An Analysis of 3,555 Cases of Renal Biopsy in Thailand

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Background: *The knowledge of the epidemiology of biopsied renal diseases provides useful information in clinical practice. There are several epidemiologic population-based studies of biopsy-proven nephropathies with detailed clinicopathologic correlations that could be different according to the country analyzed.*
Objective: *To identify the prevalence of primary and secondary glomerular diseases and to study the trend of the pattern changes of the glomerulopathy in Thailand.*
Material and Method: *A retrospective study of percutaneous renal biopsies during a 23-year period of 1982 to 2005 was performed. A total of 3,555 consecutive native kidney biopsies in adult patients between 12 and 84 years of age were analyzed for the prevalence and changes in the 5-year interval over the two decades.*
Results: *From the clinical trial of 3,275 patients, the ratio between primary and secondary glomerular diseases was 2:1 (2154:1121). The most common primary glomerular disease (2154 patients) were IgM nephropathy (n = 986, 45.8%) followed by IgA nephropathy (n = 386, 17.9%); membranous nephropathy (n = 341, 15.8%); diffuse endocapillary proliferative glomerulonephritis (n = 114, 5.3%) and diffuse crescentic glomerulonephritis (n = 71, 3.3%). Lupus nephritis was the most prevalent cause of secondary glomerulonephritis in the present study (n = 992, 88.5%). Examination of the 5-year interval along the study period revealed a significant increase in the prevalence of IgA nephropathy and diabetic nephropathy. Prevalence of focal and segmental glomerulosclerosis rose by five times over the last two decades in contrast to IgM nephropathy, which prevalence is decreasing.*
Conclusion: *There is high prevalence of IgM nephropathy, IgA nephropathy, and lupus nephritis in Thailand which is different from other countries. It could be due to various races and altered environments. The information obtained from these results is an important contribution for the understanding of the prevalence in renal diseases in Thailand. It can be used as the baseline data for making efficient research into the appropriate and beneficial way of management in the future.*

Keywords: *Glomerulonephritis, Native kidney, Pathology, Prevalence, Renal biopsy*

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The knowledge of the epidemiology of biopsied renal diseases provides useful information in clinical practice. There are several epidemiologic population-based studies of biopsy-proven nephropathies with detailed clinicopathologic correlations that could be different according to the country analyzed[1-9].

The aim of the present study was to identify the prevalence of primary and secondary glomerular diseases and study the trend of changes in the pattern of the glomerulopathy in Thailand.

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This report is intended to serve as a resource for nephrologists, healthcare providers, researchers, and government officials to stimulate new analysis and investigations, to improve treatment of renal diseases and to help national and regional governments to develop protocols for preventive medicine

Material and Method

The histopathological diagnoses of renal tissue were analysed retrospectively from 3,555 consecutive native kidney biopsies performed in adult patients (≥ 12 years of age) at the Department of Pathology, Siriraj Hospital, Mahidol University in Bangkok during a 23-year-period (1983-2005). 3,275 glomerular and 280 non glomerular diseases were found. All patients were admitted to the Renal Division, Department of Medicine, Siriraj Hospital due to some certain significant abnormal urinary findings and clinical data of 2,683 patients from 1987 to 2005 were reviewed.

The renal biopsy specimens were studied by light, immunofluorescence and/or immunoperoxidase, and electron microscopy. The criteria for diagnosis and classification of the glomerular diseases were those published by W.H.O. Collaborating centre for the Histological Classification of Renal Diseases in 1995[10] with minor modification. Only glomerular diseases of the native kidney are subjected for this analysis.

The clinical data were obtained from the request form for renal biopsy and included sex, age, date of biopsy and evidence of renal disease comprised edema, significant proteinuria (≥ 500 mg/24 hours), significant hematuria (≥ 5 red blood cells/high power field) and nephrotic range proteinuria (≥ 3.5 gm of 24 hours urine protein). Other pertinent clinical findings, namely hypertension (blood pressure ≥ 140/90 mm Hg), and creatinine level, are also included. The prevalence of the diseases in each 5-year period were compared and correlated with some certain pertinent clinical findings including age, sex, significant abnormal urinary findings, and hypertension

Statistical analysis

Distribution of the various renal biopsy diagnoses during 1983-2005 was compared by using

Table 1. Percentage of primary glomerular disease in 2,154 renal biopsies

	1983-1987	1988-1992	1993-1997	1998-2002	2003-2005	Total
IgM nephropathy	450 (62.5%)	225 (62.3%)	126 (44.4%)[a,b]	125 (28.8%)[c,d,e]	60 (16.9%)[f,g,h,i]	986 (45.8%)
IgA nephropathy	74 (10.3%)	36 (10.0%)	40 (14.0%)	111 (25.6%)[c,d,e]	125 (35.2%)[f,g,h]	386 (17.9%)
Membranous GN	78 (10.8%)	51 (14.1%)	68 (23.9%)[a]	80 (18.4%)	64 (18.0%)	341 (15.8%)
Diffuse endocapillary proliferative GN	48 (6.7%)	14 (3.9%)	17 (6.0%)	23 (5.3%)	12 (3.4%)[f]	114 (5.3%)
Diffuse crescentic GN	7 (1.0%)	8 (2.2%)	7 (2.5%)	25 (5.8%)[c]	24 (6.8%)[f]	71 (3.3%)
Mesangiocapillary GN type 1	9 (1.3%)	11 (3.0%)	13 (5.0%)	16 (3.7%)	16 (4.5%)	65 (3.0%)
Focal & segmental GN	12 (1.7%)	-	-	17 (3.9%)	32 (9.0%)	61 (2.8%)
Diffuse sclerosing GN	12 (1.7%)	3 (0.8%)	9 (3.2%)	12 (3.0%)	4 (1.1%)	40 (2.0%)
Mesangial proliferative GN	14 (2.0%)	6 (1.7%)	3 (1.0%)	10 (2.3%)	4 (1.1%)	37 (1.7%)
Unclassified GN	16 (2.2%)	6 (1.6%)	1 (0.4%)	8 (1.8%)	6 (1.7%)	37 (1.7%)
Minimal change	-	1 (0.3%)	-	7 (1.6%)	8 (2.3%)	16 (0.7%)
Total	720	361	284	434	355	2154

Data were presented as number (%), GN, glomerulonephritis
a, Difference of prevalence between year 1983-1987 and 1993-1997
b, Difference of prevalence between year 1988-1992 and 1993-1997
c, Difference of prevalence between year 1983-1987 and 1998-2002
d, Difference of prevalence between year 1988-1992 and 1998-2002
e, Difference of prevalence between year 1993-1997 and 1998-2002
f, Difference of prevalence between year 1983-1987 and 2003-2005
g, Difference of prevalence between year 1988-1992 and 2003-2005
h, Difference of prevalence between year 1993-1997 and 2003-2005
i, Difference of prevalence between year 1998-2002 and 2003-2005
p-value < 0.05

Pearson's chi-square test[11]. The chi-square test was also used to compare prevalence within 5 years in each group. The chi-square analysis showed a significant difference in the distribution of diagnoses among five periods (p values < 0.05).

Results

Prevalence of primary glomerular diseases

Data listed in Table 1 demonstrate the prevalence of adult primary glomerular diseases in the presented overall renal biopsy population from January 1983 to December 2005. The percentage of primary glomerular diseases in the present study was 65.8 (2,154 from a total of 3,275 glomerular diseases). The five most common glomerular diseases were IgM nephropathy (986 cases, 45.8%) followed by IgA nephropathy (386 cases, 17.9%), membranous nephropathy (341 cases, 15.8%), diffuse endocapillary proliferative glomerulonephritis (GN) (114 cases, 5.3%) and diffuse crescentic GN (71 cases, 3.3%) respectively.

The relative frequency of IgA nephropathy increased significantly from 10.3% in the first period (1983 to 1987) to 35.2% in the last period (2003 to 2005), $p < 0.05$. Although, there were a small number of focal segmental glomerulonephritis in the present series, the prevalence increased five times during the two decades (1.7% to 9% respectively). The relative frequency of IgM nephropathy decreased significantly from 62.5% in the first period to only 16.9% in the last period ($p < 0.05\%$).

Prevalence of secondary glomerular diseases

Data listed in Table 2 demonstrate the prevalence of adult secondary glomerular diseases in the percentage of 34.2 of total glomerular diseases (1,121 from 3,275). The most common etiology is lupus nephritis, 88.5% (992 from 1,121) and followed by diabetic nephropathy (58 cases, 5.2%), amyloidosis (24 cases, 2.1%), nephritis in Henoch-Schonlein purpura (20 cases, 1.8%), and Alport's syndrome (17 cases, 1.5%) respectively. The relative frequency of diabetic nephropathy increased significantly from 1.9% in the first period to 8.5% in the last period, $p < 0.05$.

In the authors' experience, there are some other glomerular diseases on top of diabetic nephropathy; four IgA nephropathy, three membranous nephropathy, two IgM nephropathy, two lupus nephritis, one diffuse crescentic glomerulonephritis and one membranoproliferative glomerulonephritis. In addition, there are two IgM nephropathy and one focal segmen-

Table 2. Percentage of secondary glomerulonephritis in 1,121 renal biopsies

Secondary GN	1983-1987	1988-1992	1993-1997	1998-2002	2003-2005	Total
Lupus nephritis	197 (91.2%)	131 (92.3%)	146 (89.0%)[a]	276 (87.3%)[c,d]	242 (85.5%)[f,g]	992 (88.5%)
Diabetic nephropathy	4 (1.9%)	3 (2.1%)	9 (5.5%)[a]	18 (5.7%)[c]	24 (8.5%)[f,g]	58 (5.2%)
Amyloidosis	5 (2.3%)	2 (1.4%)	2 (1.2%)	10 (3.2%)	5 (1.8%)	24 (2.1%)
Nephritis in Henoch-Sch nlein purpura	5 (2.3%)	1 (0.7%)	4 (2.4%)	5 (1.6%)	5 (1.8%)	20 (1.8%)
Alport's syndrome	5 (2.3%)	5 (3.5%)	3 (1.8%)	2 (0.6%)	2 (0.7%)	17 (1.5%)
Thrombotic micro-angiopathy including toxemia of pregnancy	-	-	-	5 (1.6%)	5 (1.8%)	10 (0.9%)
Total	216	142	164	316	283	1121

Data were presented as number (%), GN, glomerulonephritis
a, Difference of prevalence between year 1983-1987 and 1993-1997
b, Difference of prevalence between year 1988-1992 and 1993-1997
c, Difference of prevalence between year 1983-1987 and 1998-2002
d, Difference of prevalence between year 1988-1992 and 1998-2002
e, Difference of prevalence between year 1993-1997 and 1998-2002
f, Difference of prevalence between year 1983-1987 and 2003-2005
g, Difference of prevalence between year 1988-1992 and 2003-2005
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i, Difference of prevalence between year 1998-2002 and 2003-2005
p-value < 0.05

tal glomerulonephritis (negative immunofluorescent and electron microscopic deposition) in lupus nephritis and three anti-glomerular basement membrane with positive high anti-GBM titre without lung involvement and one Fabry disease, the first case report in Thailand, is found in the present study.

Discussion

The present study may be representative of a range of renal diseases in Thailand, even though it was done in one single tertiary centre, there where referred patients from all provinces included. The authors had data on 3,555 biopsies over 23 years up to now. There were no reports with a large number of biopsies that have been published in Thailand.

In Thailand, idiopathic IgM nephropathy is the most frequent biopsied renal pathology in adults. However, there has been a significant decrease in the frequency of IgM nephropathy since 1993. It could be from the reason that the authors did not perform every GN patient when there was a good response to the treatment and IgM nephropathy in Thailand has a response rate up to 60 percent. The geographical difference in various types of primary glomerulonephritis is shown in Table 3 which compares the prevalence in Western and Asian countries.

The next two common glomerulonephritis in Thailand are IgA nephropathy (17.9%) and membranous nephropathy (15.8%). The difference of these two diseases is the increasing prevalence of IgA nephropathy during the 23 years from 10.3 to 35.2 percent. All these patients had clinical and laboratory abnormalities from biopsy indications. Therefore, the true numbers of IgA nephropathy must be much higher than 17.9 percent. The change in the prevalence of IgA nephropathy may be from the biopsy policies that were used for the treatment. The prevalence of membranous GN remained constant from 1983 to 2005.

In Thailand the prevalence of lupus nephritis has remained high for the last 20 years. It could be from genetic, infections, and environments of Asian populations. In contrast, the authors observed a significant increase in the prevalence of diabetic nephropathy during these two decades which follows the high prevalence of diabetes mellitus. Even though, there are small numbers of focal segmental glomerulonephritis in the present series compared with countries having Western populations (Table 3). It may be associated with racial dif-ference especially in Blacks and Hispanic[12-15]. The five times increasing prevalence for the past two decades (1.7% to 9%) is similar to the Western countries[12,16-18]. In 2000, Braden GL et al[17] showed the raising prevalence of FSGS from 13.7% to 25% for the two decades. In 2005, Dragovic et al[12] also reported the increasing prevalence of FSGS from 13.7% to 25% during the two decades. In 2004, Bahiense-Oliveira M et al[18] demonstrated that FSGS was the most common primary glomerulonephritis in Brazil and seemed to be increasing from 22.3% to 34% during twenty one years. Nevertheless, this finding is different from the report in Singapore that there was no change in the prevalence of FSGS over the past two decades[19]. The variation in the pre-valence of glomerular diseases and their changes may exist among populations, races, environment and differences in the biopsy policies.

The nephrotic syndrome and nephrotic nephritic syndrome are the frequent pathological conditions in which renal biopsy is a necessary investigation for diagnosis. The leading symptom of IgM nephropathy and membranous GN is nephrotic range proteinuria. While nephrotic nephritic manifestation with

Table 3. Nephrotic syndrome: Main pathologies involved (%)

	Thailand	Italy[1]	Spain[16]	Denmark[6]	Korea[9]	Japan[7]	United Arab Emeritis[23]
MCD	0.7	12	17.1	23.5	59.4	37.7	26.2
FSGS	2.8	12.3	14.1	8	11.1	9	15.4
MN	15.8	32.9	22.9	22.4	15.9	23.3	28.3
IgAN	17.9	2.4	4.5	17.5	3.3	19.2	3.2
MPGN	1.7	4.6	6.5	9.9	6.8		
IgMN	45.8	1.9					

Abbreviation are: FSGS, focal and segmental glomerulonephritis; IgAN, IgA nephropathy; MCD, minimal change disease; MN, membranous glomerulonephritis; MPGN, Membranoproliferative glomerulonephritis; IgMN, IgM nephropathy

hypertension and renal dysfunction are prominent findings in IgA nephropathy and lupus nephritis. It seems that these two diseases have a trend of increasing severity or otherwise the authors perform renal biopsy in rather complicated patients.

IgA nephropathy was most frequently found in chronic renal insufficiency thus confirming that this disease is the primary cause of end-stage kidney disease, as shown by some European reports[20-22].

Conclusion

In conclusion, this analysis of 3,555 adult native kidney biopsies during a 23-year period shows that the frequency in the main groups of glomerulonephritis and the distribution of different glomerulonephritis change in some forms over a long period. Their correlations with new generation of infections or environments and races or genetics still remain to be solved. The information obtained from these results is an important contribution to the understanding of the frequency of renal diseases in Thailand and will permit comparisons with renal biopsies in other countries of the world and permit future research into the appropriate way of taking care of these patients as well.

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โรคไตอักเสบชนิดปฐมภูมิและทุติยภูมิที่พบในการตรวจชิ้นเนื้อไตของผู้ป่วยไทยจำนวน 3,555 ราย

ไพศาล ปาริชาติกานนท์, รัตนา ชวนะสุนทรพจน์, ชัยรัตน์ ฉายากุล, บุณยฤทธิ์ ชื่นสุชน, สมเกียรติ วสุวัฏฏกุล, เกรียงศักดิ์ วารีแสงทิพย์, ทวี ชาญชัยรุจิรา, สุชาย ศรีทิพยวรรณ, อรรถพงศ์ วงศ์วิวัฒน์, นลินี เปรมัษเฐียร, ไกรวิพร เกียรติสุนทร, รัตนา ลาภกิจขจร, ลีนา องอาจยุทธ

จากการสำรวจผลชิ้นเนื้อไตทางพยาธิวิทยาจากผู้ป่วยที่มารักษาที่หน่วยโรคไต ภาควิชาอายุรศาสตร์ โรงพยาบาลศิริราช นาน 23 ปี ระหว่างปี พ.ศ. 2525 ถึงปี พ.ศ. 2548 จำนวนรวม 3,555 ราย พบผู้ป่วยโรคไตอักเสบชนิดปฐมภูมิ (2154 ราย) IgM nephropathy มากที่สุดคือ 986 ราย (45.8%) รองลงมาคือ IgA nephropathy 386 ราย (17.9%) ตามด้วย membranous nephropathy 341 ราย (15.8%), diffuse endocapillary proliferative glomerulonephritis 114 ราย (5.3%) และ diffuse crescentic glomerulonephritis 71 ราย (3.3%) ตามลำดับ ส่วนโรคไตอักเสบชนิดทุติยภูมิ (1,121 ราย) เป็น lupus nephritis มากที่สุด คือ 992 ราย (88.5%) แนวโน้มของโรคไตอักเสบ IgM จะลดลง แต่ FSGS, IgA และ diabetic nephropathy จะมากขึ้นอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) สถิติชนิดโรคไตอักเสบในผู้ป่วยไทยมีความแตกต่างกับของผู้ป่วยทางยุโรปและอเมริกา ซึ่งอาจมีปัจจัยจากเชื้อชาติ ความเป็นอยู่ สิ่งแวดล้อม ซึ่งข้อมูลเหล่านี้จะ เป็นประโยชน์อย่างยิ่งในการสืบค้นหาสาเหตุ พยาธิกำเนิด ตลอดจนแนวทางการรักษาผู้ป่วยไทยต่อไปในอนาคต