Sir Salimullah Medical College Journal

Sir Salimullah Med Coll J 2023; 31: 26-33

Original Article

DOI: https://doi.org/10.3329/ssmcj.v31i1.69357

Histomorphological Patterns of Focal Segmental Glomerulosclerosis and Their Clinical Correlation in Tertiary Care Hospitals in Bangladesh

Nafisa Abedin[1], Saumitra Chakravarty[2], Afsana Papry[3], Nafisa Sermin[4], Tanushree Paul[5], Syeeda Shiraj-Um-Mahmuda[6], Md. Akhtaruzzaman[7], Umama-Tun-Nesa Emita[8], Farhana Alam[9], Sultana Gulshana Banu[10]

Article information
Received: 03-10-2022
Accepted: 05-02-2023

Cite this article:
Abedin N, Chakravarty S, Papry A, Sermin N, Paul T, Mahmuda SS. Histomorphological Patterns of Focal Segmental Glomerulosclerosis and Their Clinical Correlation in Tertiary Care Hospitals in Bangladesh. Sir Salimullah Med Coll J 2023; 31: 26-33

Key words:
FSGS, histomorphological variants, Interstitial fibrosis and tubular atrophy, thick walled blood vessels.

Abstract:

Background: *Being one of the commonest glomerular diseases in adults and a major etiology of the nephrotic syndrome, Focal Segmental Glomerulosclerosis (FSGS) gradually progresses towards end-stage renal disease (ESRD). According to pathogenesis, FSGS can be classified into primary or secondary ones and in both instances, histomorphological findings are nearly indistinguishable. Five histomorphological variants of primary as well as secondary focal segmental sclerosis have already been accepted, for instance, NOS (not otherwise specified), tip, cellular, perihilar, and collapsing variants. Nonetheless, primary FSGS is a diagnosis of exclusion and all the time, primary and secondary FSGS can not be distinguished discernibly. For this reason, correlation with clinical and biochemical parameters are extremely important. The present study was undertaken to identify various histomorphological patterns of FSGS by light microscopy and immunofluorescence study at tertiary care hospitals in Bangladesh as well as to correlate those patterns with clinical, biochemical parameters and additional histologic findings.*

Methods: *This is an observational & cross sectional study which was conducted among 57 paraffin blocks of renal biopsy specimens of histologically confirmed FSGS cases including all age groups and both sexes, which were collected from department of Pathology, BSMMU & Kidney foundation hospital & research institute, Mirpur, Dhaka. Renal biopsies received for light microscopy only and biopsies that contained less than eight glomeruli were exluded from the study . Routine Haematoxylin & Eosin (H&E), Periodic Acid Schiff (PAS), Jones silver & Masson's trichrome stains were used to evaluate renal biopsy specimens & histomorphological patterns of FSGS were identified. Data regarding clinical & biochemical parameters were collected from patient's medical records. Statistical analyses were performed by SPSS-22.*

Result: *In our study, it was observed that, among 57 biopsies, 35(61.4%) biopsies were diagnosed as NOS, 12(21.1%) biopsies as perihilar, 4(7.0%) biopsies as tip, 3(5.3%) biopsies as collapsing and 3(5.3%) biopsies as cellular variant. No clinical and biochemical*

1. Curator, Department of Pathology, Sir Salimullah Medical College, Dhaka, Bangladesh.
2. Assistant Professor, Department of Pathology, BSMMU, Dhaka.
3. Lecturer, Department of Pathology, Sir Salimullah Medical College, Dhaka, Bangladesh.
4. Clinical Pathologist, Department of Clinical Pathology, Dhaka Medical College Hospital, Dhaka
5. Senior Lecturer, Department of Pathology, MH Samorita Hospital & Medical College, Tejgaon, Dhaka.
6. Lecturer, Department of Pathology, Dhaka Medical College, Dhaka.
7. Lecturer, Department of Pathology, Pabna Medical College, Pabna
8. Pathologist, Khulna Medical College Hospital, Khulna.
9. Lecturer, Department of Pathology, Colonel Maleque Medical College, Manikganj
10. Associate Professor, Department of Pathology, BSMMU, Dhaka

Address of Correspondence: Dr. Nafisa Abedin, Curator, Department of Pathology, Sir Salimullah Medical College, Dhaka, Bangladesh. ORCID : 0000-0001-6682-7842

parameters were significantly associated with these histomorphological patterns of FSGS. Regarding additional histologic features, thick walled blood vessels was significantly associated with histomorphological patterns.

Conclusion: *This study was conducted on only two tertiary level hospitals in Bangladesh, therefore, the result may not reflect the exact scenario of Bangladesh. It is the need of the moment to mention the histomorphological patterns of FSGS in renal histopathology reports. Moreover, logistic support is a necessity to institute nephro-pathology section in the pathology department of all the tertiary care hospitals in order to identify renal glomerular disease precisely.*

Introduction:

Focal segmental glomerulosclerosis (FSGS) is one of the common causes of kidney disease globally and a major glomerular cause of end stage renal disease (ESRD) in adults as well as in children.[1] This clinicopathological condition is characterized by proteinuria, usually nephrotic range proteinuria (protein excretion of more than 40 mg/m^2/h or more than 3.5 gm/24 hours), progressively developed renal failure as well as focal and segmental sclerotic glomerular lesion in renal biopsy.[2]

The incidence of FSGS is gradually increasing in both developing and developed countries. Commonly, FSGS incidence rates are higher in males being around 1.5 times higher than in females. During the last three decades, FSGS has transcended all other causes of adult nephrotic syndrome (NS) in countries like USA, Brazil, Singapore and South-East Asian countries specially in India and Pakistan. Global incidence rate of FSGS varies from 0.2 to 1.8/100,000 population, per year.[3] In Bangladesh, a small number of studies are done to document FSGS as one of the principal causes of adult NS, as a result of limited access of kidney biopsy facilities in the country. [4]

FSGS is characterized by a number of histological forms sharing an usual pattern of podocyte injury and exhaustion. In accordance with Columbia classification, FSGS can be categorized into five histomorphologic variants, namely, not otherwise specified (NOS), tip, cellular, perihilar and collapsing types. All of these histological variants seem to be related to well defined clinical features, prognostic and therapeutic inferences. Some histologic variants of FSGS are predominantly present in specific diseases, for example, perihilar and collapsing groups are found mostly in secondary form of FSGS and virus associated FSGS specially HIV-associated nephropathy (HIVAN) respectively.[5]

This study was conducted to evaluate histo-morphological variants of FSGS in renal biopsies and correlate those various with demographic, clinical and biochemical parameters. Although treatment regimen of FSGS is not directly related to the histomorphological patterns, appropriate and precise diagnosis of the patterns is extremely important because the prognostic outcomes vary in different subtypes, for instance, collapsing variant shows poorer prognosis with more chance of development of ESRD than do NOS and tip variants. Therefore, these analyses will eventually guide selection of therapeutic strategies and will provide therapeutic insight, thereby reducing morbidity associated with FSGS.

Materials and method:

This is a cross sectional observational study which was conducted from March, 2020 to February, 2022 among 57 paraffin blocks of renal biopsy specimens of histologically confirmed FSGS cases including all age groups and both sexes, which were collected from two tertiary care hospitals in Bangladesh. Sample size was calculated by Cochran and modified Cochran formula where sample proportion was 0.45 and accepted standard error 0.05.

Tissue sections stained with routine H&E, PAS, Jones silver & Masson's trichrome stains were evaluated & five histomorphological patterns of FSGS were identified. The association between histomorphological patterns of FSGS and clinical-biochemical parameters was observed. Data regarding clinical & biochemical parameters were collected from patient's medical records. All relevant data were placed in a data sheet. Statistical analyses were performed on the tabulated data by Chi-square and ANOVA test.

Results:

Among 57 patients of FSGS, more than one fourth 15(26.3%) patients belonged to age group 21-30 years. The mean age was 27.4±16.2 years ranged from 1 to 72 years. Nearly two thirds 34(59.6%) of patients were male and 23(40.4%) were female. The mean duration of disease before biopsy was 1.73±0.96 years ranged from 0.5 to 4.4 years. Five (8.8%) patients had previous history of biopsy and 3(5.3%) had positive family history (Table I).

Table I. Distribution of the study patients by demographic profile (n=57)

Demographic profile	No. of patients	Percentage
Age (years)		
1-10	9	15.8
11-20	12	21.1
21-30	15	26.3
31-40	9	15.8
41-50	7	12.3
>50	5	8.8
Mean±SD	27.4±16.2	
Range (min-max)	1-72	
Sex		
Male	34	59.6
Female	23	40.4
Duration of disease (years)		
Mean±SD	1.73±0.96	
Range (min-max)	0.5-4.4	
Previous history of biopsy		
Yes	5	8.8
No	52	91.2
Family history		
Yes	3	5.3
No	54	94.7

Among 57 patients of FSGS, nearly two thirds, 34(59.6%) of patients were male and 23(40.4%) were female.

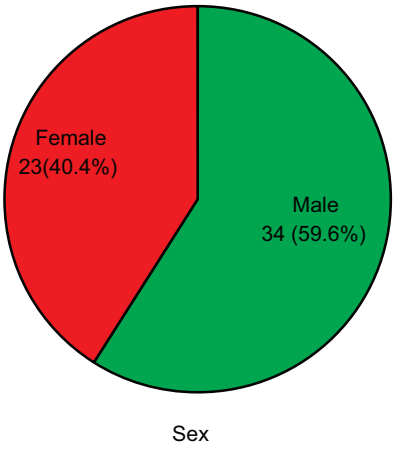

Fig.-1: *Pie chart showing the distribution of the study patients by sex (n=57)*

In this study, evaluated clinical parameters were bedside estimated proteinurea, nephrotic syndrome, isolated proteinurea, haematuria, renal Failure, HTN and oedema , although none of these was significantly (p>0.05) associated with histomorphological patterns of FSGS (Table-II)

Table-II Association between histomorphological patterns of FSGS with clinical symptoms (n=57)

Clinical symptoms	Histomorphological patterns										P value
	NOS(n=35)		Perihilar(n=12)		Tip(n=4)		Collapsing(n=3)		Cellular(n=3)		
	n	%	n	%	n	%	n	%	n	%	
Proteinurea											
2+	11	31.4	1	8.3	1	25.0	0	0.0	1	33.3	
3+	23	65.7	11	91.7	3	75.0	3	100.0	2	66.7	0.804^{ns}
4+	1	2.9	0	0.0	0	0.0	0	0.0	0	0.0	
Nephrotic syndrome	21	60.0	5	41.7	0	0.0	3	100.0	1	33.3	0.062^{ns}
Isolated proteinurea	14	40.0	7	58.3	4	100.0	0	0.0	2	66.7	
Haematuria											
Yes	16	45.7	5	41.7	3	75.0	1	33.3	1	33.3	0.766^{ns}
No	19	54.3	7	58.3	1	25.0	2	66.7	2	66.7	
Renal Failure											
Yes	3	8.6	1	8.3	0	0.0	0	0.0	0	0	0.922^{ns}
No	32	91.4	11	91.7	4	100.0	3	100.0	3	100	
HTN											
Yes	6	17.1	3	25.0	1	25.0	1	33.3	2	66.7	0.386^{ns}
No	29	82.9	9	75.0	3	75.0	2	66.7	1	33.3	
Oedema											
Yes	34	97.1	12	100.0	3	75.0	2	66.7	3	100.0	0.058^{ns}
No	1	2.9	0	0.0	1	25.0	1	33.3	0	0.0	

NOS : Not otherwise specified

The biochemical parameters that were used in our study were 24-hrs urinary protein, Urinary protein/ creatinine ratio, serum albumin, serum cholesterol, serum creatinine and low serum C3. However, no biochemical parameter was significantly associated with histomorphological patterns (p>0.05) (Table-III).

In this study, all of the 57 cases had segmental sclerosis while more than half of the cases (61.4%) showed global sclerosis. Increased mesangial matrix was the most frequent (94.7%) histologic finding in the sclerosed glomeruli followed by increased mesangial cellularity (87.7%), thickened glomerular basement membrane(29.8%) and endocapillary proliferation(3.5%) (Table V).

Table III. Association between histomorphological patterns of FSGS with biochemical parameters (n=57)

Biochemical parameter	Histomorphological patterns										P value
	NOS (n=35)		Perihilar (n=12)		Tip (n=4)		Collapsing (n=3)		Cellular (n=3)		
24-hrs urinary protein (gm) Mean±SD	5.31±3.21		4.76±2.02		5.25±2.35		2.69±0.53		6.5±3.91		[a]0.437[ns]
U.protein/ creatinine ratio Mean±SD	1.75±2.18		1.91±2.46		2.32±2.31		1.5±1.31		1.87±1.85		[a]0.987[ns]
S. albumin Mean±SD (gm/dl)	2.33±0.45		2.41±0.6		1.95±0.71		2.27±0.46		2.33±0.76		[a]0.656[ns]
Raised S. Cholesterol (mg/dl)											
Yes	17	48.6	4	33.3	2	50.0	3	100.0	1	33.3	[b]0.336[ns]
No	18	51.4	8	66.7	2	50.0	0	0.0	2	66.7	
S. Creatinine (mg/dl) Mean±SD	1.58±1.37		2.33±2.57		1.42±0.91		1.36±0.92		1.03±0.15		[a]0.615[ns]
S. C3 (Low)											
Yes	2	5.7	0	0.0	0	0.0	1	33.3	0	0.0	[b]0.213[ns]
No	33	94.3	12	100.0	4	100.0	2	66.7	3	100.0	

After evaluation of histomorphological patterns, NOS was the most frequent(61.4%) along with collapsing and cellular was the least frequent (5.3%) variants of FSGS (Table-IV).

Table-IV. *Distribution of the study patients by histomorphological patterns (n=57)*

Histomorphological patterns	Number of patients	Percentage
NOS	35	61.4
Perihilar	12	21.1
Tip	4	7.0
Collapsing	3	5.3
Cellular	3	5.3

Table V. *Distribution of the study patients by histological findings (Glomerulus) (n=57)*

Glomerulus	No. of patients	Percentage
Number of Glomerulus		
Mean±SD	13.97±4.05	
Range (min-max)	9-28	
Segmental sclerosis		
Present	57	100.0
Mean±SD	2.56±1.84	
Range (min-max)	1-8	
Global sclerosis		
Present	35	61.4
Absent	22	38.6
Mean±SD	2.76±2.82	
Range (min-max)	1-14	
Increased mesangial matrix	54	94.7
Increased mesangial cellularity	50	87.7
Thickened glomerular basement membrane	17	29.8
Endocapillary proliferation	2	3.5

Table VI : Association between histomorphological patterns of FSGS with additional histological findings (n=57) of tubulo interstitial compartment

Tubulo interstitial compartment	Histomorphological patterns										P value
	NOS (n=35)		Perihilar (n=12)		Tip (n=4)		Collapsing (n=3)		Cellular (n=3)		
	n	%	n	%	n	%	n	%	n	%	
Interstitial fibrosis	34	97.1	12	100.0	4	100.0	3	100.0	3	100.0	0.169^{ns}
Interstitial fibrosis and tubular atrophy (IFIA)	21	60.0	5	41.7	2	50.0	1	33.3	1	33.3	0.690^{ns}
Thick walled blood vessels	23	65.7	8	66.7	0	0.0	0	0.0	0	0.0	0.006^{s}
Chronic inflammation	19	54.3	5	41.7	2	50.0	1	33.3	1	33.3	0.871^{ns}
Interstitial oedema	18	51.4	2	16.7	3	75.0	1	33.3	1	33.3	0.180^{ns}
Arteriolar hyalinosis	9	25.7	3	25.0	0	0.0	0	0.0	0	0.0	0.519^{ns}
Tubular injury	5	14.3	0	0.0	1	25.0	0	0.0	0	0.0	0.472^{ns}
Others (Int.granulom)	1	2.8	0	0.0	0	0.0	0	0.0	0	0.0	-

s=significant, ns= not significant, p value reached from Chi-square test. NOS : Not otherwise specified

Considering additional pathologic findings of tubulo interstitial compartment, thick walled blood vessels were found in 23(65.7%) of NOS variant and 8(66.7%) of perihilar. No case of tip, collapsing or cellular variant had thick walled blood vessels. Thick walled blood vessels was significantly (p<0.05) higher in perihilar variant. Other additional histological findings (interstitial fibrosis, interstitial fibrosis with tubular atrophy, chronic inflammation, interstitial oedema, arteriolar hyalinosis, tubular injury and interstitial granuloma) were not significantly (p>0.05) associated with histomorphological patterns (Table 6, Figure 2, figure 3)

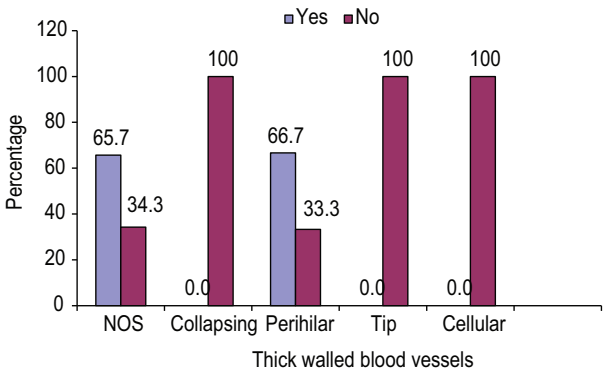

Fig.-2: *Bar diagram showing the association between histomorphological patterns with thick walled blood vessels*

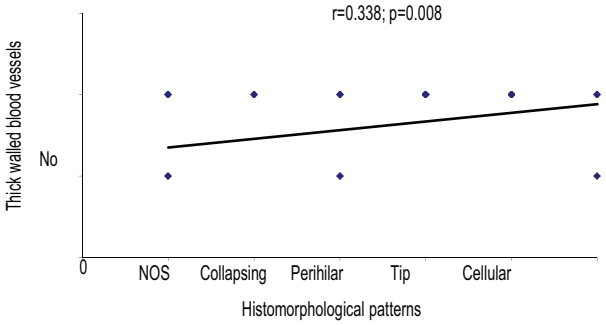

Fig.3: *Scatter diagram showing correlation between histomorphological patterns with thick walled blood vessels.*

Discussion:

In this study, it was observed that more than one fourth (26.3%) patients belonged to age between 21-30 years. The mean age was 27.4±16.2 years ranging from 1 to 72 years. Nearly two thirds (59.6%) patients were male and 40.4% were female. The mean duration of disease prior to biopsy was 1.73±0.96 years ranging from 0.5 to 4.4 years. Five (8.8%) patients had previous history of biopsy and 3(5.3%) patients had positive family history. In a study by Shakeel et al., there were 120 (65.2%) males and 64 (34.8%) females and the mean age of the patients was 30.62±12.02 years.[6] In another study by Das et al., among 65 patients of FSGS, 46 were males and 19 were females. In that study 24 biopsies were derived from children (<18 years of age), while only two patients were more than 50 years in age. [7]

Table VII. Results of different studies on histological variants of FSGS

Study, (Year)	Country	Total cases	Histomorphological variants (%)				
			NOS	Perihilar	Tip	Collapsing	Cellular
Present study, 2022	Bangladesh	57	35(61.4%)	12(21.1%)	4(7.0%)	3(5.3%)	3(5.3%)
Kawaguchi et al.[12]	Japan	194	145(48%)	47(15%)	57(19%)	5(15%)	40(13%)
Swarnalatha et al.[9]	India	116	78(62.2%)	13(11.2%)	9(7.7%)	5(4.3%)	11(9.4%)
D'Agati et al.[5]	Belgium	148	94(68%)	10(7%)	14(10%)	16(12%)	4(3%)
Arias et al.[13]	Colombia	288	224(78%)	14(5%)	40(14%)	10(3%)	-
Shakeel et al.[6]	Pakistan	184	141(77%)	2(1%)	18(9.6%)	22(11.9%)	1(0.5%)
Taneda et al. [14]	Japan	80	19(24%)	13(16%)	24(30%)	13(16%)	11(14%)
Thomas et al.[10]	USA	196	83(42%)	52(2%)	34 (17%)	22(11%)	6(3%)
Stokes et al.,[15]	USA	225	87(38.6%)	-	60(26.7%)	56(24.9%)	22(9.7%)
Chun et al.[16]	USA	87	36(41.3%)	-	11(12.8%)	40(45.9%)	-

In the mentioned two studies, FSGS, NOS was the most frequent, both in children and adults while collapsing FSGS was the least frequent in children and cellular variant was the least frequent in adults.[6,7]

In the present study, regarding histomorphological patterns, it was observed that 35(61.4%) biopsies were diagnosed as not otherwise specified (NOS), 12(21.1%) biopsies as perihilar, 4(7.0%) biopsies as tip, 3(5.3) biopsies as collapsing and 3(5.3) biopsies as cellular variant. Distribution of different variants of FSGS have been evaluated by many studies and there is variation in their observation (Table VII)

In the present study, all four patients of tip variant had isolated proteinuria, three (75.0%) patients had oedema and haematuria, no patient of tip variant had NS or renal failure. In a similar study, Kwon YE et al reported that, at presentation, nephrotic-range proteinuria occurred more commonly in tip lesion than in other variants.[8]

Swarnalatha G et al observed that majority of patients with tip variant had nephrotic range proteinuria and the amount of proteinuria was highest in this variant than in other variants. Regarding biochemical parameters, urinary protein/ creatinine ratio was highest in tip variant (2.32±2.31).[9] Thomas et al in their study found that at presentation, tip lesion had severe NS with mean 24-h protein excretion of 9.7 g/day.[10] Deegens et al showed that renal function was significantly better in patients with the tip variant compared with NOS ($P < 0.05$). More patients with tip variant presented with NS compared with patients with NOS and perihilar variants ($P < 0.01$).[11]

In this study, all the patients of collapsing variant presented with nephrotic syndrome (NS), one patient (33.3%) had haematuria, one patient (33.3%) had hypertension and no patient had renal faiure. Regarding biochemical parameters, raised serum cholesterol was found in all patients of collapsing variant. Swarnalatha G et al observed that majority of patients with collapsing variant had nephrotic range proteinuria. They also observed that a higher percentage of patients with the collapsing and cellular variants had renal failure at the time of presentation.[9] Thomas et al in their study found that at presentation, collapsing lesion had severe NS with mean 24-h protein excretion of 10.0 g/day.[10]

In our study, one (33.3%) patient of cellular variant had NS, one (33.3%) patient had haematuria and 2(66.7%) patients had hypertension. The mean 24-hrs urinary protein was highest in cellular variant (6.5±3.91 gm/day). Das et al. found mean serum creatinine level 0.96±0.2 mg/dL in the cellular variant compared with 4.43±3.25 mg/dL in the collapsing variant in their study.[7]

In this study, among 12 cases of perihilar variant, 5(41.7%) cases had NS, 5(41.7%) cases had haematuria and 3(25%) cases had hypertension. Highest level of serum creatinine was found in perihilar variant (2.33±2.57 mg/dl).

Among 35 patients of NOS, 21(60%) patients presented with NS, 16(45.7%) patients had haematuria, 3(8.6%) patients had renal failure and 6(17.1%) patients had hypertension. Thomas et al in their study found that at presentation perihilar and NOS variant had less proteinuria with mean

24-h urinary protein excretion 4.4 and 5.5 g/day, respectively.[10] In a similar study, D'Agati et al. observed that individuals with NOS variant were more likely to have subnephrotic proteinuria (P=0.01).[5]

In our study, however, no clinical and biochemical parameter was significantly associated with histomorphological patterns.

Regarding additional histologic findings, it was observed that 54(94.7%) cases had increased mesangial matrix, 50(87.7%) cases had increased mesangial cellularity; 17(27.8%) had thickened glomerular basement membrane and 2(3.5%) had endocapillary proliferation. The mean number of glomerulus showing segmental sclerosis was 2.56±1.84 ranging from 1 to 8. The mean number of glomerulus showing global sclerosis was 2.76±2.82 ranging from 1 to 14. In a study, Alsaad and Herzenberg observed that the earliest morphological change in FSGS was mesangial expansion due to increased mesangial matrix deposition and a mild increase in mesangial cellularity and hypertrophy of mesangial cells. [17]

In our study, regarding additional histologic findings of tubulo interstitial compartment, it was observed that 56(98.2%) biopsies had interstitial fibrosis, 31(54.4%) had thick walled blood vessels, 30(52.6%) had interstitial fibrosis with tubular atrophy, 28(49.1%) had chronic inflammation, 25(43.9%) had interstitial oedema, 11(19.3%) had arteriolar hyalinosis, and one (1.8%) biopsy had interstitial granuloma. Farris and Colvin showed that tubular atrophy (TA) was considered as a result of vascular compromise and resulted in loss of specialized transport and metabolic activity.[18] Histologically, TA is typically manifested by small tubules with cells having pale cytoplasm or dilated and thin tubules. They also observed that TA was usually associated with interstitial fibrosis (IF). In a recent study, Leatherwood et al. reported that interstitial fibrosis and tubular atrophy (IFTA) and thick walled blood vessels were frequent histologic features of FSGS in renal biopsies.[19] Haruhara et al. reported that among the histopathological characteristics, only the severity of interstitial fibrosis and/or tubular atrophy exhibited a significant association with hypertension. In addition, a moderately advanced grade of interstitial fibrosis and tubular atrophy was found to be significantly associated with overt proteinuria and impaired renal function.[20]

In this study, 8(66.7%) cases of perihilar variant had thick walled blood vessels and 23(65.7%) of NOS had the same histologic finding. No biopsy of tip, collapsing or cellular variant had thick walled blood vessels. Therefore, thick walled blood vessels was significantly (p<0.05) higher in perihilar variant. Other histological findings (interstitial fibrosis, interstitial fibrosis with tubular atrophy, chronic inflammation, interstitial oedema, arteriolar hyalinosis, tubular injury and interstitial granuloma) were not significantly (p>0.05) associated with histopathologic variants. In a study, Nanayakkara et al. reported that interstitial fibrosis and tubular atrophy with or without nonspecific interstitial mononuclear cell infiltration was the dominant histopathological observation in FSGS. [21] In the same study, features of vascular pathology such as vascular wall thickening and arteriolar hyalinosis were also common.[21]

In our study, a Spearman's weak positive correlation was observed between histomorphological variants with thick walled blood vessels (r=0.338; p=0.008).

Conclusion:

This study was conducted to observe various histomorphological patterns of FSGS intended for prognosis of the patients and to correlate those patterns with clinical and biochemical parameters. Cases were collected from two tertiary care hospitals in Bangladesh. It was observed that among 57 cases of FSGS, 35(61.4%) were categorized as NOS, 12(21.1%) were perihilar, 4(7%) were tip, 3(5.3%) were collapsing and 3(5.3%) were cellular variants. However, no clinical or biochemical parameter was significantly associated with histomorphological variants. However, considering additional histologic findings, thick walled blood vessels was significantly associated with histomorphologic patterns of FSGS. Larger scale multicentric studies with detailed clinical information, complete light, immunofluorescence and electron microscopic examinations as well as genetic testing may explore significant associations of histomorphological patterns with clinical and biochemical parameters.

References:

1. Rosenberg, A.Z. and Kopp, J.B., Focal segmental glomerulosclerosis. Clinical Journal of the American Society of Nephrology, 2017. *12*(3), pp.502-517.
2. John R.goldblum, et al. Rosai and Ackerman's surgical pathology. (Kambham, N., Ed.)Advances in Anatomic Pathology, 2012, 11th editiion vol-1, Mosby, london, PP. 1101- 1210.
3. McGrogan, A., Franssen, C. F. M., and De Vries, C. S. The incidence of primary glomerulonephritis worldwide: A systematic review of the literature. Nephrology Dialysis Transplantation, 2011, 26(2) ,pp. 414–430
4. Islam, S. M. J., Alam, S. M., and Islam, M. M. U. Trend of Changing Morphological Pattern of Adult Nephrotic Syndrome, Global and Bangladesh Perspective. Journal of Armed Forces Medical College, Bangladesh , 2016, 12(1) ,pp. 100–108.
5. D'Agati, V. D., Alster, J. M., Charles Jennette, J., Thomas, D. B., Pullman, J., Savino, D. A., Cohen, A. H., Gipson, D. S., Gassman, J. J., Radeva, M. K., Moxey-Mims, M. M., Friedman, A. L., Kaskel, F. J., Trachtman, H., Alpers, C. E., Fogo, A. B., Greene, T. H., and Nast, C. C., Association of histologic variants in FSGS clinical trial with presenting features and outcomes. Clinical Journal of the American Society of Nephrology, 2013, 8(3) ,pp. 399–406.
6. Shakeel, S., Mubarak, M., Kazi, J.I., Jafry, N. and Ahmed, E., Frequency and clinicopathological characteristics of variants of primary focal segmental glomerulosclerosis in adults presenting with nephrotic syndrome. Journal of nephropathology, 2013, *2*(1), pp.28-35.
7. Das, P., Sharma, A., Gupta, R., Agarwal, S.K., Bagga, A. and Dinda, A.K., Histomorphological classification of focal segmental glomerulosclerosis: A critical evaluation of clinical, histologic and morphometric features. Saudi Journal of Kidney Diseases and Transplantation, 2012, *23*(5), pp.1008-1016.
8. Kwon, Y.E., Han, S.H., Kie, J.H., An, S.Y., Kim, Y.L., Park, K.S., Nam, K.H., Leem, A.Y., Oh, H.J., Park, J.T. and Chang, T.I., Clinical features and outcomes of focal segmental glomerulosclerosis pathologic variants in Korean adult patients. BMC nephrology, 2014, 15(1), pp.1-9.
9. Swarnalatha, G., Ram, R., Ismal, K.M., Vali, S., Sahay, M. and Dakshinamurty, K.V., Focal and segmental glomerulosclerosis: does prognosis vary with the variants? Saudi Journal of Kidney Diseases and Transplantation, 2015, *26*(1), pp.173-181.
10. Thomas, D.B., Franceschini, N., Hogan, S.L., Ten Holder, S., Jennette, C.E., Falk, R.J. and Jennette, J.C., Clinical and pathologic characteristics of focal segmental glomerulosclerosis pathologic variants. Kidney international, 2006, *69*(5), pp.920-926.
11. Deegens, J.K., Steenbergen, E.J., Borm, G.F. and Wetzels, J.F., Pathological variants of focal segmental glomerulosclerosis in an adult Dutch population—epidemiology and outcome. Nephrology Dialysis Transplantation, 2008, *23*(1), pp.186-192.
12. Kawaguchi, T., Imasawa, T., Kadomura, M., Kitamura, H., Maruyama, S., Ozeki, T., Katafuchi, R., Oka, K., Isaka, Y., Yokoyama, H. and Sugiyama, H, Focal segmental glomerulosclerosis histologic variants and renal outcomes based on nephrotic syndrome, immunosuppression and proteinuria remission. Nephrology Dialysis Transplantation. 2021, 25(2), pp.153-159
13. Arias, L.F., Jimenez, C.A. and Arroyave, M.J, Histologic variants of primary focal segmental glomerulosclerosis: presentation and outcome. Brazilian Journal of Nephrology, 2013, 35, pp.112-119.
14. Taneda, S., Honda, K., Uchida, K., Nitta, K., Yumura, W., Oda, H. and Nagata, M., Histological heterogeneity of glomerular segmental lesions in focal segmental glomerulosclerosis. International urology and nephrology, 2012, *44*(1), pp.183-196.
15. Stokes, M.B., Valeri, A.M., Markowitz, G.S. and D'Agati, V.D, Cellular focal segmental glomerulosclerosis: clinical and pathologic features. Kidney international, 2006, 70(10), pp.1783-1792.
16. Chun, M.J., Korbet, S.M., Schwartz, M.M. and Lewis, E.J., Focal segmental glomerulosclerosis in nephrotic adults: presentation, prognosis, and response to therapy of the histologic variants. Journal of the American Society of Nephrology, 2004, *15*(8), pp.2169-2177.
17. Alsaad, K.O. and Herzenberg, A.M., Distinguishing diabetic nephropathy from other causes of glomerulosclerosis: Journal of clinical pathology, 2007, 60(1), pp.18-26.
18. Farris, A.B. and Colvin, R.B., Renal interstitial fibrosis: mechanisms and evaluation in: current opinion in nephrology and hypertension. Current opinion in nephrology and hypertension, 2012, 21(3), pp.289-300.
19. Leatherwood, C., Speyer, C.B., Feldman, C.H., D'Silva, K., Gómez-Puerta, J.A., Hoover, P.J., Waikar, S.S., McMahon, G.M., Rennke, H.G. and Costenbader, K.H., Clinical characteristics and renal prognosis associated with interstitial fibrosis and tubular atrophy (IFTA) and vascular injury in lupus nephritis biopsies. In Seminars in arthritis and rheumatology, 2019, 49(3), pp. 396-404.
20. Haruhara, K., Tsuboi, N., Koike, K., Fukui, A., Miyazaki, Y., Kawamura, T., Ogura, M. and Yokoo, T., Renal histopathological findings in relation to ambulatory blood pressure in chronic kidney disease patients. Hypertension Research, 2015, 38(2), pp.116-122.
21. Nanayakkara, S., Komiya, T., Ratnatunga, N., Senevirathna, S.T.M.L.D., Harada, K.H., Hitomi, T., Gobe, G., Muso, E., Abeysekera, T. and Koizumi, A., Tubulointerstitial damage as the major pathological lesion in endemic chronic kidney disease among farmers in North Central Province of Sri Lanka. Environmental health and preventive medicine, 2012, 17(3), pp.213-221.