Distribution of Renal Histopathology in Guilan
A Single-center Report

Ali Monfared,[1,2] Masoud Khosravi,[1,2] Mohammadkazem Lebadi,[1,2]
Seyed Amin Mosavian Roshan Zamir,[2] Saba Hoda,[2,3]
Seyed Mahmoud Habibzadeh,[2,3] Sepiedeh Besharati[2]

[1]Division of Nephrology, Department of Internal Medicine, Guilan University of Medical Sciences, Rasht, Iran
[2]Urology Research Center, Guilan University of Medical Sciences, Rasht, Iran
[3]Department of Pathology, Guilan University of Medical Sciences, Rasht, Iran

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Introduction. Glomerulonephritis is the third most common cause of end-stage renal disease. Epidemiological data of kidney disease is population-based and has great geographic variability. The aim of this study was to assess the results of all kidney biopsies in a 5-year period in the Guilan province.

Materials and Methods. In a retrospective study of 336 kidney biopsies recorded in the Department of Nephrology in Razi Hospital of Rasht, capital city of Guilan province, from August 2001 to September 2006, data consisting of age, gender, indication of kidney biopsy, and histopathological diagnosis were collected and analyzed.

Results. A total of 336 kidney biopsies were reviewed (73.8% males; mean age, 40.12 ± 16.78 years). Nephritic syndrome (42.5%) and nephrotic syndrome (38.7%) were the most frequent indications of biopsy. Overall, pathologic examinations were indicative of glomerulonephritis in 272 (81.0%) biopsies and nonglomerular diseases in 64 (19.0%). The most common cause of secondary glomerulonephritis was lupus nephritis (82.6%). Focal and segmental glomerusclerosis (20.5%) was the most common pathologic diagnosis, followed by membranous glomerulonephritis (14.9%), minimal change disease (11.6%), tubulointerstitial nephritis (8.9%), and IgA nephropathy (3.6%). The most common pathologic finding among glomerular diseases was focal segmental glomerusclerosis (25.4%), while tubulointerstitial nephritis (46.9%) was the most common among nonglomerular diseases, followed by diffuse glomerulosclerosis, interstitial fibrosis, and tubular atrophy indicative of end-stage renal disease (23.4%).

Conclusions. In our study, FSGS was the most common pathologic finding in kidney biopsies, and the frequency of IgA nephropathy was much lower than that in other studies.

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INTRODUCTION

Several registries have reported the results of renal biopsies all over the world.[1] In North Carolina, membranous glomerulonephritis (MGN) was reported to be the most frequent renal pathology, followed by focal segmental glomerulosclerosis (FSGS), lupus nephritis (LN), and Immunoglobulin A nephropathy (IgAN).[1] In the Spanish registry that includes both children and adult patients, MGN was the most frequent followed by minimal change disease (MCD).[1] Studies from France and Finland reported IgAN as the most common pathology.[1] Most East Asian studies have also reported IgAN as the most common glomerular disease.[1]

Chronic kidney disease (CKD) is a common and costly health problem in the Middle East

and is a major cause of morbidity and mortality worldwide.[2] Epidemiological data of kidney diseases is population-based and has notable changes related to the socioeconomic condition, geographic area, race, indication for biopsy, and variation of genetic tendency and environmental exposure.[3-6] In developing countries, limited financial resources and lack of infrastructure organizations restrict health policies considering the increasing burden of CKD.[7]

Kidney biopsy was introduced into regular clinical practice by Iverson and Brun in 1951, and from that time it presented an irreplaceable tool for diagnosis of many renal diseases.[8] A percutaneous kidney biopsy may be obtained for a number of reasons, including establishment of the exact diagnosis, as an aid to determine the nature of the recommended therapy or to help decide when treatment is futile, and to ascertain the degree of activity or chronicity of changes.[9,10] The indications for performing a kidney biopsy varies among nephrologists determined in part by the presenting sign and symptoms.[9-11] There is limited data about kidney disease frequency in our region due to lack of a national kidney disease registry. Hence, we investigated renal pathology results during a 5-year period.

MATERIALS AND METHODS

In a retrospective study, we analyzed 336 kidney biopsy reports performed in Guilan, Iran, from August 1st, 2001 to September 31st, 2006. Our exclusion criteria were the absence of immunofluorescence or light microscopy report, insufficient tissue (the count of glomeruli less than 5), age less than 12 years, and biopsy from transplant kidneys.

The biopsies had been performed in the nephrology department of Guilan University of Medical Sciences. The indications for kidney biopsy were nephrotic syndrome, nephritic syndrome, nephrotic-nephritic syndrome, acute kidney failure with unknown etiology, systemic disease with hematuria and proteinuria, and microscopic hematuria with proteinuria more than 500 mg/d. Kidney biopsies were processed for light and immunofluorescence microscopy in all specimens, without electron microscopy study, by 2 pathologists. All data related to the final diagnosis, age, gender, and clinical indication for biopsy were recorded.

Nephritic syndrome was defined as proteinuria ($\geq$ 500 mg/d) and hematuria (> 3 to 5 erythrocytes per high-power field) with hypertension and/or a rise in serum creatinine (> 1.4 mg/dL), usually with edema. Nephrotic syndrome was defined as proteinuria ($\geq$ 3500 mg/d) associated with or without hyperlipidemia, hypoalbuminemia, and edema. Azotemia was defined as a serum creatinine level greater than 1.4 mg/dL. Acute kidney failure was defined as a rise in serum creatinine in a few hours or days. Rapidly progressive glomerulonephritis was defined as proteinuria and hematuria associated with progressive kidney failure within 1 to 3 months. Asymptomatic urinary abnormality was defined as subnephrotic proteinuria and/or hematuria with no clinical symptoms or signs. Cases not fulfilling any of the mentioned definitions were classified as unknown presentation.

Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 16.0, SPSS Inc, Chicago, Ill, USA). Categorical values were expressed as absolute frequencies and percentages.

RESULTS

A total of 336 kidney biopsies performed during a 5-year period were reviewed. Of the patients, 248 (73.8%) were males. The mean age was 40.12 ± 16.78 years. Nephritic syndrome (42.5%) and nephrotic syndrome (38.7%) were the most frequent indications for kidney biopsy (Table 1).

Overall, pathologic examinations were indicative of glomerulonephritis (GN) in 272 (81.0%) biopsies and nonglomerular diseases in 64 (19.0%). Secondary GN consisted of 47 cases of GNs (17.4%); the most common cause of secondary GN was SLE (82.6%). Focal and segmental glomerusclerosis (20.5%) was the most common pathologic diagnosis, followed by MGN (14.9%), MCD (11.6%), tubulointerstitial nephritis (8.9%), and IgAN (3.6%; Table 2). The most common pathologic finding among glomerular diseases was FSGS (25.4%), followed by MGN (18.4%), and MCD (14.3%; Table 3), while

Table 1. Presentations Indicating Kidney Biopsy

Presentation	Number (%)
Nephritic syndrome	147 (42.5)
Nephrotic syndrome	134 (38.7)
Acute kidney failure with unknown etiology	34 (9.8)
Nephritic-nephrotic syndrome	13 (3.8)
Not documented	18 (25.2)

TIN (46.9%) was the most common pathologic finding among nonglomerular diseases, followed by diffuse glomerulosclerosis, interstitial fibrosis, and tubular atrophy indicative of end-stage renal disease (23.4%; Table 4).

Table 2. Distribution of Renal Pathologic Findings*

Pathology	Number (%)
FSGS	69 (20.5)
MGN	50 (14.9)
MCD	39 (11.6)
SLE nephritis	39 (11.6)
TIN	30 (8.9)
MPGN	24 (7.1)
Diffuse glomerulosclerosis, interstitial fibrosis, and tubular atrophy (ESRD)	15 (4.5)
IgAN	12 (3.6)
Crescentic GN	15 (4.5)
Amyloidosis	7 (2.1)
ATN	4 (1.2)
Others	32 (9.5)
Total	336 (100)

*FSGS indicates focal segmental glomerulosclerosis; MGN, membranous glomerulonephritis; MCD, minimal change disease; SLE, systemic lupus erythematosus; TIN, tubulointerstitial nephritis; MPGN, membranoproliferative glomerulonephritis; ESRD, end-stage renal disease; IgAN, immunoglobulin A nephritis; GN, glomerulonephritis; and ATN, acute tubular necrosis.

Table 3. Distribution of Glomerular Disease Pathologic Findings*

Pathology	Number (%)
FSGS	69 (25.4)
MGN	50 (18.4)
MCD	39 (14.3)
SLE nephritis	39 (14.3)
MPGN	24 (8.8)
IgAN	12 (4.4)
Crescentic GN	15 (5.5)
Amyloidosis	7 (2.6)
Others	17 (6.3)
Total	272 (100)

*FSGS indicates focal segmental glomerulosclerosis; MGN, membranous glomerulonephritis; MCD, minimal change disease; SLE, systemic lupus erythematosus; MPGN, membranoproliferative glomerulonephritis; IgAN, immunoglobulin A nephritis; and GN, glomerulonephritis.

Table 4. Distribution of Nonglomerular Disease Pathologic Findings

Pathology	Number (%)
TIN	30 (46.9)
Diffuse glomerulosclerosis, interstitial fibrosis, and tubular atrophy (ESRD)	15 (23.4)
ATN	4 (6.3)
Others	15 (23.4)
Total	64 (100)

*TIN indicates tubulointerstitial nephritis; ESRD, end-stage renal disease; and ATN, acute tubular necrosis.

DISCUSSION

In this study, FSGS was the most common type of pathologic finding among kidney biopsy specimens, constituting about one fifth of the pathologic diagnoses, followed by MGN, MCD, and LN. In addition, FSGS was the most common type of glomerulonephritis. There are several studies which depict the distribution of glomerular disease in kidney biopsies.[12-19] A study in Brazil showed that FSGS was present in 34.8% of biopsies, followed by IgAN (11.8%), MGN (10.6%), and LN (10.7%).[12] Another study in Zaire presented the prevalence of FSGS as high as 41%, followed by MCD (14%), mesangioproliferative GN (MPGN; 8%), and end-stage renal disease (7%).[13] Another study in Saudi Arabia indicated that the most common histological lesions were FSGS (40.8%), MPGN (21.1%), MGN (13.6%), IgAN (13.6%), MPGN (9.5%), and MCD (1.4%), and lupus nephritis was the common cause of secondary glomerulonephritis (48.5%), whereas amyloidosis was absent.[14] Another study in Saudi Arabia reported that IgAN was the most common pathologic finding.[15]

A study from Iran reported that the most common GN was FSGS in their patients (37.1%) followed by MGN (16.5%) and lupus nephritis (13.4%).[16] Another study from Iran showed that the most frequent type of biopsy-proven GNs were MGN (26.8%), IgAN (11%), LN (11%), FSGS (10%), and MCD (8.3%).[1] A third study from Iran reported that MGN was the most common type of GN (23.6%), followed by IgAN (13.5%), MPGN (11.5%), LN (10.6%), FSGS (10.3%), and MCD (9.8%).[17] Our study and many other studies showed that FSGS is the most common type of glomerulonephritis.[19-23] Whether this is truly an increase in the incidence of FSGS or whether the condition has been better defined and more readily diagnosed by nephrophathologists is debatable. The absence of electron microscopy data as a major limitation of this study may limit the accuracy of conclusions. Nonetheless, for the past years, the yearly incidence of primary FSGS has risen from less than 10% to approximately 25% of adult nephropathies.[24] A substantial portion of this increase may be attributable to an increase in the collapsing glomerulopathy variant of FSGS and obesity.[25,26]

There are studies that indicate IgAN as the most common cause of glomerulonephritis,[21,27] and one of the studies from Iran identified IgAN as the

second most common cause of GN[17]; however, in our patients, IgAN had a low incidence (3.4%). Also a study in Peru showed that IgAN was rare (0.9%).[26] Low incidence of lgAN in our study and the littoral regions, like Guilan, may be due to the use of sea foods as a main course. In addition, we do not perform kidney biopsy in patients with isolated hematuria or hematuria with proteinuria less than 500 mg/24 h. Animal studies and observational studies in human indicate that the blood pressure-lowering effect of fish oil results from a reduction in systemic vascular resistance.[27,28] In vitro studies demonstrate that n-3 polyunsaturated fatty acid induces nitric oxide production, modulates endothelial activation, and modifies the location and function of cell membrane caveolae proteins, including endothelial nitric oxide synthase.[28,29] In short-term, fish oil consumption increases biomarkers of nitric oxide production in human, mitigates peripheral vasoconstrictive responses to norepinephrine and angiotensia II, improves arterial wall compliance, and enhances vasodilatory responses.[30-32]

These effects could account for lowering of systemic vascular resistance. The blood pressure-lowering effect of fish oil did not appear to be dose-dependent.[33] Also, observational studies demonstrated that at lower dietary doses, the dose-response maybe more linear.[27]

Furthermore, fish oil may have anti-inflammatory effects. Potential anti-inflammatory effects of fish oil have received much attention in review articles and the lay press, given the role of eicosapentaenoic acid and decosahexaenoic acid as precursors to specific eicosanoics and other inflammatory mediators. Controlled trials have generally not detected significant effects of fish oil intake on C-reactive protein levels.[34-35] Conversely, fish oil supplementation does appear to inhibit production of cytokines, including interleukin-1β and tumor necrosis factor-α.[36] Several randomized trials in human have demonstrated that fish oil consumption also lowers circulation markers of endothelial dysfunction, such as E-selecting, vascular cell adhesion molecule-1, and intercellular adhesion molecule-1.[35] In spite of these data, the possible role of sea foods and fish oil in IgAN which might act by anti-inflammatory mechanisms is not well defined. Thus, we suggest a well-designed study for establishment and to find the cause-and-effect role of this possible association in our region.

Renal involvement is common in idiopathic systemic lupus erythematosus. An abnormal urinalysis with or without an elevated plasma creatinine concentration is present in a large proportion of patients at the time of diagnosis and may eventually develop in up to 75% of cases.[38] Like other studies,[39-43] our study showed that LN was the most common cause of secondary glomerulonephritis.

CONCLUSIONS

In our study, FSGS was the most common pathologic finding overall, and also the most common GN. On the other hand, the frequency of IgAN was much lower than that in other studies. A kidney biopsy registry is required to collect more comprehensive data in our region.

CONFLICT OF INTETEST

None declared.

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Correspondence to:
Ali Monfared, MD
Urology Research Center, Razi Hospital, Sardar Jangal St, Rasht, Iran
E-mail: drmonfared2009@gmail.com
Tel: +98 131 552 5259
Fax: +98 131 552 5259

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