

The Incidence of Primary vs Secondary Focal Segmental Glomerulosclerosis: A Clinicopathologic Study

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Abstract

Objectives: To describe the change in the incidence rates of primary and secondary focal segmental glomerulosclerosis (FSGS) from 1994 through 2013 in Olmsted County, Minnesota, and to identify the clinical and biopsy characteristics that distinguish primary from secondary FSGS.

Patients and Methods: Olmsted County adult residents with native kidney biopsy from January 1, 1994, through December 31, 2013, and FSGS as the only glomerulopathy were identified. The clinical and pathologic characteristics of primary and secondary FSGS were described and compared, and incidence rates were calculated.

Results: Of 370 adults biopsied, 281 had glomerular diseases, of which 46 (16%) had FSGS. From 1994-2003 to 2004-2013, there were significant increases in kidney biopsy rates (14.7 [95% CI, 12.1-17.3] vs 22.9 [95% CI, 20.0-25.7] per 100,000 person-years, 17% increase per 5 years; $P < .001$) and total FSGS rates (1.4 [95% CI, 0.6-2.2] vs 3.2 [95% CI, 2.1-4.3] per 100,000 person-years, 41% increase per 5 years; $P = .02$). Compared with patients with limited foot process effacement ($< 80\%$), patients with diffuse effacement ($\geq 80\%$) without an identifiable cause had lower serum albumin levels ($P < .001$), had higher proteinuria ($P < .001$), and were more likely to have nephrotic syndrome (100% vs 4%; $P < .001$). Patients with diffuse effacement without an identifiable cause were classified as primary FSGS, which accounted for 3 of 12 patients (25%) during 1994-2003 and 9 of 34 (26%) during 2004-2013.

Conclusion: Although the incidence of FSGS has increased, the proportions of primary and secondary FSGS have remained stable.

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The incidence of focal segmental glomerulosclerosis (FSGS) in adults has increased during the past few decades. This temporal trend has been observed in large metropolitan areas and in small rural communities, regardless of racial and ethnic background (Table 1).¹⁻⁷ Now, FSGS accounts for 20% to 40% of all biopsy-proven glomerular diseases in adults.³⁻⁸ However, the previous studies have important limitations. First, most studies reported trends in relative disease frequencies in biopsied patients rather than true population-based incidence rates of FSGS. This approach can result in misleading conclusions because a change in the proportion of one disease automatically affects the

proportions of other diseases. Furthermore, as the referral population for kidney biopsy changes over time, so do the relative frequencies of different diseases. Another important limitation in the previous studies is the approach of reporting FSGS as a single disease entity.²⁻⁸ We now know that FSGS is a histologic pattern of injury that characterizes a broad spectrum of diseases with different pathophysiologies. Primary FSGS is presumed to be due to a circulating permeability factor diffusely toxic to podocytes, which may respond to immunosuppressive treatment.⁹ On the other hand, secondary FSGS is a response to reduction in the number of functioning nephrons (eg, unilateral renal agenesis)



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TABLE 1. Summary of Studies That Have Evaluated FSGS Frequency or Incidence

Reference, year	Time period	Location	Type of FSGS	Type of study	Findings
Haas et al, ¹ 1995	1974-1993	Chicago, IL	Excluded patients with clear risk factors for secondary glomerulonephritis	Relative disease frequency	FSGS relative frequency increased from 4% in 1974-1979 to 12.2% in 1987-1993
Korbet et al, ² 1996	1975-1994	Chicago, IL	Total FSGS	Relative disease frequency	FSGS accounted for 57% of glomerular lesions in blacks and 23% in whites; FSGS relative frequency increased from 39% in 1975-1984 to 64% in 1985-1994 in blacks
Braden et al, ³ 2000	1974-1994	Springfield, MA	Total FSGS	Relative disease frequency	Relative frequency of FSGS increased from 13.7% in 1975-1979 to 25% in 1990-1994; the increase was most notable in blacks and Hispanics, with only modest increases in whites
Swaminathan et al, ⁴ 2006	1974-2003	Olmsted County, MN	Total FSGS	Population based	Rate of FSGS increased from 0.1 per 100,000 person-years in 1974-1983 to 1.8 per 100,000 person-years in 1994-2003
Sim et al, ⁶ 2016	2000-2011	Southern California	Total FSGS	Population based	FSFS was the most common diagnosis (38.9%) across all race and ethnic groups; incidence rate increased from 1.6 per 100,000 person-years in 2000 to 5.3 per 100,000 person-years in 2011
Murugapandian et al, ⁵ 2016	2004-2014	Tucson, AZ	Total FSGS	Relative disease frequency	FSGS was the most common histopathologic diagnosis (22%)
O'Shaughnessy et al, ⁷ 2017	1986-2015	Chapel Hill, NC	Total FSGS	Relative disease frequency	Relative frequency of FSGS increased over 3 decades from 22.6% to 29.7%

FSGS = focal segmental glomerulosclerosis.

or from an abnormal stress on initially normal nephrons.⁹ The treatment is centered around unloading the pressure on glomeruli using renin-angiotensin-aldosterone system (RAAS) inhibition.

To better evaluate the incidence of FSGS, it is critical to distinguish primary FSGS from

secondary forms in a population-based study. Olmsted County in Minnesota is particularly well suited to perform a population-based study of glomerular diseases. The aim of this study was to describe the change in the incidence rates of primary and secondary FSGS from 1994 through 2013 in Olmsted County

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