopsy i.e., interstitial fibrosis and tubular atrophy (IFTA) was seen mostly in the tip variant as compared to others. There have been varied observations in tip lesions with regard to interstitial fibrosis and tubular atrophy. While some studies have shown it to be at a relatively increased proportion in tip variant as compared to other variants, others have shown percentage of IFTA less in patients of tip variant.[5,8] Also, there are some studies which did not find any difference in the chronicity of biopsy and the variant of FSGS.[13]

Limitation

The limitations of this study were less number of cases and limited follow-up of patients.

CONCLUSIONS

FSGS is a pattern of injury which shows histological variations. Although it most commonly affects males, tip and cellular variants show female preponderance. Massive proteinuria was mostly seen in collapsing and tip variants and the features of chronicity were mostly seen in tip variant. Larger studies are required for the differences in treatment protocols and prognosis of different variants.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Wani AS, Zahir Z. Histological pattern of focal segmental glomerulosclerosis and its clinical correlation. Int J Res Med Sci 2022;10:360-3.