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FREQUENCY OF FOCAL AND SEGMENTAL GLOMERULOSCLEROSIS (FSGS) DIAGNOSED ON RENAL BIOPSY AT TERTIARY CARE HOSPITAL IN KARACHI

** Abdul Rehman Qureshi, ** Naila Asif, *** Naureen Durrani, **** Alvia Saad*

* Department of Nephrology, Memon Medical Institute Hospital, Karachi. ** Department of Nephrology, Liaquat National Hospital, Karachi. *** Statistics and Quality Assurance Department, Memon Medical Institute Hospital, Karachi. **** Registrar Medicine ,Memon Medical Institute Hospital, Karachi.

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***Correspondence Author:*:**
DR. ABDUL REHMAN QURESHI
R-275, Haroon Bunglows, Phase-1, Scheme -33, Sector - 38/A University Road Karachi.
Contact no: 03452399012
Email: rehmanqureshi20155@gmail.com

ABSTRACT

Background: There has been marked variation in the trend of frequency of Glomerulonephritis around the world. Retrospective data showed that focal segmental glomerulosclerosis (FSGS) was the most common form of Primary Glomerulonephritis. Similar retrospective analysis done in Pakistan showed focal segmental glomerulosclerosis (FSGS) as the leading histopathological diagnosis. To our knowledge there was no prospective data available in Pakistan that showed the frequency of focal segmental glomerulosclerosis (FSGS) in renal biopsy patients at tertiary care hospital. Rationale of our study was to see frequency and burden of focal segmental glomerulosclerosis (FSGS) diagnosed on renal biopsies done at a tertiary care setting. **Methods**: It was a cross sectional study conducted at Aga Khan University Hospital, Nephrology Section from 2nd December 2011 to 2nd June 2012.Total seventy nine patients of either sex were included undergoing renal biopsy for evaluation of cause of proteinuria. Patients demographics were recorded. On discharge they were asked for follow up with report of histopathology of biopsy. Quantitative variables like age, 24 hour urinary protein excretion or protein-creatinine ratio was presented as mean ± standard deviation whereas qualitative variables i.e. gender, outcome (histopathological diagnosis) was taken as categorical. **Results:** Frequency of focal segmental glomerulosclerosis (FSGS) diagnosed at renal biopsy was 16.5 %. Among FSGS patients 9 were males (69.2%) and 4 were females (30.8%). **Conclusion:** FSGS is a common histopathological diagnosis which could be anticipated in patients with nephrotic syndrome. Large prospective trial in our part of the world is required to determine the frequency of FSGS so that approximate burden of patients suffering from focal segmental glomerulosclerosis (FSGS) could be established.

Key Words: Focal Segmental Glomerulosclerosis, Renal Biopsy, Proteinuria

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INTRODUCTION

There has been a marked variation in the trend of frequency of

Glomerulonephritis around the world and it depends on geographic areas, socioeconomic conditions, race, age and indications for renal biopsy [1-3].

In a retrospective study done by Dragovic D et al at Lenox Hill Hospital, New York showed that focal segmental glomerulosclerosis(FSGS) was the most common form of Primary Glomerulonephritis representing 37.8% of all Primary Glomerulonephritis [1]. In another research done at Northern Germany hospital showed that most frequent glomerulonephritis subtype was mesangioproliferative glomerulonephritis followed by focal and segmental glomerulosclerosis [2] .

In our part of the world a retrospective review of native renal biopsies performed in adult patients was undertaken at the Sindh Institute of Urology and Transplantation (SIUT) during the period from July 1995 to December 2008 which showed focal segmental glomerulosclerosis (FSGS) as the leading histopathological diagnosis, found in 29% of Primary Glomerulonephritis (21.2% of all renal biopsies) [3].

Similar retrospective study was done at Aga Khan University Hospital Karachi to determine the indications and pathological patterns of kidney biopsies of children which showed that the most common histopathology was minimal change disease in (37%), followed by focal segmental glomerulosclerosis in (12%) of the biopsies [4].

Primary focal segmental glomerulosclerosis is a heterogeneous disorder with differences in clinical presentation, prognosis, and response to treatment in different patients (5-10). Approximate burden of patients suffering from primary focal segmental glomerulosclerosis, that may require long term treatment, is mandatory for future health care plans.

METHODOLOGY

This Cross sectional study was conducted in Aga KhanUniversity Hospital, Department of Medicine, Nephrology Section from 2nd December 2011 to 2nd June 2012 . From the previous literature [3], frequency of (FSGS) (focal and segmental glomerulosclerosis) in kidney biopsies was 21%. Therefore taking the frequency (21%) with a bound on error of 0.09 (9 %) and with a 95% CIs, a sample of at least 79 was required. Sampling technique was nonprobability consecutive sampling. Adult patients of either sex above the age of 18 years were included undergoing renal biopsy for evaluation of cause of proteinuria. Patients who had a history of renal biopsy previously and having a prior diagnosis of systemic disease known to effect kidneys were excluded.

Focal Segmental Glomerulosclerosis was defined by [11] light microscopic evidence of areas of glomerular scarring in some glomeruli (focal lesions) in some parts of the glomerular tufts (segmental lesions). Proteinuria was defined by urinary protein level exceeding 3.5 gm per 1.73 m^2 of body-surface area per day [12] estimated by 24 hour urinary protein excretion or protein–creatinine ratio in a random urine sample [13].

We selected patients from general medicine ward admitted for renal biopsy after scrutiny for inclusion and exclusion criteria. An informed consent was taken prior to enrolment. Patients demographics like age, sex and degree of proteinuria (measured by 24hour urinary protein excretion or protein-creatinine ratio) was recorded on a preformed Performa (enclosed annexure 1). On discharge they were asked for follow up after the histopathology of biopsy is reported. On follow up biopsy report was recorded as per operational definition.

All analyses were conducted by using the Statistical package for social science SPSS (Release 17.0, standard version, copyright © SPSS; 1989-02). Quantitative variables like age,24 hour urinary protein excretion or protein-creatinine ratio were presented as mean ± standard deviation whereas for qualitative variables i.e. gender, outcome (histopathological diagnosis) were taken as categorical. Frequency of outcome variable (FSGS) focal segmental glomerulosclerosis was calculated and stratified by age, gender, 24hour urinary protein excretion or protein-creatinine ratio to control the effect modifier. Chi-square test was applied to compare different . p-value 0.05 was taken as significant.

RESULTS

Patient demographics are mentioned in Table I. Among the study population, 44 were males (55.7%) and 35 were females (44.3%).We had patients aged between 17 – 74 yrs. Mean age of all the patients was 42.65±15.1 years. Mean protein to creatinine ratio or 24 hour urinary protein was 7.73±4.9. Frequency of focal segmental glomerulosclerosis diagnosed at renal biopsy was 16.5 % (figure 1).Among the patients with focal segmental glomerulosclerosis (FSGS), 9 were males (69.2%) and 4 were females (30.8%) as mentioned in Table II showing male predominance with the p-value of 0.28(statistically

FSGS DIAGNOSED ON RENAL BIOPSY

ANNEXURE 1
PERFORMA

Medical record no: _____

Age: _____ Gender: _____

24 hour urinary protein: _____ OR Protein - creatitine ratio: _____

Outcome (Histopathological diagnosis):

1. FSGS Y / N

TABLE I

	No.	**Mean(SD)**
Total	79	
Males	44	
Females	35	
Age(y)	17 – 74	42.65±15.1
Protein to creatinine ratio or 24 hour urinary protein		7.63±4.6

PATIENT DEMOGRAPHICS

TABLE II

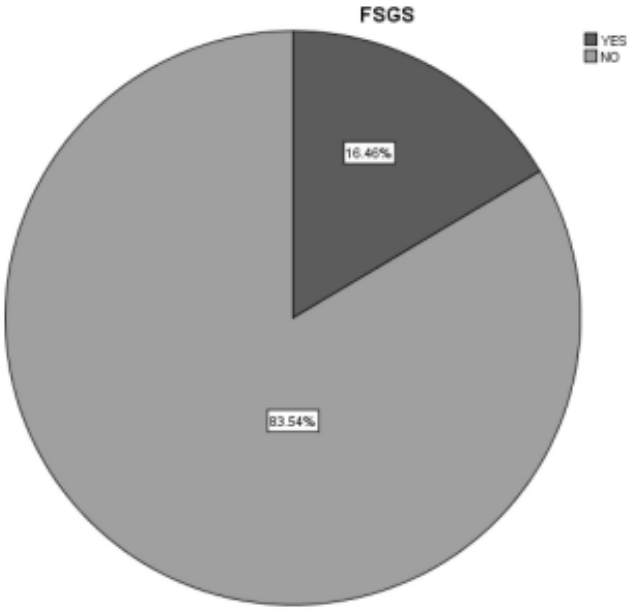
Characteristics	**FSGS yes**	**FSGS no**	**P- Value**
Total(n=79)	13	66	
Male	9	35	0.28
Female	4	31	
Protein to creatinine ratio or 24 hour			
urinary protein	7.63±4.6	7.63±5.0	
Age			
<25	1	12	
25-35	2	17	
36-45	1	10	
46-55	2	15	
>55	7	12	

OUTCOME

FSGS DIAGNOSED ON RENAL BIOPSY

FIGURE 1

FREQUENCY OF FSGS



not significant). Mean protein to creatinine ratio or 24 hour urinary protein in patients with focal segmental glomerulosclerosis was 7.63±4.6. Total 7 patients in focal segmental glomerulosclerosis group (53.8%) were more than 55 years of age while 1 patient in focal segmental glomerulosclerosis (FSGS) group (7.6%) was less than 25 years of age which showed that focal segmental glomerulosclerosis is usually diagnosed or associated with increasing age group.

DISCUSSION

Focal segmental glomerulosclerosis (FSGS) is a type of nephrotic syndrome [14] and an important cause of kidney injury in adults causing ESRD in with a prevalence of 4% [11-12] in developed world. Focal segmental glomerulosclerosis accounts for only a small percentage of cases of idiopathic nephrotic syndrome in children, it represents as many as 35% of cases in adults [13]. There have been an increased prevalence of focal segmental glomerulosclerosis (FSGS) in both adults and children in a number of different countries on different continents [15]. Early recognition of the disease is important for timely management of the disease.

Most patients with idiopathic focal segmental glomerulosclerosis present with either asymptomatic proteinuria or full nephrotic syndrome [13]. In children,10% to 30% of patients with asymptomatic proteinuria are most commonly detected on routine checkups and sports physical examinations; in adults, asymptomatic detection occurs at military induction examinations,obstetric checkups, and insurance of employment physical examination. The incidence of nephrotic-range proteinuria at onset in children is 75 to 90 %, whereas only 50% to 60 % of adults with focal segmental glomerulosclerosis presents with nephrotic syndrome [14]. Edema is, by far, the most common manifestation of focal segmental glomerulosclerosis (FSGS). Secondary forms of focal segmental glomerulosclerosis associated with hyperfiltration, such as remnant kidney and obesity – related glomerulopathy, typically have lower levels of proteinuria, and many such patients have subnephrotic proteinuria and a normal serum albumin concentration [14].

Hypertension is found in 30% to 50 % of children and adults with focal segmental glomerulosclerosis (FSGS) at the time of diagnosis [14]. Microscopic hematuria is found in 25% to & 5% of these patients, and a decreased GFR (Glomerular filtration rate) is noted at presentation in 20% to 30 % [13]. Daily urinary protein excretion ranges from less than 1 to more than 30g/day. Proteinuria is typically nonselective. Complement levels and other serologic test results are normal. Occasional patients will have glycosuria, aminoaciduria, phosphaturia, or a concentrating defect indicating functional tubular damage as well as glomerular injury [14].

Although primary focal segmental glomerulosclerosis is potentially treatable and curable in many patients, the optimal type and duration of immunosuppressive therapy as well as adjunctive therapy remains controversial.However,in recent trials using longer(>6 months) courses of corticosteroids, the results have been much more promising [13,16-17].A number of studies have used low dose cyclosporine to treat corticosteroid-resistant focal segmental glomerulosclerosis [18-19]. Complete plus partial remission rates of 60% to 70% have been achieved versus only 17% to 33% in the placebo groups.

The natural history of focal segmental glomerulosclerosis is varied. Without therapy or response to therapy, the majority of patients with primary focal segmental glomerulosclerosis will experience progressive increase in proteinuria and progression to renal failure (20). Only 5 % to 25 % of patients undergo a spontaneous remission of proteinuria. Both unresponsive children and adult have a similar course; most develop

End Stage Renal Disease 5 to 20 years after presentation, with approximately 50 % of such patients reaching End Stage Renal Disease by 10 years [21].

The approach to a diagnosis of focal segmental glomerulosclerosis has been problematic because the morphologic features are nonspecific and can occur in a variety of other conditions or superimposed on other glomerular processes. As mentioned above the defining glomerular lesion is focal, it may not be adequately sampled in small needle biopsies. Focal segmental glomerulosclerosis represents a common phenotypic expression of diverse clinicopathologic syndromes with distinct etiologies [22]. Causes are as varied as genetic mutations in podocyte proteins, circulating permeability factors, viral infections, drug toxicities, maladaptive responses to reduced number of functioning nephrons, and hemodynamic stress place on an initially normal nephron population.

As mentioned earlier there has been a marked variation in the trend of frequency of focal segmental glomerulosclerosis [1-4] around the world depending upon the geographic areas, socioeconomic conditions, race, age and indications for renal biopsy. Dragovic D et al found out at Lenox Hill Hospital, New York that focal segmental glomerulosclerosis was the most common form of Primary Glomerulonephritis representing 37.8% of all Primary Glomerulonephritis [1].Similarly in Brazil, focal segmental glomerulosclerosis (FSGS)is currently the most common primary renal disease [23].

Recent retrospective data analysis done at the Sindh Institute of Urology and Transplantation (SIUT) Pakistan during the period from July 1995 to December 2008 showed that the frequency of focal segmental glomerulosclerosis was 21.2% of all renal biopsies [3].When comparing our study from study done at SIUT, there is variation in outcome of biopsy results. This may be due to small sample size as compare previous study [3], duration of study and inclusion criteria of renal biopsies as we included patients only with nephrotic syndrome and proteinuria of more than 3.5 gm/24 hours.

There was a study done at Aga Khan University Hospital Karachi by Absar A et al [4] to determine the indications and pathological patterns of kidney biopsies of children which showed that the most common histopathology was minimal change disease in (37%), followed by focal segmental glomerulosclerosis in (12%) of the biopsies. This retrospective analysis was done specifically in children and as we know minimal change disease is the most common histopathological pattern of nephrotic syndrome in pediatric population [14]. We included adult population at same tertiary care center and when comparing our study' result (frequency of focal segmental glomerulosclerosis) with the above mention ten year experience of renal biopsies [4], it is clear that our frequency of focal segmental glomerulosclerosis is higher. This may reflect the study population age group as pattern of nephrotic syndrome varies with pediatric to adult population [14].

Our study also showed that focal segmental glomerulosclerosis is more common in males as compared to in females (statistically not significant).

From this study, it can be visualized that focal segmental glomerulosclerosis is a fairly common entity in patients with nephrotic syndrome and its frequency can be varied depending upon geographic areas, socioeconomic conditions, race, age and biopsy indication.

CONCLUSION

Focal segmental glomerulosclerosis is a common histopathological diagnosis which could be anticipated in patients with nephrotic syndrome. Large prospective trial in our part of the world is required to determine the frequency of focal segmental glomerulosclerosis so that approximate burden of patients suffering from focal segmental glomerulosclerosis could be established.

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Authors contribution:
* Concept of study, literature search, data coollection, ** Data collection and manuscript writing, *** Data analyysis, **** Data collection and results interpretation.

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