REV SEN
rev-sen.ec

OPEN ACCESS

Characterization and treatment of adult patients with focal and segmental glomerulosclerosis: A multicenter observational study.

Nathaly Elizabeth Rivadeneira Guillen [ID] [1] *, Junior Rafael Gahona Villegas [ID] [1], Ramiro Iván López Pulles [ID] [1]

1. Postgraduate Nephrology, Faculty of Medical Sciences, Universidad Central del Ecuador.

Received: Jun 12, 2022
Accepted: Aug 13, 2023
Published: Aug 26, 2023
Editor: Dr. Franklin Mora Bravo.

Cite:
Rivadeneira N, Gahona J, Lopez R. Characterization and treatment of adult patients with focal and segmental glomerulosclerosis: A multicenter observational study. REV SEN 2023;11(2):136-146.

DOI: http://doi.org/10.56867/62
Sociedad Ecuatoriana de Nefrología, Diálisis y Trasplantes.

ISSN-L: 2953-6448

Abstract

Introduction: Glomerulopathies constitute the third cause of chronic kidney disease. Within these, focal segmental glomerulosclerosis (FSGS) is one of the most prevalent in Latin America, with varied clinical presentation and etiology, as well as different treatment and evolution for each patient. The study aimed to characterize patients with histological diagnosis of FSGS based on their clinical presentation, evolution, and treatment in three public nephrology reference hospitals in Quito-Ecuador.

Methods: The present observational, longitudinal, retrospective study was conducted from January 2012 to December 2020 at the Hospitals Carlos Andrade Marín, Eugenio Espejo, and Hospital de las Fuerzas Armadas N1. The variables were demographic, clinical, laboratory, and treatment. Descriptive statistics, proportions, and confidence intervals for a proportion are used. A follow-up of 6, 12, and 24 months was carried out.

Results: 98 FSGS records were analyzed, constituting 15.2% of all kidney pathologies. This pathology was more frequent in men (60.2%) and Hispanics (98%), with a median age of 40. 95.9% and 67.3% of the patients had no history of diabetes or hypertension, respectively. The main symptom at diagnosis was nonnephrotic proteinuria (65.3%), and 7.1% of patients needed dialysis at the onset of the disease. At six months, only 24% of patients achieved remission. The most common first-line treatments were corticosteroids, followed by mycophenolate, while the most frequently used second-line drug was cyclosporine.

Conclusion: Less than half of the patients achieved remission at six months, and a small percentage of patients deteriorated renal function at two years.

Keywords:

MeSH: Glomerulosclerosis, Focal Segmental; Cyclosporine; Adrenal Cortex Hormones; Observational Study; Renal Insufficiency, Chronic; Nephrology; Proteinuria.

* Corresponding author

Email: Nathaly Elizabeth Rivadeneira Guillen < naty_rigui09 @hotmail.com >/Address: Iquique 132, Quito 170136. Postgraduate Department, Medicine Campus. Central University of Ecuador. Telephone: (02) 252-8810 REV SEN. 2023;11(2):136-145 |

Focal and segmentary glomerulosclerosis (FSGS) represents a group of diseases with a typical histological pattern with injury to the podocyte [1]. Kidney damage is characterized by the presence of sclerosis/hyalinosis lesions that affect a variable percentage of glomeruli (focal) and only a part of them (segmental) [1]. The approximate annual incidence of FSGS is 1.4 to 25 cases per million inhabitants [2]. Its prevalence has increased in recent years worldwide with variations due to geographical, genetic, age, and sex factors [3]. In a retrospective study conducted at the Cleveland Clinic from 2015 to 2021, FSGS was the most common diagnosis found (15%), along with diabetic nephropathy [4].

Ethnicity plays an essential role in the presentation of this pathology, having an incidence five times higher in African patients than in Caucasian patients. This difference is due to the presence of two risk variants, apolipoprotein L1 (APOL1) and myosin heavy chain 9 (MYH9), found in 60% of black patients compared to Caucasian patients, where it is only found in 5% [1]. In a retrospective study, the difference in nephrotic syndrome in adults was observed according to the patient's ethnicity. It was found that FSGS was the most frequent cause of nephrotic syndrome in patients of African ethnicity [5].

It occurs more frequently in men than in women at a ratio of 1.5 to 1 [2]. Although this pathology can occur at any age, it is more common in adult patients and is responsible for 20 to 30% of nephrotic syndrome in adults and 7 to 10% in children [1]. Among the diseases causing primary nephrotic syndrome, FSGS is the one that most frequently progresses to end-stage CKD [1]. It recurs in kidney transplantation in 30 to 40% of patients [6].

Although the exact cause has not yet been identified, the presence of an unknown circulating factor has been mentioned as an etiological agent. The existence of this factor is supported by the immediate reappearance of this pathology in 20 to 50% of patients undergoing kidney transplantation and up to 80% in those with a history of rejection in a previous graft [7].

Different molecules have been implicated in the pathogenesis of this glomerulopathy. These include apA1b (an isoform of ApoA1), corticotrophin-like cytokine factor, anti-CD40 antibody, and soluble urokinase receptor (suPAR) [7]. In particular, suPAR has attracted significant interest recently due to its ability to cause diffuse pedicellar fusion and proteinuria [7]. According to a study by Wei et al., suPAR levels were elevated in 70% of patients with FSGS, and these levels were significantly higher than those in patients with other glomerulopathies (membranous nephropathy and minimal change disease) or healthy controls [7]. Given that this factor is also elevated in other pathologies that are not associated with proteinuria and kidney damage, such as rheumatoid arthritis, sepsis, tumors, and liver cirrhosis, its role as a pathogenic factor in this glomerulopathy remains the subject of debate [7, 8].

Among the secondary causes of FSGS are viral infections, drug use, and adaptive causes that can occur with a reduced number of nephrons or with several nephrons within the normal range, such as obesity or hyperfiltration in type diabetes. 2 [6].

A specific group is the genetic type FSGS. In most cases, the age of presentation begins in early childhood. Nine genes have been implicated in the development of this pathology: ACTN4, NPHS2, TRPC-6, PLCE1, INF-2, WT1, CD2AP, LAMB2, and NPHS1 [6, 9].

The objective of the present study was to determine the frequency of FSGS and characterize it based on its clinical presentation, evolution, and treatment in a group of patients treated in three public reference hospitals in Quito-Ecuador.

Materials and methods

Study design

The study is a longitudinal descriptive observational study. The source is retrospective.

Scenery

The study was carried out in the nephrology and pathological anatomy service of the Eugenio Espejo public hospitals of the Ministry of Public Health; Carlos Andrade Marín Specialty Hospital of the Ecuadorian Institute of Social Security and Specialty Hospital of the Armed Forces No. 1, in Quito/Ecuador. The retrospective study period was from Jan 1, 2012, to Dec 31, 2020.

Participants

Cases of patients older than 17 who underwent renal biopsy due to proteinuria, hematuria, or alteration of renal function were included. Medical and laboratory controls were included after the start of treatment. Undiagnosed cases or incomplete records were excluded. Transplant patients were excluded.

Variables

The variables studied were as follows:

- Demographics: age, sex, ethnicity.
- Clinical features: edema, albumin, hypercholesterolemia, hypertriglyceridemia, body mass index, hypertension at diagnosis, comorbidities, glomerular filtration rate, proteinuria, and hematuria.
- Treatment and outcomes: initial treatment, need for dialysis, subsequent treatment and unconventional treatments.

Data sources/measurements

The source was indirect. The information was collected in an electronic database created by the authors from the medical records found in the institutions' archives. Biochemical measurements, biopsies, and treatments were part of the institution's regular activity of the institution, and they were routinely carried out in diagnostic and control studies, which were collected from each institution's laboratory and pathology systems.

Biases

To avoid possible interviewer, information, and memory biases, the data were kept at all times by the principal researcher with a guide

and records approved in the research protocol. Observation and selection bias were avoided with the application of participant selection criteria. All clinical and paraclinical variables from the period already mentioned were recorded. Two researchers independently analyzed each record in duplicate, and the variables were recorded in the database once their agreement was verified.

Study size

The population consisted of patients with chronic kidney disease associated with glomerulopathies. A total of 19,400 cases in Ecuador of patients with CKD stage 5 occurred in 2022 [10], of which it is known that FSGS is responsible for 10% of the cases [10]; that is, it would have a projection of 1940 cases as the universe. With a confidence level of 95%, an expected frequency of 10%, and a confidence limit of 5.9%, the sample size was 94 cases. Epi Info ™ Version 7.0 was used. (CDC. Atlanta, GA: Centers for Disease Control and Prevention, 2023) for sample calculation.

Quantitative variables

Descriptive and inferential statistics were used. The results were expressed on a scale of means and standard deviation. Categorical data are presented in proportions. The Kolmogorov – Smirnov normality test was used. The mean and standard deviation were applied for the normally distributed variables, while the nonnormally distributed variables were expressed using the median and 10th and 90th percentiles.

Statistical analysis

The Sturges test was used for the age variable, thus determining the ideal interval to divide the age groups.

The variables associated with follow-up (proteinuria, glomerular filtration rate, and dialysis) were evaluated at the time of diagnosis, at six months, at one year, and at two years to describe the characteristics of the evolution. The χi2 test evaluated the association between remission and the need to start dialysis. The results will be expressed with their respective 95% confidence index. The statistical package used was SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

Results

Study participants:

A total of 759 renal biopsy records were analyzed. The GEFS analysis was performed based on 92 cases at the end of the study (Figure 1). The prevalence of FSGS was established with the total number of cases requiring biopsies (Table 1).

Prevalence of FSGS

The present study included 759 biopsy records in patients over 18 years of age with a diagnosis of both primary and secondary glomerulopathies, of which the most frequent diagnosis was lupus nephropathy in 37.5% (n= 285), followed by focal glomerulosclerosis and segmental glomerulosclerosis in 15% (n=116) (Table 1).

Characteristics of the study population

Of the total number of patients with FSGS, 15 who did not have follow-up or laboratory results and three who died were excluded. The median age was 40, with 26.6% (n=26) of the patients aged between 28 and 36. A total of 60.2% (n=59) of the patients were men, 98% (n=96) were mixed race, and only 2% (n=2) were African American. A total of 18.4% (N=18) were obese, and 53.1% (n=52) were of average weight.

Among comorbidities, 32.7% (n=32) of patients had a history of hypertension, 4.1% (n=4) had diabetes, and 1% (n=1) had a previous diagnosis of HIV infection. Table 2 summarizes the characteristics of the study population.

Regarding the clinical characteristics at diagnosis, it is evident that 65.3% (n=64) of the patients presented with proteinuria in the nonnephrotic range, most of which were in stages 1 and 2 of chronic kidney disease. No hematuria was observed in 53.1% (n=52), edema was observed in 62.2% (n=61), and only 20.4% (n=20) presented high blood pressure at the time of diagnosis.

Figure 1. Flowchart of study participants.

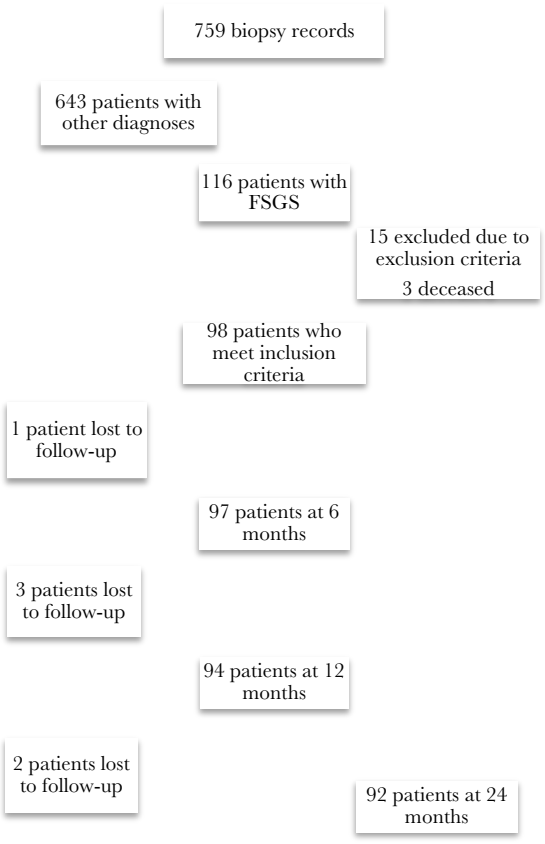


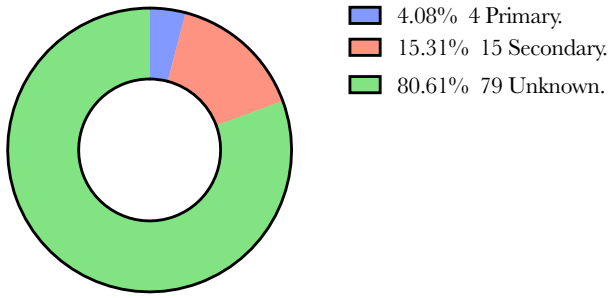
Table 1. Prevalence of glomerulopathies.

Glomerulopathy	Total= 759 n (%)
Lupus nephritis	285 (37.5%)
GEFS	116 (15.2%)
membranous	111 (14.6%)
GNMP	68 (8.96%)
NIGA	35 (4.61%)
NDE	25 (3.29%
diabetic nephropathy	13 (1.71%)
Amyloidosis	6 (0.79%)
myeloma	3 (0.40%)
Others	97 (12.7%)

FSGS: focal segmental glomerulosclerosis; MPGN: Membranoproliferative glomerulonephritis; NIGA: IgA nephropathy; MDE: Minimal Change Disease.

The presumptive etiology of the pathology was evaluated, classifying it as primary, secondary, and unknown cause. Figure 2 shows that 80.6% (n=79) of the patients presented with an unknown cause, and only 4.1% (n=4) had a primary cause as a presumptive diagnosis.

Figure 2. Distribution of cases by type of FSGS.



Total=98

Patient evolution

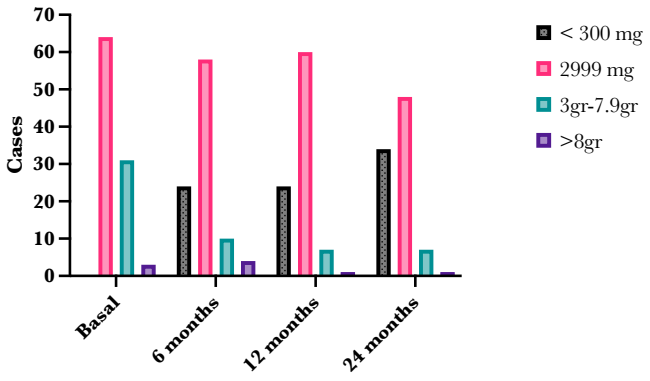
Regarding the evolution of the patients concerning proteinuria, it was observed that at six months and one year, 24.5% (n=24) of the patients had a proteinuria value of less than 300 milligrams in 24 hours, while within two years, this percentage increased to 34.7% (n=34). The highest percentage of patients during follow-up persisted with proteinuria in the nonnephrotic range, with 59.2% (n=58), 61.2% (n=60), and 49% (n=48) at 6, 12, and 24 months, respectively. At the time of diagnosis, 31.6% of patients presented nephrotic proteinuria; this percentage decreased to 10.2% at six months and 7.1% at 12 and 24 months. Patients lost during follow-up were also observed, as detailed in Figure 3.

Table 2. Demographic and clinical characteristics of the population diagnosed with focal and segmental glomerulosclerosis.

	Total = 98 n (%)
Sex	
Female	39 (39.8%)
Male	59 (60.2%)
Age (years)*	40 (29.7 - 52) 38.35 – 44.59
Age ranges	
18 - 27	19 (19.4%)
28 - 36	26 (26.5%)
37 - 45	21 (21.4%)
46 - 54	12 (12.2%)
55 - 63	9 (9.2%)
64 - 72	7 (7.1%)
73 or more	4 (4.1%)
Ethnicity:	
Half-Blood	96 (98%)
Afro-Ecuadorians	2 (2%)
BMI	24.2 (21.72 – 33.15) 24.90 - 26.74
BMI Classification	
Underweight	eleven%)
Normal	52 (53.1%)
Overweight	27 (27.6%)
Obesity	18 (18.4%)
Comorbidities	
Diabetes	4 (4.1%)
Arterial hypertension	32 (32.7%)
HIV infection	eleven%)
Proteinuria	
Nonnephrotic	64 (65.3%)
Nephrotic	31 (31.6%)
Massive	3 (3.1%)
Symptoms and signs	
Hematuria	46 (46.9%)
Edema	61 (62.2%)
Hypertension	20 (20.4%)
Hypercholesterolemia	71 (72.4%)
Hypertriglyceridemia	74 (75.5%)
Hypoalbuminemia	55 (56.1%)
Glomerular filtration rate	
Stadium 1	29 (29.6%)
Stage 2	24 (24.5%)
Stadium 3a	14 (14.3%)
Stadium 3b	15 (15.3%)
Stage 4	11 (11.2%)
Stadium 5	5 (5.1%)

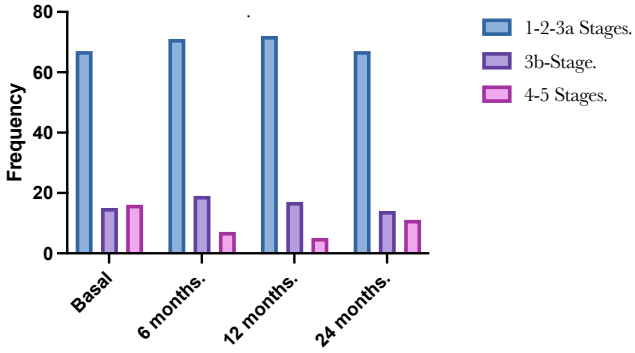
***** Age is shown as median with its respective interquartile range.

Figure 3. Evolution of proteinuria over 24 hours.



According to the CKD stages, most patients were in stage 1 at the time of diagnosis, reaching 29.6% (n=29). At six months, an increase in the percentage of patients in stage 2 was observed, reaching 34% (n=33); however, a smaller number of patients in stage 5 were also observed for diagnosis (3.2%). At 12 months of follow-up, 28.7% (n=27) of patients remained in stage 1, 36.2% (n=34) were in stage 2, and only 2.1% (n=2) reached stage 5. In contrast, at 24 months of follow-up, patients in stages 2 and 5 increased to 32.6% (n=30) and 8.7% (n=8), respectively (Figure 4).

Figure 4 . Evolution of the functional stage of patients with FSGS.



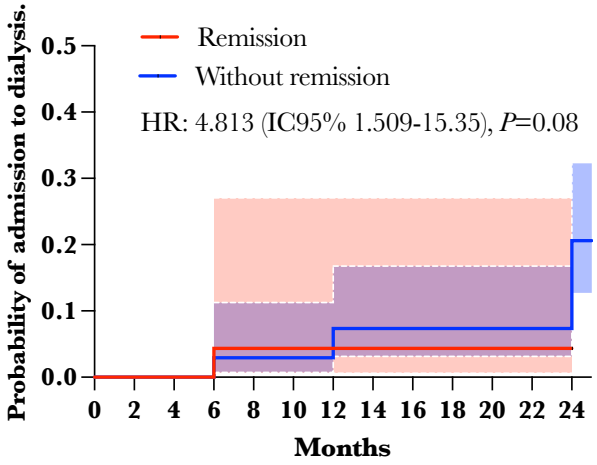
In the evolution of the disease according to the need for dialysis, 7.1% (n=7) of the patients needed initiation of dialysis at the time of diagnosis, with a slight increase in this percentage observed at the 24-month follow-up (Table 3).

Table 3. Evolution of the disease according to the need for dialysis.

Dialysis	At diagnosis n (%)	Six months n (%)	12 months n (%)	24 months n (%)
Yes	7 (7.1%)	3 (3.1%)	3 (3.2%)	9 (9.8%)
No	91 (92.9%)	94 (96.9%)	91 (96.8%)	83 (90.2%)
Total	98 (100%)	97 (100%)	94 (100%)	92 (100%)

The association between remission at six months and the need to start dialysis during follow-up was analyzed, where it was observed that at 24 months, 100% (n=9) of the patients on dialysis did not present remission. However, this association was not statistically significant ($P > 0.05$) (Figure 5).

Figure 5. Survival ratios.



Established treatment

A total of 98% (n=96) of the patients received antiproteinuric-based supportive treatment at diagnosis, as shown in Table 4. The most frequent initial treatment after corticosteroids was mycophenolate in 20.4% (n=20), followed by cyclosporine in 11.2% (n=11), and tacrolimus and azathioprine in 3.1% (n=3) each. Eighty patients received corticosteroids at the beginning of treatment, 32 used corticosteroids with another immunosuppressant, and 48 patients began treatment with corticosteroids alone.

Table 4. Initial Treatment of Patients with Focal and Segmental Glomerulosclerosis.

	With steroids	No steroids
	n (%)	n (%)
None additional	48 (60.0%)	13 (72.2%)
MMF/Azathioprine	19 (23.8%)	4 (22.2%)
Ciclosporin/Tacrolimus	13 (16.3%)	1 (5.6%)

MMF: mycophenolate.

The initial treatment was compared with the degree of proteinuria at six months, finding that remission was achieved in 13.7% (n=14) of patients who were treated only with corticosteroids, followed by 5.9% (n=6) of patients who were treated with corticosteroids plus mycophenolate. Among the patients who persisted with nonnephrotic proteinuria, 25.5% (n=26) were treated with a corticosteroid, 8.8% (n=9) with a corticosteroid plus mycophenolate and 7.8% (n=8) with a corticosteroid plus cyclosporine. It was also observed that none of the patients treated with immunosuppressants presented massive proteinuria at six months. Figure 3 summarizes the degrees of proteinuria at six months with initial treatment.

Table 5. Initial treatment and degree of proteinuria at six months.

	Remission	Non-Nephrotic	Nephrotic	Massive
ST	14 (13.7%)	26 (25.5%)	4 (3.9%)	3 (2.9%)
ST + MMF/AZA	7 (6.9%)	11 (10.8%)	1 (1%)	0 (0%)
ST+ CSA/FK	0 (0%)	9 (8.8%)	3 (3%)	0 (0%)
Medium	2 (2%)	9 (8.8)	1 (1%)	1 (1%)
MMF	1 (1%)	2 (2%)	1 (1%)	0 (0%)
CSA	0 (0%)	1 (1%)	0 (0%)	0 (0%)

ST: steroid. MMF: mycophenolate. AZA: Azathioprine. FK: tacrolimus. CSA: Cyclosporin.

For subsequent immunosuppressive treatment, it was found that the majority of patients did not receive any additional immunosuppressant as second-line treatment, representing 45.4% (n=44), 38.3% (n=36) and 45.7% (n=42) 6 months, one year and two years, respectively. At six months, the most common immunosuppressant was cyclosporine (27.8%, n=27), followed by mycophenolate (18.6%, n=18). This distribution is maintained at one and two years of follow-up, where it is evident that 29.8% (n=28) and 23.9% (n=22) of patients were treated with cyclosporine and 23.4% (n=22) and 21.7% (n=20) with mycophenolate. Table 6 summarizes the subsequent treatment used.

Table 6. Subsequent immunosuppressive treatment.

Treatment	Six months N=97	12 months N=94	24 months N=92
	n (%)	n (%)	n (%)
None	44 (45.4%)	36 (38.3%)	42 (45.7%)
Mycophenolate	18 (18.6%)	22 (23.4%)	20 (21.7%)
Cyclosporin	27 (27.8%)	28 (29.8%)	22 (23.9%)
Tacrolimus	4 (4.12%)	5 (5.3%)	6 (6.5%)
Azathioprine	4 (4.12%)	3 (3.2%)	2 (2.2%)

Among the nonconventional treatments, 5.1% (n=5) received cyclophosphamide during their follow-up, 4.1% (n=4) received plasmapheresis, and 1% (n=1) received rituximab.

Discussion

In the present study, the prevalence of FSGS was 15.2%, the second most common glomerulopathy after lupus nephropathy and the one that occupies first place within the primary glomerulopathies. It is known that the epidemiology of glomerulopathies varies according to the geographic region; for example, in Europe, the most common glomerulopathy is IgA (22%) [11]; in the United States and Latin America, FSGS, lupus nephropathy, and diabetes are the most prevalent diagnoses. In studies carried out in Peru and Mexico between 2007-2016 and 2011-2020, respectively, FSGS was the most common primary glomerulopathy, with a prevalence of 36% and 46.6% [12, 13]. These percentages differ from the present study because, in both studies, a distinction was made between primary and secondary glomerulopathies.

The present study found that at the time of diagnosis, half of the patients were under 40 years of age. Although this pathology can occur in pediatric and adult patients, the age ranges vary. These data are compared to a Japanese population between 19 and 64 (62.2%), with a median age less than or equal to 43 years [6]. In another study in Peru, the mean age was 37.2 ±16 years [14].

Regarding sex, in the present study, FSGS was more prevalent in men, data that agree with those reported by Rosenberg and Jafry, where it is mentioned that the incidence of this pathology is higher in this group with a 2:1 ratio [2, 15, 16].

Regarding ethnicity, a higher prevalence of this pathology has been described in African-American patients. This type of epidemic is demonstrated by the studies by Kitiyara and Kopp, who reported in these patients a 3 to 5 times greater risk of presenting FSGS than the general population [17, 18]. Mkbakop also reported that the most common injury pattern in African-American patients with nephrotic syndrome was FSGS [19]. These reports differ from those found in our study, where 98% of the patients were Mestizo and only 2% were Afro-Ecuadorian. This difference can be explained since ethnicity is a subjective perception of the person, and most patients in the study perceived themselves as mestizo.

With BMI (body mass index), half of the study population had a value equal to or less than 24.2, and the proportion of obese patients was 18.4%. These data are consistent with those previously found [6, 15]. Other studies, such as those by Kambham and Chen [20, 21], have studied the relationship between obesity and FSGS; however, both studies, unlike ours, included obese patients where it was shown that the most frequent histopathological pattern was FSGS, but the frequency of obesity in patients with this histopathological diagnosis was not studied.

Regarding comorbidities, 4.1% of patients had a history of diabetes, 32.7% had hypertension, and only 1% had HIV infection. The low prevalence of diabetic patients could be explained since, in these patients, renal biopsy is only indicated when there is an atypical presentation with suspicion of nondiabetic renal nephropathy [3]. Regarding hypertension, 67.3% of patients had no history of hypertension at diagnosis. These data are similar to those reported in another study in our country, where 74.3% of patients with FSGS did not present with hypertension [15]. Regarding HIV-associated nephropathy, there is an established relationship between infection with this virus and the development of collapsing-type FSGS, which is also associated with the APOL-1 gene [1]. The low prevalence of HIV infection in this study is explained by the fact that not all patients with renal involvement due to HIV are biopsied, since the indications for biopsy in these patients are similar to those of the general population.

When considering the clinical presentation at diagnosis, it was observed that although more than half of the patients presented with edema, hypoalbuminemia, and dyslipidemia, the majority of these presented nonnephrotic proteinuria at diagnosis, data consistent with those presented in studies carried out. In Ecuador, 57.1% of patients

with FSGS presented nonnephrotic proteinuria [15]. In Colombia, half of the patients with FSGS had urinary proteinuria excretion equal to or less than 688 mg in 24 hours [22]. Although FSGS is responsible for 20 to 30% of cases of nephrotic syndrome in adults, it is essential to highlight that the degree of proteinuria in this glomerulopathy varies depending on its etiology. Thus, in the primary causes, diffuse pedicellar effacement occurs abruptly, so these patients present nephrotic proteinuria in 50% to 60% of cases [23, 24]. In contrast, in secondary causes, it has been seen that the percentage of glomerular area affected by pedicellar effacement is approximately 30%, so protein excretion occurs in the nonnephrotic range [23]. The aforementioned is corroborated by the studies carried out by Jafry and Kambhan [2, 20] in patients with primary and secondary FSGS, where the mean proteinuria at diagnosis was 4697 mg in 24 hours for patients with primary FSGS and more than half of the patients with FSGS secondary to obesity presented proteinuria in the nonnephrotic range [20].

As previously mentioned, although the characteristic of FSGS is proteinuria, it has also been reported that 30% to 45% of patients present with hematuria, hypertension, and kidney damage, which could misdiagnose this pathology [25]. In the present study, at the time of diagnosis, 46.9% of the patients presented hematuria, 20.4% debuted with hypertension, and 44.1% were found in stages 3, 4, and 5 of chronic kidney disease, data similar to those reported in a study carried out in Quito, where patients with FSGS presented hematuria in 41.4%, but the percentage of patients with chronic kidney disease in stages 3, 4 and 5 was 22.4% [15]. Similar results in the percentage of hematuria were described by Ozeki et al., where this finding occurred in 32.2% of patients with FSGS [6].

When analyzing the presumptive etiology of FSGS, it was observed that 80.6% of the patients had no known cause, and a primary cause was suspected in 4.1%. The differential diagnosis between the different causes of this pathology continues to be challenging, since there is currently no specific biomarker that allows distinguishing between primary and secondary causes. In a study conducted at the Mayo Clinic, where the incidence of primary versus secondary FSGS was compared in twice, it was shown that primary FSGS represented 25% of all diagnosed patients [26]. In another study, Deegens et al. [5] evaluated the usefulness of pedicellar effacement to differentiate idiopathic from secondary FSGS and found that 17 of the 29 patients presented idiopathic FSGS. It is important to note that both studies worked with a few patients and used electron microscopy for differential diagnosis. Since we do not have this technique or genetic tests in our country, it is difficult to precisely determine the etiology of this glomerulopathy in the population.

Regarding the evolution of the patients, a follow-up was carried out at 6, 12, and 24 months, considering variables such as proteinuria, glomerular filtration rate, and need for dialysis. All patients in the study received treatment; 81.6% received corticosteroids alone or with another immunosuppressant, and 18.4% received immunosuppressive or antiproteinuric treatment. Regarding proteinuria, a gradual increase in patients who achieved remission was observed, 24.5% at six months and 34.7% at 24 months. The percentage of patients with nonnephrotic proteinuria remained at approximately 60% during the first year, with a decrease to 49% at two years. These results are similar to those reported by Rojas et al. [14], where the probability of partial or complete remission of patients with FSGS was 30.8% at 12 months.

Similarly, in another study conducted in Pakistan with 401 patients with primary FSGS, 25.5% achieved complete remission within three months [2]. In another study carried out in 5 hospitals in the United Kingdom, it was observed that the percentage of complete remission of patients was 36.8% [3]. It is essential to highlight that although the percentages of complete remission do not differ significantly, the studies above, unlike the present study, were carried out in patients with primary FSGS, where they evaluated the remission rate of the treatment instituted, which was mainly based on corticosteroids because, as we already mentioned, they are treated in patients with primary FSGS.

Regarding the glomerular filtration rate, during the 2-year follow-up, it was observed that most patients remained in stage 1. However, it is essential to highlight that an increase in patients in stage 5 was also observed. 5.1% to 8.7% during the two years of follow-up. This prevalence is reflected in the need for dialysis, where an increase is also observed in the percentage of patients who needed renal replacement therapy from diagnosis to 24 months of follow-up. No association was found between the remission of proteinuria at six months and the need for dialysis because of the small population included in our study since, as has been reported in several bibliographies, there is a direct relationship between the degree of proteinuria and the deterioration of renal function [9]. Thus, the study by Troost et al., where pediatric and adult patients were included, showed that a proteinuria value <1.5 g or a 40% reduction strongly correlates with renal survival in patients with primary FSGS [7].

Similarly, Kopp et al. [17] report that the response to corticosteroids strongly predicts renal survival, being 30% ten years after diagnosis. Along the same lines, Jafry et al. [2] analyzed the long-term clinical evolution of patients with primary FSGS, where none of the group of patients who responded to corticosteroids developed CKD or died. In contrast, 10.4% reached CKD in corticosteroid-resistant patients, and 3% died. In this study, the histopathological findings were also evaluated regarding the response to corticosteroids and remission, finding that the presence of moderate tubular atrophy was more frequent in corticosteroid-resistant patients and that patients with the "typ variant" achieved remission more frequently. Percentage with those who presented the collapsing variant. Similarly, in the study by Rojas et al. [14], it was observed that patients who were treated with corticosteroids and achieved remission had less clinical and histological severity in the renal biopsy than those who did not achieve remission, and a 12-month renal survival of 88.7% was shown. The present study differs from the latter since the findings reported in pathology were not considered.

When analyzing the treatment, it was observed that after corticosteroids, mycophenolate was the immunosuppressant most used as

initial therapy, followed by calcineurin inhibitors. However, this relationship is reversed when observing subsequent treatment after six months, when calcineurin inhibitors take first place. This data report is interesting since, as indicated by the KDIGO guidelines, the treatment of FSGS differs depending on its etiology, with corticosteroids being the basis of therapy for primary FSGS, leaving calcineurins and mycophenolate as second- and third-line treatments and secondary causes, and those of unknown etiology should not receive immunosuppressive treatment and should be treated only with antiproteinuric drugs [9]. Several studies have evaluated the efficacy of calcineurin inhibitors in patients with corticosteroid-resistant FSGS [8, 27-29]. However, the group of patients in these studies was small. In the present investigation, it was observed that more than half of the patients initially treated with mycophenolate and corticosteroids presented remission of proteinuria. In contrast, no remission was observed after six months in the group that received cyclosporine and corticosteroids.

Among the unconventional treatments for this pathology, 4.1% of patients received plasmapheresis, 5.1% cyclophosphamide, and only 1% rituximab. Several bibliographies have described plasma exchange therapy and monoclonal antibodies as adjuvant treatments for FSGS refractory to conventional treatments; however, their use is not standardized [30–33].

This study has limitations, such as the lack of uniformity of protocols in three hospitals, the greater use of mycophenolate due to the nonavailability of calcineurin inhibitors, and the initiation of immunosuppressive treatment before obtaining the histopathological result due to the delay that occurs in the report of pathology in several health homes. Despite these limitations, the study has several strengths, such as being a multicenter study and conducting a 2-year longitudinal follow-up of the study group. Future studies should evaluate 3 or 5 years of follow-up.

Conclusion

FSGS is the most common primary glomerulopathy in our environment. FSGS is more common in middle-aged men, presenting in more than half of the cases with nonnephrotic proteinuria and dyslipidemia. However, some patients also present hematuria and hypertension at diagnosis. The basis of treatment is corticosteroids and antiproteinurics. Remission of proteinuria at six months was achieved in less than half of the patients; however, few patients needed dialysis at two years of follow-up.

Abbreviations

CKD: Chronic kidney disease.
ESRD: End-stage renal disease.
RRT: renal replacement therapy.
FSGS: Focal segmental glomerulosclerosis.
MPGN: Membranoproliferative glomerulonephritis
NIGA: IgA nephropathy.
CNI: Calcineurin inhibitors.
MMF: Mycophenolate.
KDIGO: Kidney Disease Improving Global Outcomes.
SN: Nephrotic syndrome.
SLE: Systemic lupus erythematosus.
NL: Lupus nephritis.
HIV: Human immunodeficiency virus.
HCV: Hepatitis C virus.
HBV: Hepatitis B virus.

Supplementary information

Supplementary materials have not been declared.

Acknowledgments

Does not apply.

Author contributions

Nathaly Elizabeth Rivadeneira Guillen: Data curation, Formal analysis, Funding acquisition, Research, Project management, Resources, Software, Writing – original draft.
Junior Rafael Gahona Villegas: Conceptualization, Supervision, Validation, Visualization, Methodology, Writing: review and editing.
Ramiro Iván López Pulles: Supervision, Validation, Visualization, Methodology, Writing: review and editing.
All the authors have read and approved the final version of the manuscript.

Financing

None of the authors received funding for the present study. The authors paid the administrative expenses of the research.

Availability of data or materials

The data sets generated and analyzed during the current study are not publicly available due to participant confidentiality.

Statements

Ethics committee approval and consent to participate

The Human Research Ethics Committee of the Central University of Ecuador 2022 approved the research project before the retrospective data study was prepared.

All data obtained during the implementation of this project were authorized for use by the teaching and research coordination of the participating hospitals. The handling of the data collected was always confidential, using codes instead of names.

Consent for publication

Not needed for studies that do not publish patient photographs, tomography scans, or X-ray studies.

Conflicts of interest

The authors report having no conflicts of interest.

Author information

Not declared.

References

1. Melendez Rivera JG, Hashmi MF. HIV Nephropathy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023. http://www.ncbi.nlm.nih.gov/books/NBK559134/

2. Jafry N, Mubarak M, Rauf A, Rasheed F, Ahmed E. Clinical Course and Long-term Outcome of Adults with Primary Focal Segmental Glomerulosclerosis: A Retrospective Cohort Study. Iran J Kidney Dis. 2022 May;16(3):195-202. PMID: 35714214.

3. Jhonson R. Comprehensive Clinical Nephrology. Sixth edition. Vol. 1. Philadelphia: Elsevier; 2019. 219–230 p.

4. De Vriese AS, Sethi S, Nath KA, Glassock RJ, Fervenza FC. Differentiating Primary, Genetic, and Secondary FSGS in Adults: A Clinicopathologic Approach. J Am Soc Nephrol. 2018 Mar;29(3):759-774. doi: 10.1681/ASN.2017090958. Epub 2018 Jan 10. PMID: 29321142; PMCID: PMC5827609.

5. Deegens JK, Dijkman HB, Borm GF, Steenbergen EJ, van den Berg JG, Weening JJ, Wetzels JF. Podocyte foot process effacement as a diagnostic tool in focal segmental glomerulosclerosis. Kidney Int. 2008 Dec;74(12):1568-76. doi: 10.1038/ki.2008.413. Epub 2008 Aug 27. PMID: 18813290.

6. Ozeki T, Maruyama S, Imasawa T, Kawaguchi T, Kitamura H, Kadomura M, et al. Clinical manifestations of focal segmental glomerulosclerosis in Japan from the Japan Renal Biopsy Registry: Age stratification and comparison with minimal change disease. Sci Rep 2021 Jan 28;11(1):2602. doi: 10.1038/s41598-020-80931-9. PMID: 33510182; PMCID: PMC7844271.

7. Troost JP, Trachtman H, Nachman PH, Kretzler M, Spino C, Komers R, et al. An Outcomes-Based Definition of Proteinuria Remission in Focal Segmental Glomerulosclerosis. Clin J Am Soc Nephrol. 2018 Mar 7;13(3):414-421. doi: 10.2215/CJN.04780517. Epub 2017 Nov 22. PMID: 29167190; PMCID: PMC5967666.

8. Duncan N, Dhaygude A, Owen J, Cairns TD, Griffith M, McLean AG, et al. Treatment of focal and segmental glomerulosclerosis in adults with tacrolimus monotherapy. Nephrol Dial Transplant. 2004 Dec;19(12):3062-7. doi: 10.1093/ndt/gfh536. Epub 2004 Oct 26. PMID: 15507477.

9. Coresh J, Heerspink HJL, Sang Y, Matsushita K, Arnlov J, Astor BC, et al.; Chronic Kidney Disease Prognosis Consortium and Chronic Kidney Disease Epidemiology Collaboration. Change in albuminuria and subsequent risk of end-stage kidney disease: an individual participant-level consortium meta-analysis of observational studies. Lancet Diabetes Endocrinol. 2019 Feb;7(2):115-127. doi: 10.1016/S2213-8587(18)30313-9 . Epub 2019 Jan 8. PMID: 30635225; PMCID: PMC6379893.

10. Santacruz Mancheno J, Santacruz AC. Global Dialysis Perspectives: Ecuador. Kidney360. 2022 Oct 16;3(12):2131-2135. doi: 10.34067/KID.0003762022. PMID: 36591349; PMCID: PMC9802541.

11. O'Shaughnessy MM, Hogan SL, Thompson BD, Coppo R, Fogo AB, Jennette JC. Glomerular disease frequencies by race, sex and region: results from the International Kidney Biopsy Survey. Nephrol Dial Transplant. 2018 Apr 1;33(4):661-669. doi: 10.1093/ndt/gfx189. PMID: 29106637; PMCID: PMC6659026.

12. Valdez-Yánez G, Hernández-Pacheco J, Arellán-Bravo L, Velásquez-Castillo P, Matias-Tasayco V, Espinoza-Verástegui J, et al. Glomerulonephritis due to biopsy in the population treated at the Dos de Mayo National Hospital. Lima, 2007-2016. An. Fac. Med. 2018 Apr;79(2):115-118. http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S1025-55832018000200002&lng=es. doi: 10.15381/anales.v79i2.14936 .

13. Villanueva M, Pazarin H, Soto J, Barragán V, Godínez M. Morphological patterns of glomerular disease in Mexico: Report from a reference center in nephropathology. Rev Nefrol Dialysis Transpl. 2022;42(4):275-84. medigraphic/109699

14. Roja JR, Pérez M, Hurtado A, Asato C. Factores pronósticos de supervivencia renal en glomeruloesclerosis focal y segmentaria primaria [Factors predicting for renal survival in primary focal segmental glomerulosclerosis]. Nefrologia. 2008;28(4):439-46. Spanish. PMID: 18662153.

15. Cárdenas Alava ME. Relationship between the clinical and histopathological diagnosis of glomerulopathies in adult patients biopsied at the Carlos Andrade Marín Hospital, 2010 –2018 [Master thesis]. Quito: UCE; 2020. http://www.dspace.uce.edu.ec/handle/25000/21269 .

16. Rosenberg AZ, Kopp JB. Focal Segmental Glomerulosclerosis. Clin J Am Soc Nephrol. 2017 Mar 7;12(3):502-517. doi: 10.2215/CJN.05960616. Epub 2017 Feb 27. Erratum in: Clin J Am Soc Nephrol. 2018 Dec 7;13(12):1889. Doi: 10.2215/CJN.05960616 PMID: 28242845; PMCID: PMC5338705.

17. Jafry N, Mubarak M, Rauf A, Rasheed F, Ahmed E. Clinical Course and Long-term Outcome of Adults with Primary Focal Segmental Glomerulosclerosis: A Retrospective Cohort Study. Iran J Kidney Dis. 2022 May;16(3):195-202. PMID: 35714214.

18. Kitiyakara C, Eggers P, Kopp JB. Twenty-one-year trend in ESRD due to focal segmental glomerulosclerosis in the United States. Am J Kidney Dis. 2004 Nov;44(5):815-25. PMID: 15492947.

19. Mbakop C, DeVita MV, Wahl SJ, Bijol V, Rosenstock JL. Adult primary nephrotic syndrome trends by race: a diminished frequency of focal segmental glomerulosclerosis in nonblack patients. Int Urol Nephrol. 2021 Apr;53(4):719-724. doi: 10.1007/s11255-020-02658-w. Epub 2020 Nov 17. PMID: 33200335.

20. Kambham N, Markowitz GS, Valeri AM, Lin J, D'Agati VD. Obesity-related glomerulopathy: an emerging epidemic. Kidney Int. 2001 Apr;59(4):1498-509. doi: 10.1046/j.1523-1755.2001.0590041498.x. PMID: 11260414.

21. Chen HM, Li SJ, Chen HP, Wang QW, Li LS, Liu ZH. Obesity-related glomerulopathy in China: a case series of 90 patients. Am J Kidney Dis. 2008 Jul;52(1):58-65. doi: 10.1053/j.ajkd.2008.02.303 . Epub 2008 Apr 18. PMID: 18423814.

22. García Herrera HG, Restrepo Valencia CA, Buitrago Villa CA, García Herrera HG, Restrepo Valencia CA, Buitrago Villa CA. Clinical and histological characteristics of renal parenchymal diseases in a sample of renal biopsies obtained between 2002 and 2017 in the department of Caldas, Colombia. Rev Colomb Nefrol. Dec 2018;5(2):107-17. doi: 10.22265/acnef.0.0.300

23. De Vriese AS, Sethi S, Nath KA, Glassock RJ, Fervenza FC. Differentiating Primary, Genetic, and Secondary FSGS in Adults: A Clinicopathologic Approach. J Am Soc Nephrol. 2018 Mar;29(3):759-774. doi: 10.1681/ASN.2017090958. Epub 2018 Jan 10. PMID: 29321142; PMCID: PMC5827609.

24. Bose B, Cattran D; Toronto Glomerulonephritis Registry. Glomerular diseases: FSGS. Clin J Am Soc Nephrol. 2014 Mar;9(3):626-32. doi: 10.2215/CJN.05810513 . Epub 2013 Aug 29. PMID: 23990165; PMCID: PMC3944761.

25. Korbet SM. Treatment of primary FSGS in adults. J Am Soc Nephrol. 2012 Nov;23(11):1769-76. doi: 10.1681/ASN.2012040389. Epub 2012 Sep 20. PMID: 22997260.

26. Hommos MS, De Vriese AS, Alexander MP, Sethi S, Vaughan L, Zand L, Bharucha K, Lepori N, Rule AD, Fervenza FC. The Incidence of Primary vs Secondary Focal Segmental Glomerulosclerosis: A Clinicopathologic Study. Mayo Clin Proc. 2017 Dec;92(12):1772-1781. doi: 10.1016/j.mayocp.2017.09.011. Epub 2017 Oct 27. PMID: 29110886; PMCID: PMC5790554.

27. Braun N, Schmutzler F, Lange C, Perna A, Remuzzi G, Risler T, Willis NS. Immunosuppressive treatment for focal segmental glomerulosclerosis in adults. Cochrane Database Syst Rev. 2008 Jul 16;2008(3):CD003233. doi: 10.1002/14651858.CD003233.pub2. Update in: Cochrane Database Syst Rev. 2022 Feb 28;2:CD003233. PMID: 18646090; PMCID: PMC7144690.

28. Ramachandran R, Kumar V, Rathi M, Nada R, Jha V, Gupta KL, Sakhuja V, Kohli HS. Tacrolimus therapy in adult-onset steroid-resistant nephrotic syndrome due to a focal segmental glomerulosclerosis single-center experience. Nephrol Dial Transplant. 2014 Oct;29(10):1918-24. doi: 10.1093/ndt/gfu097. Epub 2014 Apr 24. PMID: 24771498.

29. Laurin LP, Gasim AM, Poulton CJ, Hogan SL, Jennette JC, Falk RJ, Foster BJ, Nachman PH. Treatment with Glucocorticoids or Calcineurin Inhibitors in Primary FSGS. Clin J Am Soc Nephrol. 2016 Mar 7;11(3):386-94. doi: 10.2215/CJN.07110615. Epub 2016 Feb 16. PMID: 26912551; PMCID: PMC4791818.

30. Hansrivijit P, Cheungpasitporn W, Thongprayoon C, Ghahramani N. Rituximab therapy for focal segmental glomerulosclerosis and minimal change disease in adults: a systematic review and meta-analysis. BMC Nephrol. 2020 Apr 15;21(1):134. doi: 10.1186/s12882-020-01797-7. PMID: 32293308; PMCID: PMC7160971.

31. Xue C, Yang B, Xu J, Zhou C, Zhang L, Gao change disease or focal segmental glomerulosclerosis: a systematic review and meta-analysis. Clin Kidney J. 2020 Nov 21;14(4):1042-1054. doi: 10.1093/ckj/sfaa191. PMID: 34094516; PMCID: PMC8173623.

32. Chen YY, Sun X, Huang W, He FF, Zhang C. Therapeutic apheresis in kidney diseases: an updated review. Ren Fail. 2022 Dec;44(1):842-857. doi: 10.1080/0886022X.2022.2073892. PMID: 35723077; PMCID: PMC9225689.

33. Raina R, Wang J, Sharma A, Chakraborty R. Extracorporeal Therapies in the Treatment of Focal Segmental Glomerulosclerosis. Blood Purif. 2020;49(5):513-523. doi: 10.1159/000506277. Epub 2020 Feb 19. PMID: 32074606.

DOI: Digital Object Identifier. PMID PubMed Identifier.

Editor's Note

REV SEN remains neutral concerning jurisdictional claims over published maps and institutional affiliations.