AJKD

Original Investigation

Distribution of Biopsy-Proven Presumed Primary Glomerulonephropathies in 2000-2011 Among a Racially and Ethnically Diverse US Population

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Background: The incidence and distribution of primary glomerulonephropathies vary throughout the world and by race and ethnicity. We sought to evaluate the distribution of primary glomerulonephropathies among a large racially and ethnically diverse population of the United States.

Study Design: Case series from January 1, 2000, through December 31, 2011.

Setting & Participants: Adults (aged ≥ 18 years) of an integrated health system who underwent native kidney biopsy and had kidney biopsy findings demonstrating focal segmental glomerulosclerosis (FSGS), membranous glomerulonephritis (MGN), minimal change disease (MCD), immunoglobulin A nephropathy (IgAN), and other.

Outcomes: Rates and characteristics of the most common primary glomerulonephropathies overall and by race and ethnicity.

Results: 2,501 patients with primary glomerulonephropathy were identified, with a mean age 50.6 years, 45.7% women, 36.1% Hispanics, 31.2% non-Hispanic whites, 17.4% blacks, and 12.4% Asians. FSGS was the most common glomerulonephropathy (38.9%) across all race and ethnic groups, followed by MGN (12.7%), MCD (11.0%), IgAN (10.2%), and other (27.3%). The FSGS category had the greatest proportion of blacks, and patients with FSGS had the highest rate of poverty. IgAN was the second most common glomerulonephropathy among Asians (28.6%), whereas it was 1.2% among blacks. Patients with MGN presented with the highest proteinuria (protein excretion, 8.3 g) whereas patients with FSGS had the highest creatinine levels (2.6 mg/dL). Overall glomerulonephropathy rates increased annually in our 12-year observation period, driven by FSGS (2.7 cases/100,000) and IgAN (0.7 cases/100,000). MGN and MCD rates remained flat.

Limitations: Missing data for urine albumin and sediment, indication bias in performing kidney biopsies, and inexact classification of primary versus secondary disease.

Conclusions: Among a racially and ethnically diverse cohort from a single geographical area and similar environment, FSGS was the most common glomerulonephropathy, but there was variability of other glomerulonephropathies based on race and ethnicity.

INDEX WORDS: Primary glomerulonephropathy; glomerulonephritis; nephrotic syndrome; focal segmental glomerulosclerosis (FSGS); membranous glomerulonephritis (MGN); minimal change disease (MCD); IgA nephropathy (IgAN); epidemiology; race/ethnic predilection; kidney biopsy; case series.

Glomerulonephropathies are major contributors to kidney failure throughout the world.[1,2] They are the most common cause of end-stage renal disease (ESRD) in certain countries. In the United States of America, glomerulonephropathies rank as the third most common cause of ESRD and thus account for a significant proportion of the $31 billion in annual Medicare costs for ESRD care.[3] The incidence of glomerulopathy-related ESRD has increased in the past 30 years, though it has steadied in the past decade.[3] Worldwide, primary glomerulonephropathy occurs at a rate of up to 2 to 3 cases per 100,000 individuals,[4] and glomerulonephropathies account for more than 100,000 patients with ESRD in the United States.[3]

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Received December 10, 2015. Accepted in revised form March 9, 2016.

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0272-6386

http://dx.doi.org/10.1053/j.ajkd.2016.03.416

The distribution and incidence of the different primary glomerulonephropathies vary across countries, race and ethnic groups, and time periods. This suggests the possibility that multiple risk factors play a role in glomerulonephropathy, including environment and innate biological properties. Although immunoglobulin A nephropathy (IgAN) has been the most prevalent glomerulonephropathy described throughout most countries,[5-17] membranous glomerulonephritis (MGN) or focal segmental glomerulosclerosis (FSGS) is the most common in other countries, including the United States.[18-23] There have been variations in time periods as well, with a trend toward increased rates of FSGS in many countries.[2,21,24] Certain race and ethnic groups have been strongly linked with specific glomerulonephropathies, such as IgAN among Asians[2,6,8,10,11] and FSGS among blacks.[22] These population-based studies have been drawn from predominantly homogeneous populations reflective of the country or area of practice. Thus, aside from identified genetic causes of certain glomerulonephropathies, the contributions of environment and/or inborn physiognomies on the risk for glomerulonephropathy is not well known, but is the subject of much speculation.

Given the heterogeneous population of the United States, it is not well known what the distributions of glomerulonephropathies are within different race and ethnic groups that reside in similar areas and environments. Specifically, it would be of interest to determine and compare the distribution of glomerulonephropathies among Hispanics and Asians in addition to whites and blacks within the United States. We sought to characterize primary glomerulonephropathies among a large ethnically diverse contemporary adult population in the Southwestern region of the United States. Using the health information for more than 3 million members of an integrated health system, we reviewed all native kidney biopsies performed over a 12-year period. Based on biopsy findings only, we identified diagnoses presumed to be primary glomerulonephropathy to determine the distribution of primary glomerulonephropathies among the general population and by different race and ethnic groups.

METHODS

Study Overview

A retrospective cohort study was performed in January 1, 2000, through December 31, 2011, within the Kaiser Permanente Southern California (KPSC) health system. KPSC is an integrated prepaid health plan with 14 medical centers and more than 200 satellite medical offices that geographically spans from Bakersfield to San Diego, CA. As of July 2015, there were more than 4 million KPSC members. The membership population is racially and ethnically diverse, reflective of the underlying population and Southern California in general.[25-27] Compared to the distribution of the US population, the KPSC membership has twice as many Asians and 3 times as many Hispanics. Members have similar access to health visits, medications, procedures, and medication and supply benefits. As part of routine clinical care, KPSC maintains all member information collected in the electronic health record (EHR). This includes information for demographics, comorbid conditions, vital signs, laboratory and imaging results, pathology reports, and medications. Race and ethnic information are entered into the EHR based on either patient self-report or provider assessment. Nearly all Hispanics within KPSC are Hispanic whites; Hispanic blacks account for $<1\%$ of KPSC members. Thus, the designation of Hispanics within our study refers to Hispanic whites. All laboratory measurements are performed and reported from an American College of Pathology/Clinical Laboratory Improvement Act (CLIA)-certified laboratory. Income information was derived using resident address and the US Census tract information. This study was approved by the local institutional review board (IRB #5815) and exempted from informed consent.

Study Population

All members 18 years and older who underwent a native kidney biopsy were identified for potential inclusion in the study cohort. Individual paper and electronic chart reviews were performed to identify and categorize biopsy findings and diagnoses. Biopsies that had a main diagnosis of primary glomerulonephropathy were included in the study. For individuals who had multiple biopsies, the first biopsy result was used in our study and analyses. Primary glomerulonephropathies to be identified on chart review included FSGS, IgAN, minimal change disease (MCD), MGN, membranoproliferative glomerulonephritis (MPGN) including dense deposit disease, pauci-immune glomerulonephritis/antineutrophil cytoplasmic antibody (ANCA)-associated glomerulonephritis, immune complex nephropathy, crescentic glomerulonephritis not otherwise specified, post-infectious glomerulonephritis, anti–glomerular basement membrane glomerulonephritis, fibrillary glomerulonephritis, and others. Exclusion criteria were members younger than 18 years at the time of biopsy, transplant biopsies, history of systemic lupus erythematous (SLE), and biopsies that demonstrated inconclusive findings or a secondary glomerulonephropathy. Secondary glomerulonephropathies that were excluded were diabetic glomerulosclerosis, SLE-associated nephritis, amyloidosis, nephrocalcinosis, Bence-Jones/cast nephropathy, myelodysplastic disorder–associated glomerulonephropathy, human immunodeficiency virus (HIV)-associated nephropathy, urate nephropathy, sarcoidosis, Alport disease, light or heavy chain deposition disease, and oxalate nephropathy.

Kidney Biopsies at KPSC

All kidney biopsy information in the study period was obtained from routine clinical practice, whereby all biopsies were determined as clinically indicated by the practitioners. Kidney biopsies are performed in both the inpatient and outpatient settings, with nearly all member biopsies occurring at a KPSC medical center.[28] Approximately 3% are performed at non-KPSC facilities, but all specimens are transported to the KPSC renal pathology department for processing and reading. All samples are received at the KPSC regional laboratory in North Hollywood, CA, for processing and preparation. All samples are separately prepared in hematoxylin-eosin, Masson trichrome, periodic acid–Schiff, and Jones methenamine silver stains for light microscopy viewing. Immunofluorescence studies and electron microscopy viewing are performed on all specimens. When prepared, samples are sent to Los Angeles Medical Center for review and interpretation by 2 renal pathologists. After each renal pathologist views the specimens separately, the final diagnoses are determined after a consensus is reached by the 2 renal pathologists.

Kidney biopsy results were extracted by chart review performed by 4 research associates (see Acknowledgements). Results were categorized based on the primary diagnoses as reported on the