Yonsei Medical Journal
Vol. 32, No. 1, 1991

□Original Article□

An Analysis of 2361 Cases of Renal Biopsy in Korea

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To evaluate the distribution pattern of renal diseases based on needle biopsy, we analyzed 2361 cases of renal biopsy and necropsy material examined at the Department of Pathology from 1973 to 1988. The average age was 21.1 years for males and 23.7 years for females. The adult cases comprised 60.2% and the child cases 39.8%. The male to female ratio was 1.6: 1 in adults and 2.3: 1 in children. Glomerular diseases were 97.8% of the total; primary glomerulonephritis (GN) 59.8% and secondary GN 27.6%. The major glomerular diseases, in descending order of frequency, were; minimal change nephrotic syndrome (MCNS; 24.2%), IgA nephropathy (IgAN; 17.8%), benign recurrent hematuria (BRH; 8.8%), membranous GN (MGN; 7.9%), acute poststreptococcal GN (APSGN; 7.3%), mesangioproliferative GN (MspGN; 5.5%), minimal mesangiopathy (5.5%), membranoproliferative GN(4.1%), and focal segmental glomerulosclerosis (FSGS; 2.7%). GN of systemic disease included 77 cases of lupus nephritis, 157 cases of Henoch-Schönlein purpura nephritis (HSPN) and 7 cases of systemic infection excluding Hepatitis B viral hepatitis. The most common glomerular diseases were MCNS, IgAN, MGN and MspGN in adults, and MCNS, BRH, HSP-N and APSGN in children. HBs antigenemia was found in 71cases, of which MGN and IgAN were the most frequent. HBs antigenemia-associated MGN was prevalent in male children, whereas IgAN was prevalent in adults. A repeated biopsy was obtained from 91 patients two to five times, either because of first biopsy failure (22 cases) or to evaluate the treatment response. Three cases of MCNS were confirmed by the second biopsy to be FSGS.

Key Words: Renal biopsy, glomerulonephritis, Korea

The prevalence of glomerular disease is somewhat differerent in various parts of the world, according to race, age and, perhaps, according to renal biopsy indications. It is well known that IgA nephropathy (IgAN) demonstrates geographic or racial differences in occurrence; that is, it is prevalent in Japan (Kitajima *et al.* 1983), Singapore (Sinniah *et al.* 1981), Austrialia (Clarkson *et al.* 1984), Italy (D' Amico 1985), France, and also in Korea (Lee *et al.* 1987), whereas, the incidence is low in the U.S. (Galla *et al.* 1984) and Canada. Acute glomerulonephritis associated with streptococcal infection is more frequent in children, whereas secondary GN is generally prevalent in adults. In Korea, Many reports (Lee *et al.* 1986, Ko *et al.* 1987), mainly have been on single glomerular disease (Lee *et al.* 1987; Kim *et al.* 1988-89), so that an overview of the distribution of glomerular diseases has been limited.

We aim to review retrospectively the renal biopsy and necropsy materials based on needle biopsy and to analyze the distribution pattern of renal diseases, especially glomerular lesions.

MATERIALS AND METHODS

The materials were composed of 2514 cases of renal biopsy/necropsy examined at the Department of Pathology, Yonsei University College of Medicine from 1973 to 1988. Cases from Yonsei University Medical Center comprised 85.6% and those referred from other hospitals inside Korea accounted for 14.4%. We excluded 57 cases of biopsy failure and 96 cases of insufficient or inadequate materials.

Received July 5, 1990
Accepted September 28, 1990

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A total of 2361 cases were studied and classified according to W.H.O. classification (Churg and Sobin 1982a and 1982b). HBs antigenemia, recorded in available cases, was examined either by radioimmunoassay or by the double diffusion method. Rebiopsy cases were collected and analyzed.

The renal biopsy specimen was routinely divided into 3 pieces for light, immunofluorescent and electron microscopy. For the light microscopical examination, the specimen was fixed in 10% neutral formalin, embedded either in paraffin or plastic, serially cut at 4-5 μ or 1 μ thickness, and stained with hematoxylin-eosin, periodic acid-Schiff, Masson's trichrome and periodic acid-Schiff-methenamine silver stains.

For the immunofluorescent microscopical examination, a portion of the fresh renal tissue was frozen, exposed to FITC-conjugated antihuman -IgG, -IgA, -IgM, -C3, -C4, -C1q and -fibrinogen (Meloy Inc) and examined with a Leitz dialoux immunofluorescent microscope. The intensity of mesangial immune deposits was divided into four categories: trace($\pm$), mild(+), moderate(++), and severe(+++).

For the electron microscopical examination a small piece of renal tissue was fixed in 3% glutaraldehyde, postfixed with Os04, embedded in Epon mixture, double stained with uanium acetate and lead citrate, and examined with a Hitachi H-500 transmission electron microscope.

All 2361 cases were studied by light microscopy. Over 90% of the cases were studied routinely by immunofluorescent microscopy, and over 60% of the cases were studied selectively by electron microscopy.

RESULTS

Age and sex distribution

Excluding 49 unrecorded cases, there were 1391 adults (60.2%) and 921 children(39.8%). The sex ratio(M: F) was 1.6: 1 in adults and 2.3: 1 in children. The average age was 22.3 years in males and 23.7 years in females.

Distribution of glomerular disease

Glomerular diseases were 97.8% of the total; primary glomerulonephropathy (GN) was 59.8% and secondary GN was 27.6% (Table 1).

Primary GN: The major primary glomerulonephritides were minimal change nephrotic syndrome (MCNS), membranous glomerulonephritis (MGN), acute poststreptococal glomerulonephritis(APSGN) mesangioproliferative glomerulonephritis(MspGN) and minimal mesangiopathy in descending order. MCNS was 559 cases(male 407, female 152). The mean age was 19.4 years in males and 26.4 years in females; it was prevalent under 30 years of age. The male to female ratio of MCNS was 2.7: 1. MGN was manifested in 183 cases, and the mean age was 31.9 years. MGN was evenly distributed from the first to sixth decades and showed male predominance. APSGN was shown in 168 cases, and predominantly affected the first and second decades (mean age: 16.0 years). The sex ratio was 1.3: 1 with slightly Male predominant. MspGN was in 134 cases, the sex ratio was 1.4: 1; it was prevalent in the middle-aged group. Ninety-five cases of membranoproliferative glomerulonephritis (MPGN) included one case of dense deposit disease, with a sex ratio of 1.8: 1 and mean age of 28.3 years. Focal segmental glomerulosclerosis(FSGS) was manifested in 62 cases and the mean age was 25.8 years. Male predominance was noted in focal GN, MGN, MCNS, and FSGS(Table 2).

Secondary GN: Secondary GN was IgAN, Henoch-Schönlein purpura nephritis(HSP-N) and lupus nephritis, in descending order. HSP-N was prevalent in children and IgAN and lupus nephritis were prevalent in adults. IgAN consisted of 411 cases, comprising 17.8% of the total. IgAN was prevalent in the second and third decades, approaching 60.8%. The mean age of IgAN was 24.7 years and the male to femal ratio was 1.7: 1; whereas, those of HSP-N were 13.6 years and 2.4: 1 (Table 3).

Lupus nephritis showed a female predominance of 3.5: 1(F: M) and was prevalent from the second to fourth decades(80.3%).

Hereditary nephritis: Among patients with hereditary nephritis, Alport syndrome was diagnosed in a patient who had a renal biopsy taken 4 times during a seven year period. The majority of the hereditary nephritis in our study was benign recurrent hematuria (BRH) comprising 203 cases, and most prevalent in children.

Distribution of tubulointerstitial and vascular diseases

Tubulointerstitial nephritis and vascular disease appeared in 51 cases, of which acute tubular necrosis, chronic pyelonephritis and interstitial nephritis occupied over 70% (Table 4).

Table 1. Distribution of glomerular diseases according to W.H.O. classification

	Total No. (%)	Aduts		Children		Unstated
		M	F	M	F	
PRIMARY GLOMERULAR DISEASES						
Minimal Change Nephrotic Syndrome	559(24.2)	233	111	168	39	8
Focal Segmental Glomerulosclerosis	62(2.7)	29	14	12	6	1
Acute Postinfectious GN	168(7.3)	28	32	66	38	4
Membranous GN	183(7.9)	98	39	10	2	1
With HBs antigenemia		8	1	20	4	
Mesangioproliferative GN	134(5.8)	55	44	19	13	3
Membranoproliferative GN	95(4.1)	52	21	9	12	1
Rapidly Progressive GN	10(0.4)	5	2	1	2	0
Focal Proliferative/Global Sclerosing GN	9(0.4)	5	2	2	0	0
Minimal Mesangiopathy	128(5.5)	43	35	23	17	10
Chronic GN	29(1.3)	18	9	1	1	0
Unclassified GN	35(1.5)	19	6	6	2	2
SYSTEMIC DISEASES						
Systemic Lupus Erythematosus	77(3.3)	8	49	9	10	1
Henoch-Schonlein Purpura Nephritis	157(6.8)	17	13	92	33	2
IgA nephropathy	411(17.8)	181	125	69	26	10
Systemic Infection	7(0.3)	4	0	2	0	1
VASCULAR DISEASES						
Hemolytic Uremic Syndrome	1(0.0)	0	0	1	0	0
Scleroderma	2(0.1)	0	1	1	0	0
METABOLIC DISEASES						
Diabetes Millitus	8(0.3)	6	2	0	0	0
A nyloidosis	1(0.0)	1	0	0	0	0
Cryoglobulinemia	1(0.0)	0	1	0	0	0
HEREDITARY DISEASES						0
Alport Syndrome	4(0.2)	0	0	4	0	0
Benign Familial Hematuria	4(0.2)	0	0	1	3	0
Congenital Nephrotic Syndrome	2(0.1)	0	0	2	0	0
Benign Recurrent Hematuria	203(8.8)	15	12	106	67	3
Others	4(0.2)	0	1	2	1	0
PREECLAMPTIC NEPHROPATHY	2(0.1)	0	2	0	0	0
END STAGE KIDNEY	11(0.5)	4	5	2	0	0
TRANSPLANTATION REJECTION	3(0.1)	3	0	0	0	0
TOTAL	2310(99.9)	832	527	628	276	47

Table 2. Distribution by age and sex in primary glomerular diseases

Glomerular diseses	Total	- 10	- 20	- 30	- 40	- 50	- 60	- 70	M: F
Minimal change nephrotic syndrome	551	131	160	154	52	23	24	7	2.7 : 1
Focal segmental glomerulosclerosis	60	11	12	14	12	7	4	1	2.0 : 1
Acute postinfectious GN	164	50	54	23	18	10	5	4	1.3 : 1
Membranous GN	182	21	28	28	38	35	24	8	3.0 : 1
Mesangioproliferative GN	131	15	17	17	36	28	14	4	1.4 : 1
Membranoproliferative GN	93	9	22	21	21	12	6	3	1.8 : 1
Rapidly progressive GN	10	3	2	0	1	3	0	1	1.5 : 1
Focal proliferative GN	9	1	2	2	2	2	0	0	3.5 : 1
Minimal mesangiopathy	118	31	9	19	31	18	6	4	1.4 : 1
Chronic GN	29	0	4	15	5	4	1	0	1.9 : 1
Unclassified GN	33	3	12	5	4	4	4	1	2.8 : 1

HBs antigenemia

The distribution of cases with HBs antigenemia is shown in Table 5. MGN and IgAN were the most frequent, although there was not a case of the two overlapping. MGN associated with HBs antigenemia was found in 24 children and 9 adults; the sex ratio was 7: 1 in children and 3: 1 in adults. IgAN was found in 12 adults and one child, and the sex ratio was 1.6: 1.

Rebiopsy

Rebiopsy was repeated two to five times in 91 patients for a total of 197 cases. Twenty-two patients had a renal biopsy repeated due to first biopsy failure or insufficient material for evaluation. In the remaining cases, rebiopsy was done for the evaluation of treatment response. The cases were MCNS, MGN, and MPGN, in descending order (Table 6).

Three cases of MCNS in the initial biopsy were confirmed to be FSGS in the follow-up biopsies. Follow-up biopsy was done in five patients with IgAN, three of whom experienced first biopsy failure. A 9-year-old male had C3, fibrinogen as well as IgA deposits in the mesangium in the first biopsy. Interval changes were not found in the second biopsy done 7 months later by both light and immunofluorescent microscopy. One case of APSGN had a rebiopsy due to persistent microscopic hematuria, which revealed minimal mesangial C3 deposit. One patient, who had four biopsies

Table 3. Comparison of age and sex distribution between IgA nephropathy and Henoch-Schonlein purpura nephritis

Age (yrs)	IgA nephropathy		H-S purpura nephritis	
Sex	M	F	M	F
- 10	34	10	48	26
- 20	69	33	55	10
- 30	84	58	3	5
- 40	36	31	1	2
- 50	17	14	2	3
- 60	5	5	0	0
- 70	5	0	0	0
Total	250	151	109	46

Table 5. Distribution of 71 cases with HBs antigenemia

Diseases	No. of cases
IgA nephropathy	13
Membranous GN	33
Acute poststreptococcal GN	7
Minimal change nephrotic syndrome	7
Membranoproliferative GN	4
Benign recurrent hematuria	3
Focal proliferative GN	1
Systemic lupus erythematosus	1
Hemolytic uremic syndrome	1
End stage kidney	1

Table 4. Distribution of tubulointerstitial and vascular diseases according to W.H.O. classification

	Total No. (%)	Adults		Children		Unstated
		M	F	M	F	
TUBULOINTERSTITIAL DISEASES						
Acute Tubular Necrosis	18(35.3)	5	2	7	2	2
Chronic Pyelonephritis	10(19.6)	5	4	1	0	0
Interstitial Nephritis	9(17.6)	7	1	1	0	0
Gouty Nephropathy	2(3.9)	1	1	0	0	0
Myeloma Kidney	2(3.9)	1	1	0	0	0
Renal Tubular Acidosis	2(3.9)	0	0	0	1	0
VASCULAR DISEASES						
Nephrosclerosis	4(7.8)	1	3	0	0	0
Infarction	1(2.0)	0	0	1	0	0
Bartter's Syndrome	2(3.9)	0	0	2	0	0
TUMOR(Wilms' tumor)	1(2.0)	0	0	1	0	0
TOTAL	51(99.9)	20	12	13	4	2

Table 6. Distribution of 197 rebiopsy cases in 91 patients

Diseases	No. of pts.	No. of biopsies
Minimal change nephrotic syndrome	27	56
Henoch-Schonlein purpura nephritis	17	44
Membranous GN	10	20
Membranoproliferative GN	6	12
IgA nephropathy	5	11
Focal segmental glomerulosclerosis	5	10
Minimal mesangiopathy	3	6
Mesangioproliferative GN	3	6
Acute poststreptococal GN	3	6
Systemic lupus erythematosus	3	6
Others*	9	20

Others: rapidly progressive GN, 1; acute tubular necrosis, 1; Alport syndrome, 1; end stage kindey, 1; benign recurrent hematuria, 1; unclassifed GN, 1; unsatisfactory, 3

had Alport syndrome; the diagnosis was made in the third biopsy by electron microscopic examination.

DISCUSSION

Distribution patterns of renal disease have been reported worldwide so far. The percentages could differ according to the age, sex or the clinician's biopsy policy, but some diseases did have geographic differences. In Korea, though representative data was not reported, the distribution patterns seemed to be no different from those of other Far East countries (Oshima and Hatano 1979, Lin 1986). This turned out to be especially true in the prevalence of IgA nephropathy and HBs antigenemia-associated glomerular lesions.

IgAN occupied 17.8% of the total and was the second most common glomerular disease next to MCNS in our series. In other hospitals in Korea, the incidence of IgAN has been reported to be 16.7% to 27.5% (Lee *et al.* 1987) in adults and 10.3% (Chung *et al.* 1986) to 16.9% (Cho *et al.* 1987) in children. This disease is highly prevalent in Japan, with the highest incidence (Kitajima *et al.* 1981 and 1983, Levy and Berger 1988), China(Galla 1988), Singapore(Sinniah, *et al.* 1981) and Australia (Clarkson *et al.* 1979). Since mass screening is popular in Japan, the difference may not be as high as the percentages indicate. Indonesia, although in Asia, has a low incidence (Sidabutar *et al.* 1986), which may reflect a racial difference. There are so many similarities between IgAN and HSP-N that these two diseases might represent a different spectrum of one disease (Choi *et al.* 1986, Waldo 1988). However, there was a difference in mean age and sex ratio, that is 24.7 years and 1.6: 1 in IgAN and 13.6 years and 2.4: 1 in HSP-N. The pathogenetic mechanisms of IgAN have been actively studied and proposed in various papers recentaly. The relationships between IgAN and HSP-N (Choi *et al.* 1986; Weldo 1988) and also mesangial IgA deposition in other conditions (Choi *et al.* 1989; Choi *et al.* 1990) are not yet fully defined. For this reason, IgAN is classified tentatively with secondary glomerular diseases in our study.

HBs antigenemia was more frequently found than in western countries, but the occurrence rate was similar to Taiwan (Hsu *et al.* 1983; Lin 1987) and Japan (Nishioka *et al.* 1975) which are also endemic for hepatitis B viral infection. The positive rate of HBs antigen in circulating blood was increased in patients with renal diseases, both in adults and children, as compared with age-matched controls (Kim 1981, Kim *et al.* 1982). Choi *et al.* (1981) and Kim *et al.* (1982) reported HBs antigen positivity to be 10.2 to 10.7% in children with nephritis. It was positive in 25.3% of adults with nephritis (Kim 1981). It is well known that MGN was the most common glomerular disease associated with HBs antigenemia (Cheong *et al.* 1989, Kleinkenecht *et al.* 1979, Southwest Pediatric Nephrology Group 1985, Takekoshi *et al.* 1978, Wiggelingkhuisen *et al.* 1983). We found 71 cases with HBs antigenemia, of which MGN was the most frequently associated (Table 5). In our present study, it is till uncertain whether or not HB antigens play an important role

in various types of glomerular diseases, particularly in the MGN type. For these reasons, MGN associated with HB antigenemia is classified tentatively, not in secondary but primary glomerular diseases, and separately classified among the primary MGN. Twenty-four out of 36 MGN cases in children were HBs antigen positive. The male to female ratio was markedly increased in HBs antigen positive children. In adults, IgAN, MPGN, MCNS as well as MGN were associated with HBs antigenemia. This differes from the reports that MPGN was the most prevalent type in adults (Choi 1978, Kim *et al.* 1977, Takeda *et al.* 1988). Recently, Lai *et al.* (1988) reported that IgAN was strongly associated with HBs antigenemia in endemic areas, supported by with our results.

MGN was the third most common glomerular disease and showed a rather wide age distribution in our series, a difference from the reports in which it was reported to usually affected middle age. This might be attributed to the prevalence of HBs antigenemia in Korea. The incidences of MCNS (Churg and Duffy 1973), APSGN (Habib 1978; Germuth and Rodriguez, 1973), MspGN and MPGN (Bohle *et al.* 1974, Cameron 1973) were similar to other reports. MCNS was the most common glomerular disease both in adults and children and occupied 25.4 and 22.9%, respectively. APSGN, HSP-N and BRH were Prevalent in children, MCNS and IgAN were prevalent in the second and third decades, and MspGN in the fourth and fifth decades.

BRH, presently known as thin GBM nephropathy, can affect children and adults. Immunofluorescent study was applied to 185 of the 203 cases of BRH while electron microscopic study was applied to 120 cases. We observed that many cases of BRH showed C3 vascular deposit, particularly on afferent arterioles by immunofluorescent microscopy, and electron microscopy commonly showed focal attenuation of the lamina densa and widening of the lamina rara interna, especially in children. However, we did not exclude the possibility that BRH may be a heterogenous group of diseases presenting hematuria, including not only hereditary but also unnoticed secondary acquired lesions. Alport syndrome was confirmed in one case, and the findings were similar to those of the reported cases.

Of rebiopsies performed in 91 patients, 24.2% were done due to initial biopsy failure. Three patients with MCNS in the first biopsy were confirmed to be FSGS. Five cases of IgAN were biopsied repeatedly, but only one case could be successfully evaluated and revealed no interval change.

Acute tubular necrosis and chronic pyelonephritis were the major tubulointerstitial diseases among needle biopsied cases, but occupied only a small portion of total biopsy materials.

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