Malaysian J Pathol 1994; 16(1): 19 – 21

The pattern of renal disease in Malaysia

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Abstract

An analysis of 1000 consecutive, adequate renal biopsies from patients of the University Hospital Kuala Lumpur between 1982 and 1991 revealed: minimal change nephritis (20.7%), focal glomerulosclerosis (2.9%), proliferative glomerulonephritides (16.0%), membranous glomerulonephritis (5.5%), IgA nephropathy (18.5%), lupus nephritis (24.9%), end stage nephropathy (3.1%) and others (8.4%). Compared with the previous decade, IgA nephropathy has emerged as a common entity. Lupus nephritis forms the largest diagnostic entity and is probably related to the selected referral of SLE patients to this hospital.

Key words: Glomerulonephritis, IgA nephropathy, systemic lupus erythematosus, epidemiology.

INTRODUCTION

Urinary tract disease ranks as the fourth most common definitive cause of hospital admissions in Malaysia and renal disease ranks as the seventh most common cause of death in our population, accounting for more than 1000 medically certified deaths annually.[1] This, without doubt, is just the tip of the iceberg: the true morbidity and mortality due to renal disease is probably much higher. This paper presents information based on renal biopsies received at the Department of Pathology, University of Malaya and seeks to provide an insight into the pattern of renal disease in the Malaysian population.

MATERIALS AND METHODS

The Department of Pathology of the University of Malaya Medical Centre started its renal biopsy interpretation service as a diagnostic service for patients of the University Hospital Kuala Lumpur (UHKL) in 1969. Currently, about 150 renal biopsies are received per year.

All biopsies are examined through the standard procedures of light, immunofluorescence and electron microscopy. For light microscopic examination, paraffin-embedded biopsy material are sectioned at 1 micron thick and stained with the Haematoxylin and eosin, PAS, silver methanamine, Masson's trichrome and Martius scarlet blue.

For immunofluorescence examination, part of the biopsy was snap frozen in the fresh state in liquid nitrogen and (cryostat) frozen sections stained for immunoreactivity against anti human C3, IgG, IgA, IgM, IgD and IgE. Immunofluorescence examination was available for about 76.8% of biopsies received (or 94% of adequate biopsies).

Material was also routinely submitted for electron microscopy in all (95%) cases but the examination was carried out only when light microscopy was inconclusive.

Since 1988, the Department of Pathology of this Medical Centre has also extended its renal biopsy diagnostic service to other Governmental Hospitals in both Peninsular and East Malaysia. Biopsies are received in two pieces: one piece fixed in formalin for light microcopy; the other mounted fresh in OCT medium and packed in dry ice. The biopsies are air-flown in by courier service. Biopsies from these outside sources now average 250 per year. To cater for biopsies which are unsuitable for IF examination, we have applied an immunoperoxidase method as an alternative method to study renal immunopathology.

RESULTS

Information based on 1000 consecutive, adequate renal biopsies received from patients of the University Hospital between 1982 and 1991 were analysed and where relevant, compared against the pattern of the preceding 1000 biopsies received between 1970 and 1981 and against the pattern of biopsies received from centres outside of UHKL.

Demographic profile:
The age range of patients was 2 yr to 74 yr. Most of the biopsies (i.e > 60%) were from the 20-40

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yr age-group. The male:female ratio was 1:1.8 showing a female preponderance. The ethnic distribution of patients were: Chinese (73.3%), Malays (16.1%), Indians (9.9%) and others (0.7%). This pattern contrasted with the ethnic distribution of admissions to the University Hospital: Chinese (46.6%), Malays (24.3%), Indians (27.8%) and others (1.3%), suggesting that renal disease is more common in the Chinese.

Clinical presentation:

About 50% of patients presented with the nephrotic syndrome. Other modes of presentation included the nephritic syndrome, systemic lupus erythematosus (SLE), proteinuria and haematuria separately or in combination, hypertension or renal failure.

Histological pattern:

Of the primary glomerular diseases, minimal change nephritis was the most common (20.7%), followed, in descending rank order by the proliferative glomerulonephritidies (16.0%), membranous glomerulonephritis (5.5%) and focal glomerulosclerosis (2.9%). Of the secondary glomerulopathies, lupus nephritis (24.9%) and IgA nephropathy (18.5%) were the most prominent. The other types of glomerular diseases, together constituting 8.4% of the biopsies, consisted of a mixture of changes due to diabetes mellitus, acute tubular necrosis, tubulointerstitial disease, hypertension, amyloidosis and transplant rejections.

Interestingly, studies in this centre have shown that about 35% of *minimal change nephritis* biopsies exhibited faint (+ to ++) deposition of IgM in the mesangium. Patients with IgM positive biopsies did not differ from IgM negative ones in age and sex prevalence, clinical presentation, renal morphology and response to therapy.[2]

Of the *proliferative glomerulonephritides*, 36% showed pure mesangial cell proliferation (mesangial proliferative GN). 5% revealed the classical features of post-streptococcal acute diffuse proliferative GN and 6% showed crescent formation indicative of a rapidly progressive downhill course. 6% showed a focal proliferative picture.

Table 1 compares the pattern of glomerular disease in 1000 biopsies in the decade 1982-1991 to that of the previous decade. An outstanding difference in pattern is the emergence of IgA nephropathy as a common entity. This is probably because IgA nephropathy was a scarsely recognised entity before the mid-1970's.

TABLE 1: Histological patterns of renal biopsies, University Hospital Kuala Lumpur

Pattern	1970 – 81	1982 – 91
Minimal change	257	207
Focal glomerulosclerosis	54	29
Proliferative glomerulonephritis	248	160
Membranous glomerulonephritis	55	55
IgA nephropathy	58	185
Lupus nephritis	184	249
End stage	40	31
Others	104	84
TOTAL	1000	1000

Furthermore, most biopsies before 1977 were not subjected to immunofluorescence examination, hence IgA nephropathy could not be diagnosed then and was probably categorised as proliferative GN.[3]

A review of proven primary *IgA nephropathy*[4] cases showed the majority of patients to be young adults in the 20-30 year age-group. There was no significant sex preponderance, the male:female ratio being 1:1.5. The ethnic distribution was 72.4% Chinese, 16.2% Malays, 10.8% Indians and 0.5% others. The preponderance of Chinese was statistically significant ($p<0.01$) when the ethnic distribution was compared against non-obstetrical and non-nursery hospital admissions during the same period. Unlike earlier reports in the literature, the most common glomerular pattern in IgA nephropathy was diffuse mesangial proliferative GN (Table 2).

Lupus nephritis formed one of the largest diagnostic entity in this study. The ages of biopsied SLE patients ranged from 6 yr to 60 yr with the majority between 20 and 40 years. The

TABLE 2: Histological pattern of IGA nephropathy

	No.	(%)
No morphological abnormality	16	(11.3)
Focal glomerulosclerosis	7	(4.9)
Focal proliferative	21	(14.8)
Diffuse mesangial proliferative	89	(62.7)
Diffuse proliferative (unspecified)	2	(1.4)
Mesangiocapillary	1	(0.7)
Chronic glomerulonephritis	6	(4.2)
TOTAL	142	(100)

TABLE 3: Histological pattern of lupus nephritis (WHO classification)

	1970 – 1981		1982 – 1991		1970 – 1991	
Class	No.	(%)	No.	(%)	No.	(%)
I	5	(2.7)	13	(5.2)	18	(4.2)
II	31	(16.8)	38	(15.3)	69	(15.9)
III	16	(8.7)	7	(2.8)	23	(5.3)
IV	89	(48.4)	159	(63.9)	248	(57.3)
V	43	(23.4)	30	(12.0)	73	(16.9)
VI	0	(–)	2	(0.8)	2	(0.5)
TOTAL	184	(100)	249	(100)	433	(100)

male:female ratio of 1:10.3 indicated a marked female preponderance, a well known feature of SLE. The ethnic distribution of SLE patients reveal the majority to be Chinese (77.9%). This was significantly excessive compared against non-obstetrical and non-nursery hospital admissions over the same period, indicating that SLE is more common among the Chinese. WHO Class IV was the predominant histological pattern of lupus nephritis encountered (Table 3).

Biopsies from outside centres:

A comparison of renal biopsies between outside centres and the UHKL, showed that the patterns were essentially similar.[5] The main difference was in a larger proportion of minimal change disease and a smaller proportion of proliferative GN in biopsies from outside centres (Table 4). This difference was probably related to differences in selection criteria for biopsy between centres. Possibly, patients with the nephrotic syndrome are biopsied more readily outside. Renal diseases with favourable prognosis, such as minimal change disease, are probably under-represented in UHKL biopsies. Since 1975, childhood nephrotics seen at the UHKL are not usually biopsied unless they are steroid-resistance, steroid-dependence or have recurrent disease.[3]

DISCUSSION

The pattern of glomerular disease in Malaysia appears similar to that described in the West and the developed countries. In contrast, it is unlike that of tropical Africa and Papua New Guinea where proliferative glomerulonephritides and malaria related nephropathies form a significant proportion of biopsies.

IgA nephropathy has emerged as an important entity and usually presents as haematuria or proteinuria or both in young adults. Lupus nephritis is another important entity and probably reflects the relatively common occurrence of SLE in young Chinese females. There is also selective referral of SLE patients to the UHKL.

Although there are limitations due to bias referral and selection of patients for biopsy, this analysis provides an insight into the problem of renal disease in the Malaysian population, particularly into those that require more serious consideration.

TABLE 4: Comparison of renal biopsy patterns between UHKL and outside centres

Pattern	UHKL	Outside Centres
Minimal change	20.7%	30.6%
Focal glomerulosclerosis	2.9%	8.7%
Proliferative glomerulonephritis	16.0%	8.7%
Membranous glomerulonephritis	5.5%	4.4%
IgA nephropathy	18.5%	13.7%
Lupus nephritis	24.9%	25.1%
End stage	3.1%	3.3%
Others	8.4%	5.5%
TOTAL	100 %	100%

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