2nd REPORT OF THE MALAYSIAN REGISTRY of RENAL BIOPSY 2008

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&

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ABOUT MALAYSIAN REGISTRY OF RENAL BIOPSY

Renal biopsy remains the main investigation in the diagnosis of renal diseases. In addition, it plays a major role in determining the management and prognosis of parenchymal renal disease. The collection of demographic, clinical and laboratory data at the time of biopsy and the set up of a database are useful tools for studying renal parenchymal diseases.

The development of a renal biopsy registry in each country promotes many advantages and these include comparison in incidence of renal diseases, identification of different policies and practices in renal biopsy in different areas, linkage with other registries such as dialysis or transplant registry and identification of rare renal diseases. Thus, the registry is a source of epidemiological data and would provide useful information in the planning of health care and in organizing prospective clinical studies.

The incidence of glomerular disease varies according to population, demographic characteristics, environmental factors, socio-economic status and the prevalence of infectious diseases. At present, there is limited information on the prevalence and incidence of glomerular disease, its potential disease burden and the temporal trend in Malaysia. Hence, the Malaysian Registry of Renal Biopsy (MRRB) was set up in 2005 to address this deficiency.

The MRRB collects information about patients who undergo renal biopsy in Malaysia. The MRRB is a new component of National Renal Registry (NRR), which has been operating the Malaysian Dialysis and Transplant Registry (MDTR) since 1993.

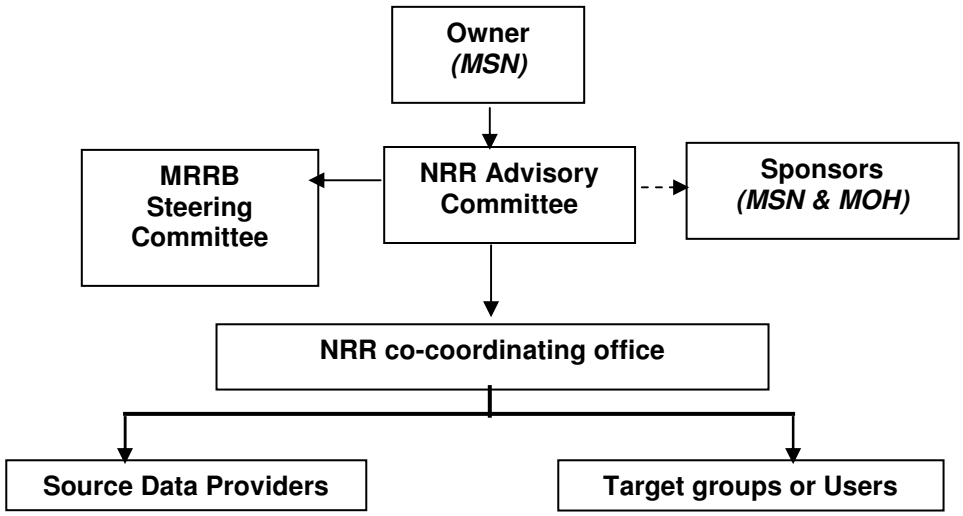
Objectives

The objectives of the MRRB registry are to:

1. Determine the disease burden attributable to glomerular disease (GD) by quantifying its incidence and prevalence, and its geographic and temporal trends in Malaysia.
2. Identify subgroups in the population at high risk of GD to whom preventive efforts should be targeted.
3. Identify potential causal and risk factors involved in GD.
4. Describe the clinical presentation and spectrum of GD.
5. Stimulate and facilitate basic, clinical and epidemiological research on GD.
6. Identify causes of allograft failure in our renal transplant population.
7. To audit the renal biopsy procedure, monitor both complications and quality of specimens in addition to identifying risk factors associated with complications.

Organization

The NRR organization is as follows:



Owner

The Malaysian Society of Nephrology (MSN) is the owner of this registry.

Sponsors

The MRRB is sponsored by the Malaysian Society of Nephrology (MSN) and the Ministry of Health, Malaysia.

NRR Advisory Committee

This is the committee established by the sponsors. The NRR Advisory Committee's role is to ensure that the MRRB stay focused on its objectives and to assure its continuing relevance and justification.

MRRB Steering Committee

The MRRB Working Committee supervises its operations.

National Renal Registry office

The NRR coordinating office is the designated coordinating center. It coordinates the data collection among the Source Data Providers (SDPs). It collaborates with Clinical Research Centre of Hospital Kuala Lumpur that provides epidemiological and statistical support for MRRB.

Source Data Providers (SDP)

These are centres that contribute the required data for MRRB. The SDP collects and enters data directly through the on-line web-base system. The pilot phase of the registry consists of SDPs from Ministry of Health.

Throughout this initial phase, we have refined and improved the database. In 2008, the registry is expanding to a national level to include participation from all nephrologists and renal physicians in Malaysia who perform renal biopsies. We hope the nephrology community will support us by submitting information, which is crucial to eventually improve the management of patients with Chronic Kidney Disease (CKD).

To participate in MRRB

Centres interested to participate in this registry please write in to NRR officially via post or email nrr@msn.org.my.

The following documents need to be completed and returned to facilitate participation.

- Centre Participation Self Reply Form
- Authorization Form
- Information Security Policy/User Agreement . One form per nominee as listed in the Authorization form. Users must have a personal mobile phone to received SMS authentication.

Upon receiving these documents, the centre shall be registered and each of the users of the MRRB shall be notified via their e-mail address.

Methodology

All patients from participating centres who undergo any kidney biopsy (native or graft) are to be enrolled into the registry.

On-line data submission is through MRRB web application or paper CRF. The data variables collected include demography, clinical presentation, and indication of biopsy, renal function, and laboratory data at presentation and at the time of biopsy, serological markers, virology status and histopathological result. In addition, an update on outcomes in terms of significant end-points such as end stage renal disease or death will be recorded annually.

DATA CONTRIBUTING CENTRES FOR THIS REPORT

Centre Name	Adult Nephrology	Paediatric Nephrology
96 Hospital Angkatan Tentera Lumut	√	
Fan Medical Renal Clinic	√	
Ipoh Specialist Hospital	√	
KPJ Ampang Puteri Specialist Hospital	√	
KPJ Selangor Specialist Hospital, Shah Alam	√	
Kuala Lumpur Hospital	√	√
Lam Wah Ee Hospital, Pulau Pinang	√	
Likas Hospital		√
Melaka Hospital	√	
Metro Specialist Hospital, Sungai Petani	√	
Normah Medical Specialist Centre, Kuching	√	
Pulau Pinang Hospital	√	√
Queen Elizabeth Hospital, Kota Kinabalu	√	
Raja Perempuan Zainab II Hospital, Kota Bharu	√	
Raja Permaisuri Bainun Hospital, Ipoh	√	
Sarawak General Hospital, Kuching	√	
Selayang Hospital	√	√
Serdang Hospital	√	
Sultan Ismail Hospital, Pandan		√
Sultanah Aminah Hospital, Johor Bharu	√	
Sultanah Bahiyah Hospital, Alor Star	√	
Sultanah Nur Zahirah Hospital, Kuala Terengganu	√	
Sunway Medical Centre	√	
Tengku Ampuan Afzan Hospital, Kuantan	√	√
Tengku Ampuan Rahimah Hospital, Kelang	√	
Tuanku Ja'afar Hospital, Seremban	√	√
Tung Shin Hospital, Kuala Lumpur	√	
University Malaya Medical Centre, Kuala Lumpur	√	

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FOREWORD

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The second report of the Malaysian Registry of Renal Biopsy (MRRB) showed an increase in the number of centers reporting. This is gratifying especially as most of the new centers were form the Universities and the private sector. The first report was confined to centers from the Ministry of Health only. The addition of data from the new centers will hopefully give a more “national” representation of the pattern of glomerular diseases in the country. The ascertainment rate, however, has dropped in 2008 to 76%. Of the 1519 biopsies that were done, 1155 were reported. This is unfortunate as a large segment of useful information is missing. It is hoped that nephrologists will take some time off their busy schedule to report on the biopsies they did.

The pattern of primary and secondary glomerular diseases was similar to that seen in the first report. Any change in pattern in the short term is more likely to be the result of more centers reporting (eg more pediatric nephrology centers) or more biopsies being done than any real change in incidence of glomerular diseases. Facilities for doing renal biopsies are now available in all major hospitals in the country. However indications for biopsies may vary between practitioners and this to some extent affects the pattern observed. Thus the real “pattern” can only be seen after the registry has matured and achieve a high ascertainment rate and there is some consistency amongst practitioners on the indications for biopsy. Nephrotic syndrome remained the most common indication for doing renal biopsy in 2008 followed by asymptomatic urinary abnormalities.

Data from registries serve not only to indicate incidence/prevalence and clinical presentation of diseases but more importantly help guide clinical practice. Data from the Malaysian Dialysis and Transplant Registry (MDTR) have helped in the formulation of clinical practice guidelines on Renal Replacement Therapy in Malaysia along with results from clinical trials. It is hoped that with information accumulated in the MRRB, we could one day develop some practice guidelines on the management of glomerular disease. The registry will have to look at means of collecting more clinical data on outcome such as renal survival, complications of glomerular disease etc before we can embark on such a task.

This year (2010) the funding for all registries by the Ministry of Health has been drastically reduced putting the long-term viability of many registries in peril. The National Renal Registry is seriously looking at measures to reduce costs and also to look for additional sources of income. It will endeavour to maintain all existing registries under its purview.

Dr Zaki Morad
Chairman, National Renal Registry

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REPORT SUMMARY

CHAPTER 1: OVERVIEW OF RENAL BIOPSY IN MALAYSIA

The second MRRB report included data from MOH centers as well as from universities and private hospitals. Universities and private hospitals contributed data to MRRB from 2008.

- Total of 33 centers contributed data in 2008. There were an additional 11 new centers.
- The first report was exclusively from 23 MOH centers only.
- Renal biopsies performed in MOH centers from 2005-2008 was also updated.
- 1519 renal biopsies were performed in 2008 and of these, 1155 were reported.
- The ascertainment rate was 92.2%, 91.05 %, 92.9% and 76.03% for the years 2005, 2006, 2007 and 2008 respectively.
- Average ascertainment rate for the years 2005 – 2008 was 86.5%.
- 89.4 % of renal biopsies in 2008 were reported in native biopsies.
- 83% of native biopsies were done in patients older than 15 years old and in this group 91.8% of the biopsies were done in patients less than 55 years of age.
- There were more females than males (ratio 3:2) due to the higher number of females amongst patients biopsied for lupus nephritis.
- 869 (23%) of the biopsies from 2005 to 2008 yielded less than 10 glomeruli.
- 38 (1%) of biopsies were classified as missing. The histopathological reports were not submitted to MRRB.
- 47.6% histopathology slides were read by pathologists in the same hospital and 52.4 % were sent to be read by pathologists in another hospital.
- Main indications for native kidney biopsies were nephrotic syndrome (46%) and urinary abnormalities (28%).
- 54 % had normal renal function and 32% had impaired renal function. Data was missing for 14%.

CHAPTER 2: PRIMARY GLOMERULONEPHRITIS

The commonest primary GN reported was Minimal Change Disease (MCD) followed by Focal Segmental Glomerulosclerosis (FSGS).

Minimal change disease

- Accounted for 33% of total primary GN
- Mean age at the time of biopsy was 29.1 ± 12.8 years.
- Male to female ratio was 2:1.
- Nephrotic syndrome was the most common clinical presentation.
- Twenty percent had e-GFR < 60 ml/min/1.73 m2 at time of biopsy
- There was a higher risk of renal impairment with increasing age.

Focal Segmental Glomerulosclerosis (FSGS)

- Accounted for 30% of total primary GN.
- Mean age at the time of biopsy was 32.5 ± 13.5 years.
- Male to female ratio was 1.3:1.
- Nephrotic syndrome was the most common clinical presentation.
- Forty-one percent had e-GFR < 60 ml/min/1.73 m2 at time of biopsy
- There was a higher risk of renal impairment with increasing age

Idiopathic Membranous Nephropathy (IMN)

- Accounted for 11% of total primary GN.
- Mean age at the time of biopsy was 45.3 + 14.7 years.
- Male to female ratio was 1.3:1.
- Nephrotic syndrome was the most common clinical presentation.
- Thirty-seven percent had e-GFR < 60 ml/min/1.73 m2 at time of biopsy.
- There was a higher risk of renal impairment with increasing age

IgA nephropathy

- Accounted for 19% of total primary GN.
- Mean age at the time of biopsy was 33.8 ± 12.5 years.
- Male to female ratio was 0.9:1.
- Asymptomatic urine abnormalities was the most common clinical presentation, followed by nephritic syndrome.
- Forty-six percent had e-GFR < 60 ml/min/1.73 m2 at time of biopsy.
- Males tend to have worse renal function at presentation compared to females.

CHAPTER 3: SECONDARY GLOMERULONEPHRITIS

The commonest secondary GN reported was lupus nephritis. Diabetic nephropathy was the second commonest glomerular disease reported.

Lupus nephritis

- Accounted for 86% of total secondary GN.
- Mean age at the time of biopsy in adult lupus nephritis was 30.3 ± 10.4 years.
- Male to female ratio was 6.9:1.
- Urine abnormality (38%) was the commonest clinical presentation followed by nephrotic syndrome (30%).
- The commonest histopathological finding was WHO or ISN/RPS class IV or IV+V (59%).
- There was no clear correlation between histopathological findings and clinical presentation. However, class IV or class IV+V were more likely to present with symptomatic renal disease.
- The prevalence of hypertension was higher in class IV or class IV +V
- The prevalence of impaired kidney function correlated with histopathological findings. Class IV was more likely to have impaired renal function.
- About 2/3 of cases with lupus nephritis fulfilled 4 or more American Rheumatological Association (ARA) criteria at presentation.
- Fulfilling the ARA criteria does not predict the severity of renal lesion.

CHAPTER 4: PAEDIATRIC RENAL BIOPSY

This chapter reports on renal biopsy in children less than 15 years of age and the summary details the report for the years 1999 -2008.

- 809 renal biopsies were performed in 755 children.
- Majority of biopsies were performed in MOH hospitals.
- 770 (95.2%) were assessed to be adequate. The success rate is comparable to reports from Thailand, UK and Japan.
- 621(77.2%) yielded more than 10 glomeruli.
- 51.9% were performed in girls.
- Nephrotic syndrome (52.9%) was the most frequent clinical presentation.41.8% of the diagnosis on biopsy was FSGS and minimal change disease in 28.7%.
- The commonest biopsy finding for nephritic syndrome was post-infectious glomerulonephritis (36.3%).
- Overall, in terms of diagnosis on biopsies for the paediatric age group, lupus nephritis was the commonest finding in 24.8%, followed closely by FSGS (24.6%) and MCD accounted for 17.27%.
- There were no difference in terms of age at presentation, race, gender, urine albumin excretion and creatinine clearance in children with FSGS and minimal change disease at biopsy.
- There was no difference in patient survival for FSGS and minimal change disease.
- There was however definite poorer renal survival, 92.4 % and 84.6% at 3 and 5 years for the FSGS group. Renal survival for the MCD group was at 95.9% at both 3 and 5 years.
- Commonest biopsy finding for the lupus group was class IV and Class V + IV (64.2%)
- Renal survival for the lupus group was 97.1 % at both 3 and 5 years.
- The complication rate for renal biopsy was 5.4%. The most common complication was bleeding which occurred in 4.1 %.

CHAPTER 5: RENAL ALLOGRAFT BIOPSY

This chapter reports on renal allograft biopsy and the summary details the report for the years 2004 - 2008.

- The number of renal allograft biopsies doubled over the last 5 years despite a decreased in the number of new transplant recipients.
- This was largely contributed by an increase in participating centres reporting to MRRB.
- 90% of renal allograft biopsies were performed in 5 centers in Klang valley.
- The biopsies were usually performed in the age group 15 to 54 years.
- Acute and chronic allograft dysfunction was the commonest indications.
- Chronic allograft dysfunction has assumed more importance in recent years. This was supported by a 5 fold increase in renal biopsies performed for this reason. (10 % in 2004 to 47% in 2008)
- In addition, there was a marked increase in the number of renal allograft biopsies performed after one year post transplant. (35% in 2004 and 55% in 2008)
- 96% of biopsies were performed under real time ultrasound guidance.
- 97% of biopsies were not associated with any complications.
- The histological diagnosis on biopsy in order of importance was acute rejection (49%), acute tubular necrosis (16%) calcineurin inhibitor toxicity (15%) and chronic allograft nephropathy. (15%)

CHAPTER 1

Overview Of Renal Biopsy In Malaysia

Wan Sha'ariah Md Yusuf
Lee Ming Lee
Lee Day Guat

1.1 Introduction

The first Malaysian Registry of Renal Biopsy (MRRB) report was published in 2009. The report provided data of renal biopsy performed and reported for year 2005 to 2007 from most of the centres providing nephrology services in the Ministry of Health Malaysia (MOH). Since 2008, the MRRB had invited participation from non MOH nephrologists and renal physicians. Thus the second MRRB report will include data from MOH centres, universities and private hospitals. Renal biopsies performed in MOH centres from 2005-2007 which were previously reported will also be updated and reported in this second MRRB report.

1.2: Renal biopsies from the participating centres

1.2.1 Ascertainment rate of total biopsy performed

From 2005 to 2008, a total of 22 centres (15 adult and 7 paediatric) from the Ministry of Health (MOH) submitted data to the MRRB. Eleven additional non MOH centres from the army, universities and private hospitals also contributed data since 2008. These participating centres will be identified by their centre identification number.

In 2005, a total 784 renal biopsies were performed and of these, 723 were reported. In 2006, 1028 renal biopsies were performed and 936 were reported. In 2007, 1037 renal biopsies were performed and of these 963 were reported. In 2008, 1519 renal biopsies were performed and of these 1155 were reported. This gives an ascertainment rate of 92.2% for 2005, 91.1% for 2006, 92.9% for 2007 and 76.0% for 2008. The average ascertainment rate for 2005-2008 was 86.5% (Table 1.2.1).

Table 1.2.1: Total number of reported and unreported renal biopsies by centres, 2005 – 2008

	2005		2006		2007		2008		Total	
	Done and reported	Done but not reported	Done and reported	Done but not reported	Done and reported	Done but not reported	Done and reported	Done but not reported	Done and reported	Done but not reported
Centre	n	n	n	n	n	n	n	n	n	n
1	97	0	107	0	101	0	120	3	425	3
2	2	0	10	1	24	0	84	1	120	2
3	97	3	104	0	65	0	55	0	321	3
4	13	0	18	0	19	0	18	0	68	0
5	28	0	38	0	44	6	3	0	113	6
6	0	30	0	0	0	0	0	0	0	30
7	31	4	45	3	55	1	50	0	181	8
8	27	0	28	0	24	0	24	0	103	0
9	10	3	5	0	11	0	11	0	37	3
10	21	0	27	0	21	0	22	0	91	0
11	68	0	81	0	61	0	94	0	304	0
12	0	0	0	0	0	0	0	0	0	0
13	0	11	42	21	4	28	31	0	77	60
14	0	0	2	0	7	1	0	7	9	8
15	18	3	6	27	0	25	0	27	24	82
16	15	0	24	0	31	1	26	11	96	12
17	39	0	50	0	44	0	0	0	133	0
18	74	0	101	10	63	0	87	0	325	10

Table 1.2.1: Total number of reported and unreported renal biopsies by centres, 2005 – 2008 (cont.)

	2005		2006		2007		2008		Total	
	Done and reported	Done but not reported	Done and reported	Done but not reported	Done and reported	Done but not reported	Done and reported	Done but not reported	Done and reported	Done but not reported
Centre	**n**	**n**	**n**	**n**	**n**	**n**	**n**	**n**	**n**	**n**
19	42	0	51	0	42	0	55	0	190	0
20	92	7	140	0	109	12	110	16	451	35
21	16	0	24	1	14	0	16	0	70	1
22	28	0	24	0	37	0	41	0	130	0
23	0	0	0	0	0	0	0	179	0	179
24	0	0	0	0	176	0	151	28	327	28
25	0	0	0	0	0	0	0	25	0	25
26	0	0	0	0	0	0	0	0	0	0
27	4	0	2	0	4	0	2	0	12	0
28	0	0	0	0	1	0	12	0	13	0
29	0	0	0	0	0	0	0	12	0	12
30	0	0	7	0	1	0	4	0	12	0
31	1	0	0	0	0	0	4	20	5	20
32	0	0	0	0	0	0	0	10	0	10
33	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	2	0	40	25	42	25
35	0	0	0	0	0	0	2	0	2	0
36	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	3	0	3	0
38	0	0	0	0	0	0	17	0	17	0
39	0	0	0	0	0	0	19	0	19	0
40	0	0	0	0	3	0	17	0	20	0
41	0	0	0	29	0	0	37	0	37	29
42	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0
Total	**723**	**61**	**936**	**92**	**963**	**74**	**1155**	**364**	**3777**	**591**

1.2.2 Type of renal biopsy performed

As expected, majority of the biopsies reported were from native kidneys: 90.2% in 2005, 87.4% in 2006, 87.1% in 2007 and 89.4% in 2008. The rest were from graft kidneys (Table 1.2.2).

Table 1.2.2: Distribution of reported native and graft renal biopsies by centres, 2005-2008

Centre	2005		2006		2007		2008		Total			
	Native	Graft	Native	Graft	Native	Graft	Native	Graft	Native		Graft	
	n	n	n	n	n	n	n	n	n	%	n	%
1	69	28	57	50	58	43	83	37	267	8	158	36
2	2	0	10	0	24	0	81	3	117	4	3	1
3	85	12	93	11	63	2	51	4	292	9	29	7
4	13	0	17	1	19	0	18	0	67	2	1	0
5	27	1	36	2	42	2	3	0	108	3	5	1
6	0	0	0	0	0	0	0	0	0	0	0	0
7	26	5	34	11	43	12	40	10	143	4	38	9
8	27	0	27	1	23	1	23	1	100	3	3	1
9	10	0	5	0	11	0	11	0	37	1	0	0
10	21	0	25	2	20	1	21	1	87	3	4	1
11	68	0	79	2	61	0	93	1	301	9	3	1
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	42	0	4	0	31	0	77	2	0	0
14	0	0	2	0	7	0	0	0	9	0	0	0
15	18	0	6	0	0	0	0	0	24	1	0	0
16	15	0	24	0	31	0	26	0	96	3	0	0
17	35	4	47	3	44	0	0	0	126	4	7	2
18	72	2	99	2	61	2	82	5	314	9	11	3
19	41	1	38	13	33	9	38	17	150	4	40	9
20	74	18	121	19	87	22	96	14	378	11	73	17
21	16	0	23	1	14	0	16	0	69	2	1	0
22	28	0	24	0	37	0	39	2	128	4	2	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	146	30	124	27	270	8	57	13
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	4	0	2	0	4	0	2	0	12	0	0	0
28	0	0	0	0	1	0	12	0	13	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0
30	0	0	7	0	1	0	4	0	12	0	0	0
31	1	0	0	0	0	0	4	0	5	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	2	0	40	0	42	1	0	0
35	0	0	0	0	0	0	2	0	2	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	3	0	3	0	0	0
38	0	0	0	0	0	0	16	1	16	0	1	0
39	0	0	0	0	0	0	19	0	19	1	0	0
40	0	0	0	0	3	0	17	0	20	1	0	0
41	0	0	0	0	0	0	37	0	37	1	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
Total	**652**	**71**	**818**	**118**	**839**	**124**	**1032**	**123**	**3341**	**100**	**436**	**100**

1.2.3: Number of renal biopsy done on each individual patient

The data captured in MRRB is year based. New biopsies and patients biopsied before 2005 were included. The number of biopsy episode/attempt per patient is recorded accordingly.

In the native biopsy group, from 2005 to 2008, 3193 patients had renal biopsy done. 2776 patients had renal biopsy for the first time, 355 patients had biopsy done twice, 54 patients had biopsy done thrice and 8 patients had four or more biopsy done on them. Therefore about 13.1% of patients had a repeat native biopsy done (Table 1.2.3(a)).

In the allograft biopsy group; over the same period, 312 patients underwent a graft biopsy. 193 patients had biopsy done once, 84 patients had biopsy done twice, 21 patients had biopsy done thrice and 14 patients had biopsy done four times or more (Table1.2.3 (b)). As expected, there was a higher rate of repeat graft biopsies (38.1%).

Table 1.2.3(a): Distribution of native renal biopsy in patients by number of episodes

Native	2005		2006		2007		2008		Total
	n	%	n	%	n	%	n	%	n
1st episode	519	85	673	87	692	87	892	88	2776
2nd episode	78	13	93	12	77	10	107	11	355
3rd episode	10	2	5	1	24	3	15	1	54
>4th episode	1	0	1	0	3	0	3	0	8
Total patient	**608**	**100**	**772**	**100**	**796**	**100**	**1017**	**100**	**3193**

Table 1.2.3 (b): Distribution of renal allograft biopsy in patients by number of episodes

Graft	2005		2006		2007		2008		Total
	n	%	n	%	n	%	n	%	n
1st episode	31	72	57	70	51	60	54	53	193
2nd episode	10	23	18	22	23	27	33	32	84
3rd episode	2	5	5	6	6	7	8	8	21
>4th episode	0	0	2	2	5	6	7	7	14
Total patient	**43**	**100**	**82**	**100**	**85**	**100**	**102**	**100**	**312**

1.2.4: Demographic distribution of renal biopsy (Native and Graft)

1.2.4.1: Age distribution

Eighty three percent of native biopsies were done in patients older than 15 years old and in this group, 91.8% of the biopsies were done in patients less than 55 years age. Very few (7%) biopsies were done in patients older than 55 years old (Table 1.2.4.1 (a)).

In the graft biopsy group, 95% were done in patients older than 15 years old and of these, 89.2% were in the age group of 15 to less than 55 years. Only 10% of the graft biopsies were done in those above 55 years of age (Table 1.2.4.1(b)).

For adults (age ≥15years old) the highest number of renal biopsy was reported in Wilayah Persekutuan (WP) Kuala Lumpur (25%), followed by Selangor (22%) and Sabah (13%). In the paediatric group (age <15 years old), the highest number of renal biopsy were reported in WP Kuala Lumpur (28%), followed by Johor (23%) and Selangor (15%) (Table 1.2.4.1(c)).

Table 1.2.4.1(a): Age distribution of native renal biopsy, 2005-2008

Age group	2005	2006	2007	2008	Total	
	n	n	n	n	n	%
<15	128	135	146	164	573	17
15-<25	173	239	217	303	932	28
25-<35	145	183	191	223	742	22
35-<45	117	125	131	134	507	15
45-<55	59	80	90	130	359	11
55-<65	18	43	43	50	154	5
≥65	12	13	21	28	74	2
Total	**652**	**818**	**839**	**1032**	**3341**	**100**

Table 1.2.4.1(b): Age distribution of renal allograft biopsy, 2005-2008

Age group (years)	2005	2006	2007	2008	Total	
	n	n	n	n	n	%
<15	0	5	7	9	21	5
15-<25	15	26	19	22	82	19
25-<35	11	25	15	20	71	16
35-<45	23	26	49	25	123	28
45-<55	12	24	24	34	94	22
55-<65	8	8	10	9	35	8
≥65	2	4	0	4	10	2
Total	**71**	**118**	**124**	**123**	**436**	**100**

Table 1.2.4.1 (c): Age group distribution of reported renal biopsies by state, 2005-2008

Year of biopsy	2005				2006				2007				2008				Total			
	Age < 15		Age ≥ 15		Age < 15		Age ≥ 15		Age < 15		Age ≥ 15		Age < 15		Age ≥ 15		Age < 15		Age ≥ 15	
State	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Johor	29	23	67	11	24	17	81	10	45	29	53	7	39	23	96	10	137	23	297	9
Kedah	0	0	2	0	0	0	10	1	4	3	20	2	3	2	83	8	7	1	115	4
Kelantan	2	2	13	2	0	0	24	3	3	2	28	3	3	2	23	2	8	1	88	3
Melaka	2	2	19	3	1	1	26	3	1	1	20	2	1	1	21	2	5	1	86	3
N.Sembilan	11	9	26	4	6	4	27	3	10	7	25	3	12	7	23	2	39	7	101	3
Pahang	0	0	0	0	6	4	38	5	5	3	6	1	1	1	30	3	12	2	74	2
Perak	3	2	29	5	2	1	38	5	0	0	49	6	0	0	17	2	5	1	133	4
Perlis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Penang	14	11	96	16	18	13	104	13	19	12	67	8	18	10	95	10	69	12	362	11
Sabah	7	5	106	18	12	9	139	17	9	6	101	12	24	14	80	8	52	9	426	13
Sarawak	0	0	0	0	0	0	7	1	0	0	1	0	0	0	4	0	0	0	12	0
Selangor	17	13	122	21	29	21	180	23	17	11	161	20	25	14	224	23	88	15	687	22
Terengganu	2	2	16	3	1	1	5	1	0	0	0	0	0	0	0	0	3	1	21	1
WP KL	41	32	99	17	41	29	117	15	40	26	279	34	47	27	286	29	169	28	781	25
Total	**128**	**100**	**595**	**100**	**140**	**100**	**796**	**100**	**153**	**100**	**810**	**100**	**173**	**100**	**982**	**100**	**594**	**100**	**3183**	**100**

1.2.4.2: Gender distribution

As in the first MRRB report, in the native renal biopsy group, there were more females compared to males (ratio 3:2). This was probably due to the higher number of females among the patients biopsied for SLE (Table 1.2.4.2(a)). However, in the graft biopsy group, there were more males (ratio 2:1)(Table 1.2.4.2 (b)). This is consistent with the trend of male predominance amongst the transplant patients as reported in the 16th Report of The Malaysian Dialysis and Transplant Registry.

Table 1.2.4.2(a): Gender distribution of native renal biopsy, 2005-2008

Gender	2005	2006	2007	2008	Total	
	n	n	n	n	n	%
Male	229	330	314	422	1295	41
Female	379	442	482	595	1898	59
Total	**608**	**772**	**796**	**1017**	**3193**	**100**

Table 1.2.4.2(b): Gender distribution of renal allograft biopsy, 2005-2008

Gender	2005	2006	2007	2008	Total	
	n	n	n	n	n	%
Male	26	54	53	62	195	63
Female	17	28	32	40	117	38
Total	**43**	**82**	**85**	**102**	**312**	**100**

1.2.4.3: Racial distribution

Among the patients who had native kidney biopsy, majority were Malays (56%), followed by Chinese (26%)(Table 1.2.4.3(a)). In the allograft biopsy group, majority of patients were Chinese (54%) followed by Malay (32%) (Table 1.2.4.3 (b)).

Table 1.2.4.3(a): Racial distribution of native renal biopsy, 2005-2008

Race	2005	2006	2007	2008	Total	
	n	n	n	n	n	%
Malay	341	436	429	569	1775	56
Chinese	149	185	226	269	829	26
Indian	40	59	58	70	227	7
Others	78	92	83	109	362	11
Total	**608**	**772**	**796**	**1017**	**3193**	**100**

Table 1.2.4.3(b): Racial distribution of renal allograft biopsy, 2005-2008

Race	2005	2006	2007	2008	Total	
	n	n	n	n	n	%
Malay	12	23	27	38	100	32
Chinese	27	49	47	46	169	54
Indian	2	7	8	11	28	9
Others	2	3	3	7	15	5
Total	**43**	**82**	**85**	**102**	**312**	**100**

1.2.5: Renal biopsy report analysis

A total of 3777 renal biopsies were performed and reported from 2005 to 2008. There were 869 (23%) of the biopsies yielded less than 10 glomeruli, which our pathologists felt was the minimum number of glomeruli required to label a biopsy as adequate. 38(1%) biopsies were classified as missing because the histopathology reports were not submitted to MRRB. The remaining 76.0% reported 10 or more glomeruli.

Table 1.2.5: Number of glomeruli obtained at each biopsy by centres, 2005-2008

Total number of glomeruli	Less 10		10 & above		Missing		Total	
Centre	n	%	n	%	n	%	n	%
1	75	9	349	12	1	3	425	11
2	15	2	105	4	0	0	120	3
3	48	6	273	10	0	0	321	8
4	7	1	61	2	0	0	68	2
5	22	3	91	3	0	0	113	3
6	0	0	0	0	0	0	0	0
7	42	5	138	5	1	3	181	5
8	17	2	86	3	0	0	103	3
9	12	1	25	1	0	0	37	1
10	38	4	53	2	0	0	91	2
11	126	14	178	6	0	0	304	8
12	0	0	0	0	0	0	0	0
13	10	1	41	1	26	68	77	2
14	2	0	7	0	0	0	9	0
15	8	1	13	0	3	8	24	1
16	37	4	59	2	0	0	96	3
17	98	11	359	13	1	3	458	12
18	0	0	0	0	0	0	0	0
19	23	3	166	6	1	3	190	5
20	79	9	368	13	4	11	451	12
21	14	2	56	2	0	0	70	2
22	60	7	70	2	0	0	130	3
23	0	0	0	0	0	0	0	0
24	108	12	219	8	0	0	327	9
25	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0
27	4	0	8	0	0	0	12	0
28	5	1	8	0	0	0	13	0
29	0	0	0	0	0	0	0	0
30	0	0	12	0	0	0	12	0
31	1	0	4	0	0	0	5	0
32	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0
34	6	1	35	1	1	3	42	1
35	0	0	2	0	0	0	2	0
36	0	0	0	0	0	0	0	0
37	1	0	2	0	0	0	3	0
38	1	0	16	1	0	0	17	0
39	4	0	15	1	0	0	19	1
40	2	0	18	1	0	0	20	1
41	4	0	33	1	0	0	37	1
42	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0
Total	**869**	**100**	**2870**	**100**	**38**	**100**	**3777**	**100**

1.2.6: Histopathology specimen distribution to histopathology laboratories

As shown in Table 1.2.6, not all biopsies performed at the centres were read by the local histo-pathologists. A number of the renal biopsy specimens were sent to other centres for processing and reporting. A total of 47.6% of HPE slides were read locally and 52.4% were sent to another laboratory (Table 1.2.6 (a)).

The histopathology laboratories were coded by a number (Table1.2.6 (b)).

Table 1.2.6(a): Distribution of biopsy specimens to histopathology laboratories by participating centres, 2005-2008

Centre	Local histopathology laboratories										Outside histopathology laboratories										All	
	2005		2006		2007		2008		Total		2005		2006		2007		2008		Total			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
1	58	14	58	14	98	23	116	27	330	78	39	9	49	12	3	1	4	1	95	22	425	100
2											2	2	10	8	24	20	84	70	120	100	120	100
3	90	28	98	31	31	10	15	5	234	73	7	2	6	2	34	11	40	12	87	27	321	100
4	13	19	17	25	11	16	1	1	42	62	0	0	1	1	8	12	17	25	26	38	68	100
5	26	23	37	33	44	39	3	3	110	97	2	2	1	1	0	0	0	0	3	3	113	100
7											31	17	45	25	55	30	50	28	181	100	181	100
8	9	9	7	7	8	8	6	6	30	29	18	17	21	20	16	16	18	17	73	71	103	100
9	8	22	5	14	8	22	11	30	32	86	2	5	0	0	3	8	0	0	5	14	37	100
10	21	23	26	29	21	23	22	24	90	99	0	0	1	1	0	0	0	0	1	1	91	100
11	68	22	81	27	60	20	94	31	303	100	0	0	0	0	1	0	0	0	1	0	304	100
13	0	0	11	14	0	0	0	0	11	14	0	0	31	40	4	5	31	40	66	86	77	100
14	0	0	0	0	0	0	0	0	0	0	0	0	2	22	7	78	0	0	9	100	9	100
15	18	75	6	25	0	0	0	0	24	100											24	100
16	0	0	0	0	10	10	22	23	32	33	15	16	24	25	21	22	4	4	64	67	96	100
17											113	25	151	33	107	23	87	19	458	100	458	100
19	36	19	37	19	41	22	52	27	166	87	6	3	14	7	1	1	3	2	24	13	190	100
20	9	2	15	3	1	0	2	0	27	6	83	18	125	28	108	24	108	24	424	94	451	100
21	2	3	0	0	0	0	0	0	2	3	14	20	24	34	14	20	16	23	68	97	70	100
22											28	22	24	18	37	28	41	32	130	100	130	100

Table 1.2.6(a): Distribution of biopsy specimens to histopathology laboratories by participating centres, 2005-2008 (cont.)

Centre	Local histopathology laboratories										Outside histopathology laboratories										All	
	2005		2006		2007		2008		Total		2005		2006		2007		2008		Total			
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
24	0	0	0	0	174	53	150	46	324	99	0	0	0	0	2	1	1	0	3	1	327	100
25																						
26																						
27											4	33	2	17	4	33	2	17	12	100	12	100
28											0	0	0	0	1	8	12	92	13	100	13	100
29																						
30											0	0	7	58	1	8	4	33	12	100	12	100
31											1	20	0	0	0	0	4	80	5	100	5	100
32																						
33																						
34	0	0	0	0	2	5	40	95	42	100											42	100
35											0	0	0	0	0	0	2	100	2	100	2	100
36																						
37											0	0	0	0	0	0	3	100	3	100	3	100
38											0	0	0	0	0	0	17	100	17	100	17	100
39											0	0	0	0	0	0	19	100	19	100	19	100
40											0	0	0	0	3	15	17	85	20	100	20	100
41											0	0	0	0	0	0	37	100	37	100	37	100
42																						
43																						
Total	**358**	**100**	**398**	**100**	**509**	**100**	**534**	**100**	**1799**	**100**	**365**	**100**	**538**	**100**	**454**	**100**	**621**	**100**	**1978**	**100**	**3777**	**100**

Table 1.2.6(b): Histopathology laboratories receiving renal biopsy specimens, 2005-2008

HistoLab	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
1	0	0	7	1	2	0	6	1	15	0
2	30	4	39	4	48	5	5	0	122	3
3	0	0	0	0	0	0	23	2	23	1
4	0	0	0	0	10	1	22	2	32	1
5	210	29	363	39	429	45	532	46	1534	41
6	19	3	6	1	6	1	1	0	32	1
7	24	3	26	3	38	4	24	2	112	3
8	105	15	125	13	42	4	16	1	288	8
9	11	2	15	2	1	0	2	0	29	1
10	17	2	13	1	16	2	17	1	63	2
11	96	13	105	11	98	10	152	13	451	12
12	0	0	11	1	0	0	0	0	11	0
13	1	0	0	0	0	0	1	0	2	0
14	38	5	71	8	1	0	0	0	110	3
15	15	2	24	3	19	2	2	0	60	2
16	0	0	0	0	2	0	42	4	44	1
17	157	22	131	14	251	26	294	25	833	22
18	0	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	11	1	11	0
20	0	0	0	0	0	0	1	0	1	0
Total	**723**	**100**	**936**	**100**	**963**	**100**	**1155**	**100**	**3777**	**100**

1.3: Native kidney biopsy

1.3.1: Clinical Indications of renal biopsy

The main indications for native kidney biopsies were nephrotic syndrome (46%) followed by urinary abnormalities (28%) (Table 1.3.1 (a)). A total of 1818 (54%) patients had normal renal function at time of biopsy, 32% had impaired renal function and for the rest, renal function was either not available or unknown at time of biopsy (Table 1.3.1 (b)).

Table 1.3.1(a): Indications for native renal biopsies, 2005-2008

Clinical presentations	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	168	26	218	27	231	28	304	29	921	28
Nephritic syndrome	61	9	66	8	62	7	90	9	279	8
Nephrotic syndrome	311	48	372	45	389	46	466	45	1538	46
Nephrotic-nephritic syndrome	21	3	38	5	52	6	99	10	210	6
Unknown	91	14	124	15	105	13	73	7	393	12
Total	**652**	**100**	**818**	**100**	**839**	**100**	**1032**	**100**	**3341**	**100**

Table 1.3.1(b): Renal function at time of biopsy

Renal function	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Normal	364	56	415	51	464	55	575	56	1818	54
Impaired	150	23	238	29	291	35	381	37	1060	32
Missing / unknown	138	21	165	20	84	10	76	7	463	14
Total	**652**	**100**	**818**	**100**	**839**	**100**	**1032**	**100**	**3341**	**100**

1.3.2: Histopathological diagnosis

In the native kidney biopsy group, the three most common primary glomerulonephritis (GN) reported were focal segmental glomerulosclerosis (FSGS) (33%), minimal change disease (33%) and IgA nephropathy (17%). Membranous nephropathy only comprises 9% of the total primary GN subgroup (Table 1.3.2).

Lupus nephritis was the commonest secondary GN; accounting for 84% of cases (Table 1.3.2).

Table 1.3.2: Histopathology of all native renal biopsies, 2005-2008

Type	Histopathological diagnosis	2005		2006		2007		2008		Total	
		n	%	n	%	n	%	n	%	n	%
Primary GN	Minimal Change Disease	94	32	107	28	128	36	174	36	503	33
	FSGS	103	35	145	38	114	32	135	28	497	33
	lg A nephropathy	37	13	62	16	58	16	99	21	256	17
	Membranous nephropathy	23	8	33	9	35	10	39	8	130	9
	Membrano-proliferative	12	4	10	3	4	1	6	1	32	2
	Mesangial Proliferative: non-IgA	16	5	10	3	12	3	11	2	49	3
	Crescentic ANCA	1	0	1	0	0	0	4	1	6	0
	Idiopathic Crescentic	6	2	9	2	3	1	4	1	22	1
	Unknown	0	0	0	0	2	1	6	1	8	1
	Subtotal	**292**	**100**	**377**	**100**	**356**	**100**	**478**	**100**	**1503**	**100**
Secondary GN	Other Infection	0	0	1	0	1	0	5	1	7	0
	Lupus Nephritis	270	89	309	85	310	82	341	81	1230	84
	Henoch Schonlein purpura	3	1	2	1	2	1	14	3	21	1
	HUS / TTP	2	1	1	0	0	0	0	0	3	0
	Amyloidosis	1	0	4	1	1	0	2	0	8	1
	Systemic vasculitis	1	0	4	1	2	1	1	0	8	1
	Post infection GN	17	6	12	3	16	4	15	4	60	4
	Polyarteritis Nodosa	0	0	0	0	0	0	0	0	0	0
	Malignancy	0	0	1	0	1	0	1	0	3	0
	Light/Heavy chain disease	0	0	0	0	1	0	1	0	2	0
	Diabetic nephropathy	8	3	27	7	40	11	37	9	112	8
	Anti GBM	0	0	0	0	0	0	0	0	0	0
	Immunotactoid /fibrillary GN	0	0	0	0	0	0	0	0	0	0
	Multiple myeloma	0	0	1	0	2	1	1	0	4	0
	Unknown	0	0	0	0	3	1	3	1	6	0
	Subtotal	**302**	**100**	**362**	**100**	**379**	**100**	**421**	**100**	**1464**	**100**

Table 1.3.2: Histopathology of all native renal biopsies, 2005-2008 (cont.)

Type	Histopathological diagnosis	2005		2006		2007		2008		Total	
		n	%	n	%	n	%	n	%	n	%
Tubulointerstitial disease	Acute interstitial nephritis	5	24	7	14	10	19	22	24	44	21
	Acute tubular-necrosis	10	48	33	67	33	61	31	34	107	50
	Chronic interstitial	6	29	9	18	11	20	37	41	63	29
	Subtotal	**21**	**100**	**49**	**100**	**54**	**100**	**90**	**100**	**214**	**100**
Vascular	Atherosclerosis	0	0	0	0	2	18	0	0	2	5
	Benign/malignant hypertension	2	100	7	100	9	82	18	95	36	92
	Missing	0	0	0	0	0	0	1	5	1	3
	Subtotal	**2**	**100**	**7**	**100**	**11**	**100**	**19**	**100**	**39**	**100**
Hereditary	Alport's syndrome	0	0	2	50	1	50	0	0	3	33
	Thin Basement membrane disease	1	50	1	25	0	0	1	100	3	33
	Others	1	50	1	25	1	50	0	0	3	33
	Subtotal	**2**	**100**	**4**	**100**	**2**	**100**	**1**	**100**	**9**	**100**
Advance GN		16	100	20	100	23	100	21	100	80	100
Others		0	0	2	100	16	100	22	100	40	100

1.3.3: Histopathology findings in common clinical presentation

1.3.3.1: Histopathological diagnosis in patients with nephrotic syndrome

In patients presenting with nephrotic syndrome, the commonest histopathology reported was minimal change (27%), followed by lupus nephritis(24%) and focal segmental glomerulosclerosis (23%) (Table 1.3.3.1).

Table 1.3.3.1: HPE diagnosis in patients presenting with nephrotic syndrome, 2005-2008

Type	Histopathological diagnosis	n	%
Primary	Minimal Change Disease	417	27
	FSGS	356	23
	lg A nephropathy	64	4
	Membranous nephropathy	89	6
	Membrano-proliferative	18	1
	Mesangial Proliferative GN-non IgA	24	2
	Crescentic	0	0
	Idiopathic crescentic	3	0
	Unknown	5	0
	Sub total	**976**	**62**
Secondary	Other infection	3	0
	Lupus Nephritis	374	24
	Henoch Schonlein Purpura	3	0
	HUS/TTP	1	0
	Amyloidosis	5	0
	Systemic vasculitis	1	0
	Post infection GN	8	1
	Polyarteritis nodosa	0	0
	Malignancy	0	0
	Light/ heavy chain disease	1	0
	Diabetic nephropathy	52	3
	Anti GBM	0	0
	Immunotactoid / fibrillary GN	0	0
	Multiple myeloma	1	0
	Unknown	3	0
	Sub total	**452**	**29**
Others		140	9
Total		**1568**	**100**

*Patients may have either one or more histopathology or not have any histopathology

1.3.3.2: Histopathological diagnosis in patients with urinary abnormalities

In patients presenting with urinary abnormalities, IgA (15%) was the commonest histopathology reported in the primary GN group; while the most common secondary GN was lupus nephritis (50%) (Table1.3.3.2).

Table 1.3.3.2: HPE diagnosis in patients presenting with asymptomatic urine abnormalities, 2005-2008

Type	Histopathological diagnosis	n	%
Primary	Minimal Change Disease	49	5
	FSGS	77	9
	lg A nephropathy	136	15
	Membranous nephropathy	29	3
	Membrano-proliferative	4	0
	Mesangial Proliferative GN-non IgA	17	2
	Crescentic	3	0
	Idiopathic crescentic	3	0
	Unknown	1	0
	Sub total	**319**	**35**
Secondary	Other infection	2	0
	Lupus Nephritis	450	50
	Henoch Schonlein Purpura	11	1
	HUS/TTP	0	0
	Amyloidosis	2	0
	Systemic vasculitis	1	0
	Post infection GN	10	1
	Polyarteritis nodosa	0	0
	Malignancy	0	0
	Light/ heavy chain disease	0	0
	Diabetic nephropathy	21	2
	Anti GBM	0	0
	Immunotactoid / fibrillary GN	0	0
	Multiple myeloma	1	0
	Unknown	2	0
	Sub total	**500**	**55**
Others		84	9
Total		**903**	**100**

* Patients may have either one or more histopathology or not have any histopathology

1.3.3.3: Histopathological diagnosis in patients with nephritic-nephrotic syndrome

In patients presenting with Nephritic-nephrotic syndrome the common histopathology among the primary GN were IgA (7%) and FSGS (7%) and among the secondary GN was lupus nephritis (49%) (Table 1.3.3.3).

Table 1.3.3.3: HPE diagnosis in patients presenting with nephritic-nephritic, 2005-2008

Type	Histopathological Diagnosis	n	%
Primary	Minimal Change Disease	14	6
	FSGS	17	7
	lg A nephropathy	15	7
	Membranous nephropathy	5	2
	Membrano-proliferative	4	2
	Mesangial Proliferative GN-non IgA	3	1
	Crescentic	0	0
	Idiopathic cresentic	2	1
	Unknown	0	0
	Sub total	**60**	**26**
Secondary	Other infection	1	0
	Lupus Nephritis	112	49
	Henoch Schonlein Purpura	3	1
	HUS/TTP	0	0
	Amyloidosis	0	0
	Systemic vasculitis	1	0
	Post infection GN	13	6
	Polyarteritis nodosa	0	0
	Malignancy	1	0
	Light/ heavy chain disease	0	0
	Diabetic nephropathy	6	3
	Anti GBM	0	0
	Immunotactoid / fibrillary GN	0	0
	Multiple myeloma	0	0
	Unknown	0	0
	Sub total	**137**	**60**
Others		31	14
Total		**228**	**100**

* Patients may have either one or more histopathology or not have any histopathology

1.3.3.4: Histopathological diagnosis in patients with nephritic syndrome

In patients presenting with acute nephritic syndrome, the commonest GN is lupus nephritis (48%) Table 1.3.3.4).

Table 1.3.3.4: HPE diagnosis in patients presenting with nephritic syndrome, 2005-2008

Type	Histopathological Diagnosis	n	%
Primary	Minimal Change Disease	16	6
	FSGS	25	9
	lg A nephropathy	22	8
	Membranous nephropathy	3	1
	Membrano-proliferative	4	1
	Mesangial Proliferative GN-non IgA	4	1
	Crescentic	2	1
	Idiopathic cresentic	6	2
	Unknown	2	1
	Sub total	**84**	**30**
Secondary	Other infection	0	0
	Lupus Nephritis	132	48
	Henoch Schonlein Purpura	2	1
	HUS/TTP	0	0
	Amyloidosis	0	0
	Systemic vasculitis	3	1
	Post infectious GN	19	7
	Polyarteritis nodosa	0	0
	Malignancy	0	0
	Light/ heavy chain disease	0	0
	Diabetic nephropathy	5	2
	Anti GBM	0	0
	Immunotactoid / fibrillary GN	0	0
	Multiple myeloma	0	0
	Unknown	0	0
	Sub total	**161**	**58**
Others		31	11
Total		276	100

* Patients may have either one or more histopathology or not have any histopathology

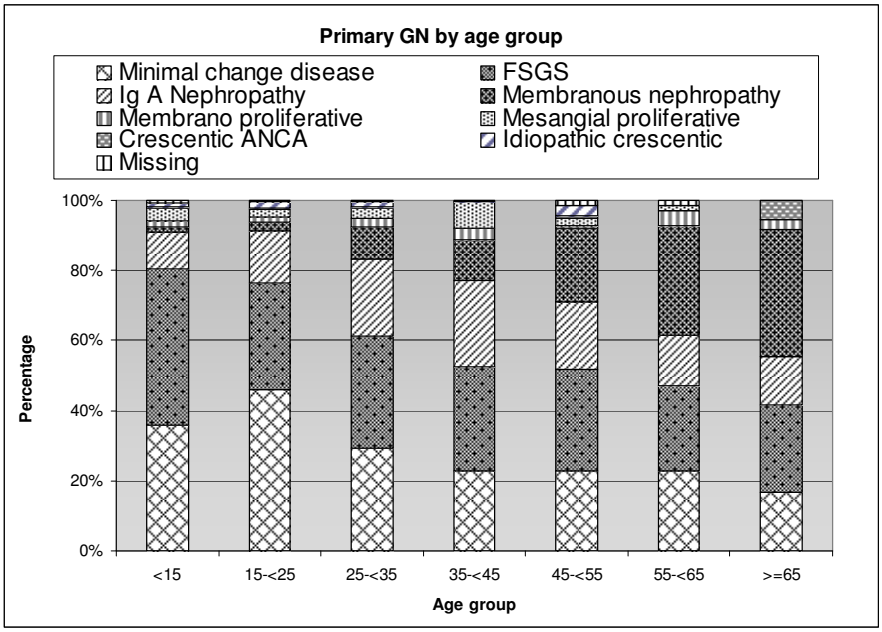
1.3.3.5 Primary GN according to various age group

FSGS was the commonest GN in the <15 year age group(45%) followed by minimal change disease(36%). In adults between 25 ≤ 55 years old, minimal change disease(34%) and FSGS(30.5%) were the two commonest GN. The commonest GN in the 15- 25 year age group was minimal change disease (46%). In patients above 55 years of age, the commonest primary GN was membranous nephropathy (33.0%) (Table 1.3.3.5).

Table 1.3.3.5: Primary GN according to the various age group, 2005-2008

Histopathological	<15		15 ≤ 25		25 ≤ 35		35 ≤ 45		45 ≤ 55		55 ≤ 65		≥ 65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Minimal change disease	114	36	199	46	91	29	46	23	31	23	16	23	6	17	503	33
FSGS	143	45	131	30	99	32	60	30	39	29	17	24	9	25	498	33
Ig A Nephropathy	33	10	64	15	68	22	50	25	26	19	10	14	5	14	256	17
Membranous nephropathy	5	2	11	3	28	9	23	11	28	21	22	31	13	36	130	9
Membrano proliferative	5	2	7	2	8	3	7	3	1	1	3	4	1	3	32	2
Mesangial proliferative	12	4	9	2	9	3	15	7	3	2	1	1	0	0	49	3
Non-Ig A Crescentic ANCA	1	0	1	0	1	0	0	0	1	1	0	0	2	6	6	0
Idiopathic crescentic	4	1	8	2	5	2	1	0	4	3	0	0	0	0	22	1
Missing	2	1	2	0	1	0	0	0	2	1	1	1	0	0	8	1
Total	**319**	**100**	**432**	**100**	**310**	**100**	**202**	**100**	**135**	**100**	**70**	**100**	**36**	**100**	**1504**	**100**

Figure 1.3.3.5: Primary GN according to the various age group, 2005-2008



CHAPTER 2

Primary Glomerulonephritis

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2.1 Introduction

This chapter covers the main primary glomerulonephritis that were reported to the MRRB from the years 2005-2008.

Minimal change disease is the commonest secondary glomerulonephritis in adult contributing 33% of all primary glomerulonephritis in Malaysia. This was followed by focal segmental glomerulosclerosis which contributed about 30% of cases. Ig A nephropathy (19%) is the third commonest primary glomerulonephritis. Idiopathic membranous nephropathy contributed only 11% of all biopsy proven primary glomerulonephritis. The other types of primary glomerulonephritis are relatively uncommon (Table 2.1).

Table 2.1: Primary Glomerulonephritis, 2005-2008

Histopathological Diagnosis	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Minimal Change Disease (MCD)	76	35	86	29	84	31	143	37	389	33
Focal Segmental Glomerulosclerosis (FSGS)	61	28	106	36	87	32	101	26	355	30
Ig A nephropathy (Ig AN)	31	14	51	17	52	19	89	23	223	19
Membranous nephropathy (IMN)	23	10	33	11	33	12	36	9	125	11
Membrano-proliferative GN (MPGN)	10	5	9	3	4	1	4	1	27	2
Mesangial Proliferative GN non Ig A	13	6	8	3	9	3	6	2	36	3
Crescentic ANCA	0	0	1	0	0	0	4	1	5	0
Idiopathic Crescentic	6	3		0	4	1	2	1	12	1
Unknown	0	0	0	0	2	1	6	2	8	1
Total	**220**	**100**	**294**	**100**	**275**	**100**	**391**	**100**	**1180**	**100**

2.2: Minimal change disease

2.2.1: Introduction

Minimal change disease (MCD) is typically characterized by normal appearing glomeruli by light microscopy and the absence of complement or immunoglobulin deposits by immunofluorescence microscopy. Glomerular size is usually normal by standard methods of light microscopy, although enlarged glomeruli may be observed.

The characteristic histologic lesion in minimal change disease is diffuse effacement (also called "fusion") of the epithelial foot processes on electron microscopy. Minimal change disease is a major cause of nephrotic syndrome in both children and adults.

2.2.2: Patient population and characteristics

A total of 389 cases of minimal change disease were reported in 2005-2008. The mean age of the patients at the time of biopsy was 29.1 ± 12.8 with a clear predominance in second and third decades of life. The frequencies of age groups 15 to <25, and 25 to <35 were 51% and 23% respectively, which is 74% when combined. However, it is important to bear in mind that children with steroid responsive nephrotic syndrome are usually not biopsied, hence the actual incidence of minimal change disease in the paediatric age group is under-represented. The diagnosis of minimal change disease is relatively rare after 55 years of age and our reported frequency was only about 6% in this age group.

There is a higher incidence of minimal change disease in males, with a ratio of 2:1 in the four-year registry data (overall 66% as compared to 34% in the female group (Table 2.2.2 (a)).

In terms of racial distribution, there was no predilection of any particular ethnic group. The racial group distribution in Malay, Chinese and Indian was 60%, 17% and 6% (Table 2.2.2 (a)). This pattern of distribution reflects the ethnic composition of patients admitted to public hospitals.

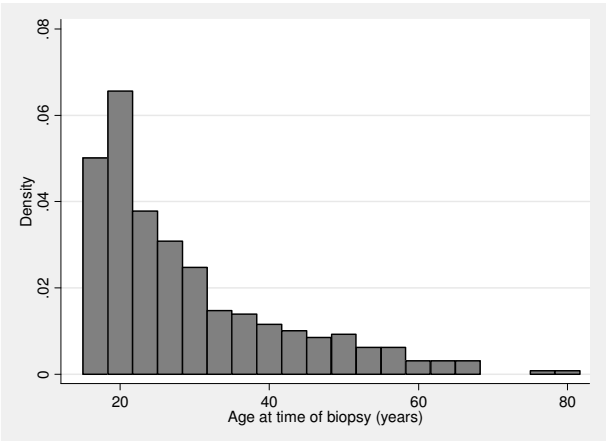
Table 2.2.2(a): Demographic characteristics for MCD, 2005-2008

Demographic Characteristics		**n =389**	**%**
Age (years)		29.1 ± 12.8	
Race	Male	258	66
	Female	131	34
Gender	Malay	234	60
	Chinese	66	17
	Indian	22	6
	Others	67	17

Table 2.2.2 (b): Age group at time of biopsy (years) for MCD, 2005-2008

Age group	**2005**		**2006**		**2007**		**2008**		**Total**	
(years)	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
15-<25	32	42	49	57	41	49	77	54	199	51
25-<35	21	28	20	23	16	19	34	24	91	23
35-<45	11	14	10	12	14	17	11	8	46	12
45-<55	10	13	4	5	6	7	11	8	31	8
55-<65	1	1	2	2	5	6	8	6	16	4
≥65	1	1	1	1	2	2	2	1	6	2
Total	**76**	**100**	**86**	**100**	**84**	**100**	**143**	**100**	**389**	**100**

Figure 2.2.2 (b): Age at time of biopsy (years) MCD, 2005-2008



2.2.3: Clinical presentation

The mean level of 24 hours urine protein was 6.4 ± 5.1g/day. Nephrotic syndrome, as expected, was the most common presentation (81%). Other presentations were asymptomatic urine abnormality (10%), nephritic syndrome (3%) and nephritic-nephrotic syndrome (3%) (Table & Figure 2.2.3(a)).

Majority of blood pressures were normal during presentation (88%) (Table 2.2.3(b)).

Most patients do not have any documented renal impairment, 58% have eGFR ≥ 90 ml/min/1.73m^2 while 23% have eGFR between 60 to 89 ml/min/1.73m^2. One fifth of patients have significant renal impairment (eGFR less than 60 ml/min/1.73m^2) (Table 2.2.3 (c)).

Table 2.2.3 (a): Clinical presentation for MCD, 2005-2008

Clinical Presentations	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	4	5	9	10	11	13	16	11	40	10
Nephritic syndrome	2	3	3	3	3	4	5	3	13	3
Nephrotic syndrome	69	91	70	81	63	75	115	80	317	81
Nephritic-Nephrotic syndrome	1	1	2	2	3	4	6	4	12	3
Missing	0	0	2	2	4	5	1	1	7	2
Total	**76**	**100**	**86**	**100**	**84**	**100**	**143**	**100**	**389**	**100**

Figure 2.2.3 (a): Clinical presentation for MCD, 2005-2008

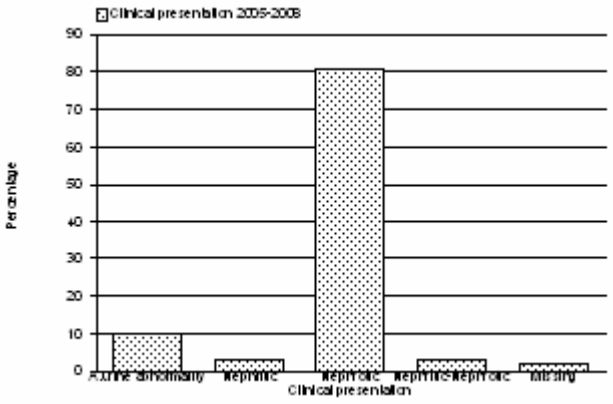


Table 2.2.3 (b): Presence of hypertension in MCD, 2005-2008

Hypertension	n	%
Present	35	9
Absent	341	88
Missing	13	3
Total	**389**	**100**

Table 2.2.3 (c): Renal function in MCD by year, 2005-2008

GFR (ml/min/1.73m^2)	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
≥90	41	54	53	62	42	50	88	62	224	58
60-89	20	26	17	20	24	29	27	19	88	23
30-59	13	17	12	14	11	13	21	15	57	15
15-29	2	3	1	1	5	6	5	3	13	3
<15	0	0	3	3	2	2	2	1	7	2
Total	**76**	**100**	**86**	**100**	**84**	**100**	**143**	**100**	**389**	**100**

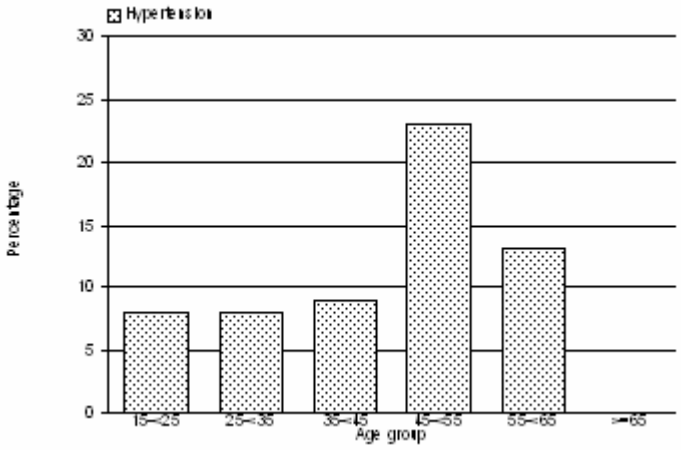
2.2.3.1: Clinical presentation by age

Nephrotic syndrome consistently predominates as the clinical presentation throughout all age groups (Table 2.2.3.1). However, the presence of hypertension increases with increasing age (Figure 2.2.3.1(b)).

Table 2.2.3.1: Clinical presentation by age group for MCD, 2005-2008

Clinical Presentations	15- <25		25-<35		35-<45		45-<55		55-<65		≥ 65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	18	9	10	11	7	16	3	10	2	13	0	0	40	11
Nephritic syndrome	5	3	5	6	1	2	1	3	0	0	1	17	13	3
Nephrotic syndrome	164	82	75	82	35	76	27	87	12	74	4	66	317	81
Nephritic-Nephrotic syndrome	10	5	0	0	1	2	0	0	0	0	1	17	12	3
Missing	2	1	1	1	2	4	0	0	2	13	0	0	7	2
Total	**199**	**100**	**91**	**100**	**46**	**100**	**31**	**100**	**16**	**100**	**6**	**100**	**389**	**100**

Figure 2.2.3.1 (b): Hypertension by age group for MCD, 2005-2008



2.2.3.2: Clinical presentation by gender

There are basically no differences between genders in terms of clinical presentation and renal function at presentation (Table 2.2.3.2 (a & b)). Both genders have relatively well preserved with renal function with less than 20% have eGFR < 60 ml/min/1.72 m^2 (Figure 2.2.3.2 (b)). The prevalence of hypertension was higher in female than male (13% vs. 7%) (Figure 2.2.3.2(c)).

Table 2.2.3.2 (a): Clinical presentation by gender for MCD, 2005-2008

Clinical Presentations	Male		Female	
	n	%	n	%
Asymptomatic urine abnormality	20	8	20	15
Nephritic syndrome	7	3	6	5
Nephrotic syndrome	215	82	102	78
Nephritic-Nephrotic syndrome	12	5	0	0
Missing	4	2	3	2
Total	**258**	**100**	**131**	**100**

Table 2.2.3.2 (b): Renal function by gender for MCD, 2005-2008

eGFR (ml/min/1.73m^2)	Male		Female	
	n	%	n	%
≥90	152	59	72	55
60-89	54	21	34	26
30-59	37	14	20	15
15-29	9	3	4	3
<15	6	2	1	1
Total	**258**	**100**	**131**	**100**

Figure 2.2.3.2 (b): Impaired renal function by gender for MCD, 2005-2008

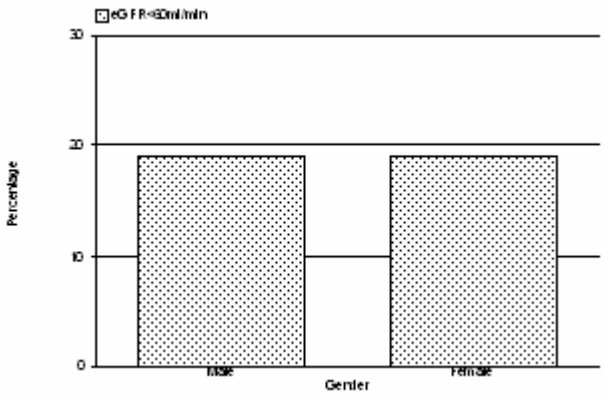
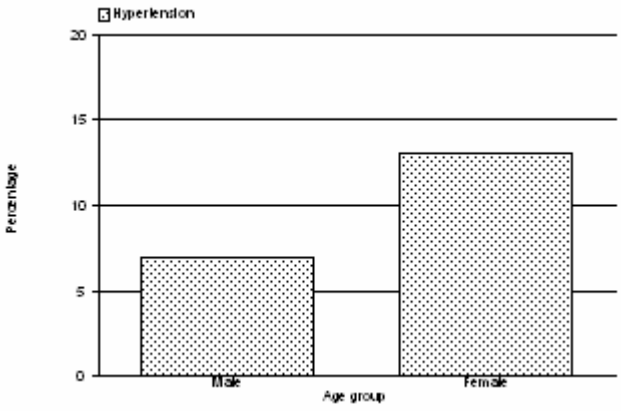


Figure2.2.3.2 (c): Hypertension by gender for MCD, 2005-2008



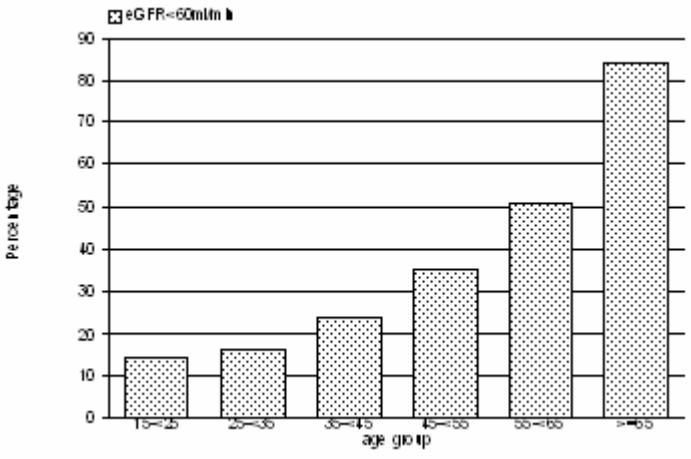
2.2.4: Renal function at presentation

About three-quarter of patients below 35-years-old have well-preserved renal function (eGFR ≥60ml/min/1.73m^2). This is in contrast to the older age group, e.g. those aged above 55 years where 50-84 % have already suffered significant renal impairment (eGFR < 60ml/min/1.73m^2) on presentation (Table & Figure 2.2.4).

Table 2.2.4: Renal function at presentation by age group for MCD, 2005-2008

eGFR (ml/min/1.73m^2)	15 ≤ 25		25 ≤ 35		35 ≤ 45		45 ≤ 55		55 ≤ 65		≥ 65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
≥90	137	69	58	64	15	33	10	32	4	25	0	0	224	58
60-89	35	18	18	20	20	43	10	32	4	25	1	17	88	23
30-59	22	11	11	12	7	15	10	32	3	19	4	67	57	15
15-29	5	3	3	3	1	2	1	3	3	19	0	0	13	3
<15	0	0	1	1	3	7	0	0	2	13	1	17	7	2
Total	**199**	**100**	**91**	**100**	**46**	**100**	**31**	**100**	**16**	**100**	**6**	**100**	**389**	**100**

Figure 2.2.4: Renal function at presentation by age group for MCD, 2005-2008



2.3: Focal Segmental Glomerulosclerosis

2.3.1: Introduction

Focal segmental glomerulosclerosis is defined on histologic criteria by segmental capillary obliteration with increased mesangial matrix deposition, intra-capillary hyaline deposits and focal adhesions of the capillary tuft to Bowman's capsule.

2.3.2: Patient Population and Characteristics

A total of 355 cases of FSGS were reported in our four-year registry data. The mean age at the time of biopsy was 32.5 ± 13.5 (Table 2.3.2 (a)). The first three decades of life were the predominant age groups in this type of renal disease. After the age of 55, the frequency rate was only 8% compared to other age groups (Table & Figure 2.3.2 (b)). FSGS was slightly more common in males (57%) compared to females (43%) (Table 2.3.2(a)). The distribution according to ethnicity was 62% in Malays, 16% in Chinese, 7% in Indians and 15% in others (Table 2.3.2(a)).

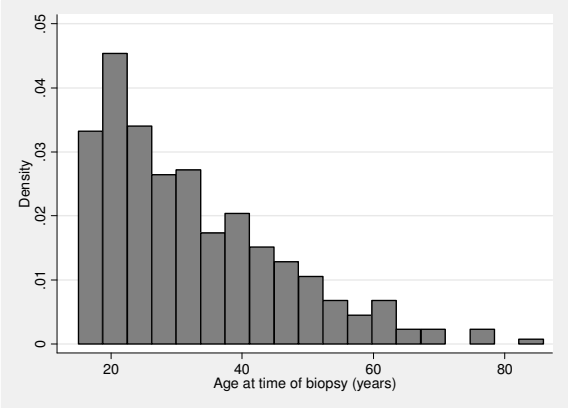
Table 2.3.2 (a): Demographic characteristics for FSGS, 2005-2008

Demographic Characteristics		n=355	%
Age (years)		32.5 ± 13.5	
Gender	Male	203	57
	Female	152	43
Race	Malay	221	62
	Chinese	56	16
	Indian	26	7
	Others	52	15

Table 2.3.2 (b): Age group at time of biopsy (years) for FSGS, 2005-2008

Age group (years)	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
15-<25	19	31	46	43	31	36	35	35	131	37
25-<35	17	28	23	22	28	32	31	31	99	28
35-<45	13	21	18	17	15	17	14	14	60	17
45-<55	8	13	9	8	9	10	13	13	39	11
55-<65	3	5	5	5	3	3	6	6	17	5
≥65	1	2	5	5	1	1	2	2	9	3
Total	**61**	**100**	**106**	**100**	**87**	**100**	**101**	**100**	**355**	**100**

Figure 2.3.2 (b): Age at time of biopsy (years) for FSGS, 2005-2008



2.3.3: Clinical Presentation

The mean level of 24 hours urine protein was 4.6±3.7g/day. Nephrotic syndrome was the most common reported clinical presentation (65%). Other reported presentations were asymptomatic urine abnormality (21%), nephritic syndrome (6%) and nephritic-nephrotic syndrome (3%) (Table & Figure 2.3.3(a)).

The majority of patients (79%) have normal blood pressure during the initial presentation (Table 2.3.3 (b)).

Table 2.3.3 (a): Clinical presentation for FSGS, 2005-2008

Clinical Presentations	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	10	16	19	18	17	20	28	28	74	21
Nephritic syndrome	4	7	5	5	5	6	6	6	20	6
Nephrotic syndrome	43	70	76	72	56	64	57	56	232	65
Nephritic-Nephrotic syndrome	1	2	0	0	6	7	4	4	11	3
Missing	3	5	6	6	3	3	6	6	18	5
Total	**61**	**100**	**106**	**100**	**87**	**100**	**101**	**100**	**355**	**100**

Figure 2.3.3 (a): Clinical presentation for FSGS, 2005-2008

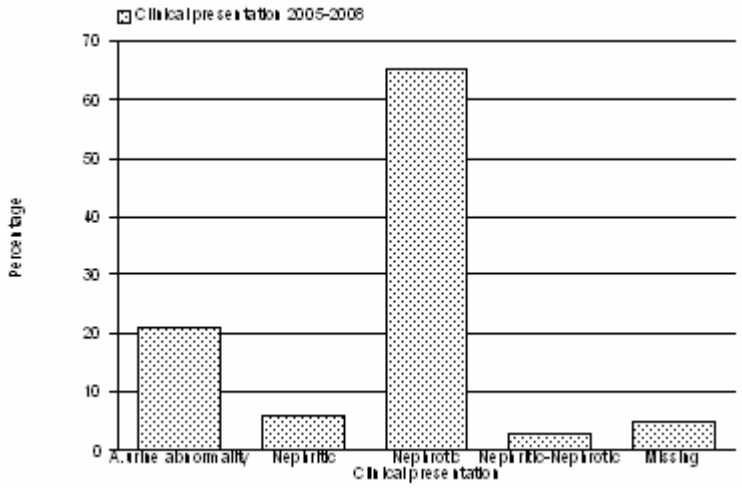


Table 2.3.3 (b): Hypertension in FSGS, 2005-2008

Hypertension	n	%
Present	63	18
Absent	281	79
Missing	11	3
Total	**355**	**100**

2.3.3.1: Clinical presentation by age

Nephrotic syndrome consistently predominates as the clinical presentation throughout all age groups particularly in the very young (below 25 years) and those above 55 (Table & Figure 2.3.3.1(a)). years. The prevalence of hypertension increases with increasing age (Figure 2.3.3.1(b)).

Table 2.3.3.1 (a): Clinical presentation by age group for FSGS, 2005-2008

Age group (years)	15 ≤ 25		25 ≤ 35		35 ≤ 45		45 ≤ 55		55 ≤ 65		≥ 65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	18	14	33	34	16	27	5	13	2	12	0	0	74	21
Nephritic syndrome	6	5	9	9	3	5	1	3	1	6	0	0	20	6
Nephrotic syndrome	100	76	49	49	36	59	26	67	14	82	7	78	232	65
Nephritic-Nephrotic syndrome	4	3	3	3	1	2	3	8	0	0	0	0	11	3
Missing	3	2	5	5	4	7	4	9	0	0	2	22	18	5
Total	**131**	**100**	**99**	**100**	**60**	**100**	**39**	**100**	**17**	**100**	**9**	**100**	**355**	**100**

Figure 2.3.3.1 (a): Clinical presentation by age group for FSGS, 2005-2008

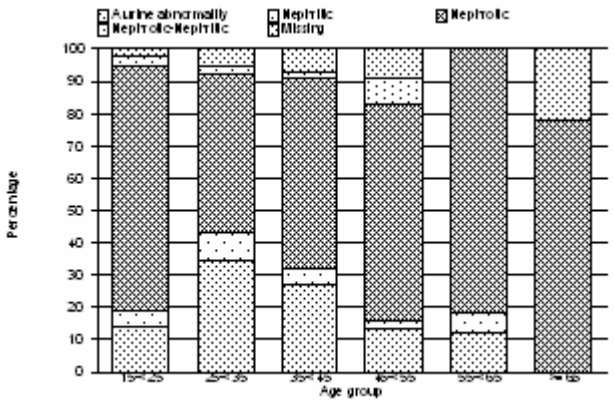
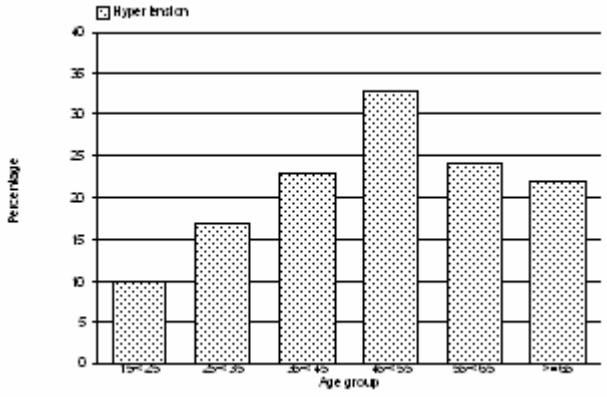


Figure 2.3.3.1 (b): Hypertension by age group for FSGS, 2005-2008



2.3.3.2: Clinical presentation by gender

From the 4 years of collected data, nephrotic syndrome appears more common in males and more females present as asymptomatic urine abnormality (Table & Figure 2.3.2 (a)). There was no difference in the prevalence of hypertension in both genders (Figure 2.3.3.2(b)).

Table 2.3.3.2 (a): Clinical presentation by gender for FSGS, 2005-2008

Clinical Presentations	Male		Female	
	n	%	n	%
Asymptomatic urine abnormality	30	16	44	29
Nephritic syndrome	11	5	9	6
Nephrotic syndrome	147	72	85	56
Nephritic-Nephrotic syndrome	8	4	3	2
Missing	7	3	11	7
Total	**203**	**100**	**152**	**100**

Figure 2.3.3.2 (a): Clinical presentation by gender for FSGS, 2005-2008

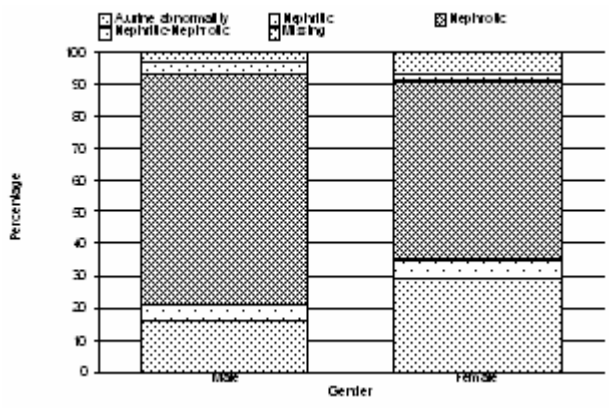
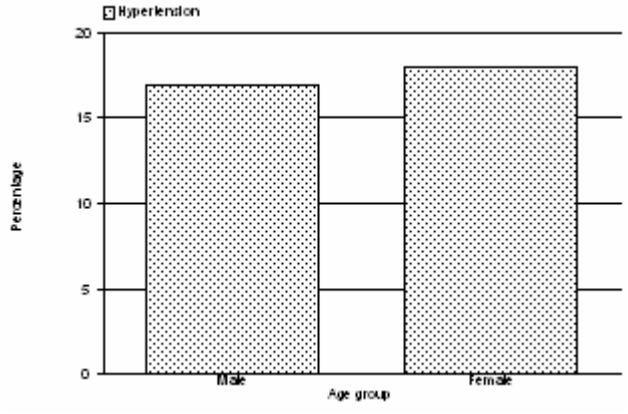


Figure 2.3.3.2 (b): Hypertension by gender in FSGS, 2005-2008



2.3.4: Renal function at presentation

About 59% have normal or well-preserved renal function (eGFR ≥60 ml/min/1.73m^2) on presentation. There were 21% of cases with eGFR range of 30-59 ml/min/1.73m^2, 11 % were 15-29 ml/min/1.73m^2 and 5% were <15 ml/min/1.73m^2 (Table 2.3.4).

Table 2.3.4: Impaired renal function in FSGS by year, 2005-2008

eGFR (ml/min/1.73m^2)	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
≥90	23	38	45	42	31	36	36	36	135	38
60-89	7	11	27	25	25	29	17	17	76	21
30-59	19	31	17	16	21	24	31	31	88	25
15-29	8	13	14	13	8	9	10	10	40	11
<15	4	7	3	3	2	2	7	7	16	5
Total	**61**	**100**	**106**	**100**	**87**	**100**	**101**	**100**	**355**	**100**

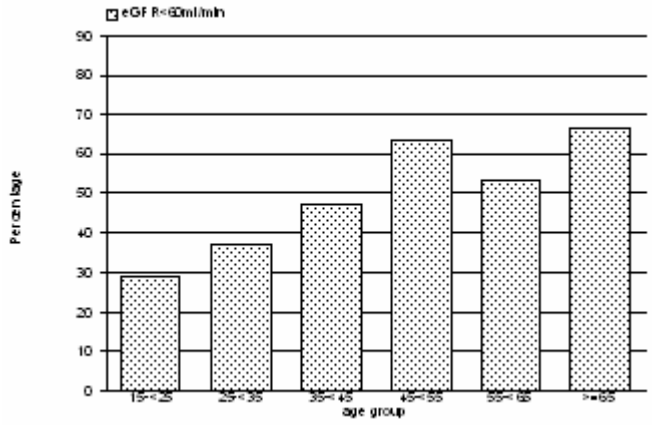
2.3.4.1: Renal function at presentation by age

There was a higher risk of renal impairment with increasing age (Table & Figure 2.3.4.1)

Table 2.3.4.1: Renal function at presentation by age group for FSGS, 2005-2008

eGFR (ml/min/1.73m^2)	15- <25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
≥90	72	55	40	40	17	28	4	10	2	12	0	0	135	38
60-89	20	15	22	22	15	25	10	26	6	35	3	33	76	21
30-59	32	24	21	21	16	27	13	33	5	29	1	11	88	25
15-29	4	3	14	14	10	17	6	15	3	18	3	33	40	11
<15	3	2	2	2	2	3	6	15	1	6	2	22	16	5
Total	**131**	**100**	**99**	**100**	**60**	**100**	**39**	**100**	**17**	**100**	**9**	**100**	**355**	**100**

Figure 2.3.4.1: Impaired renal function at presentation by age group for FSGS, 2005-2008



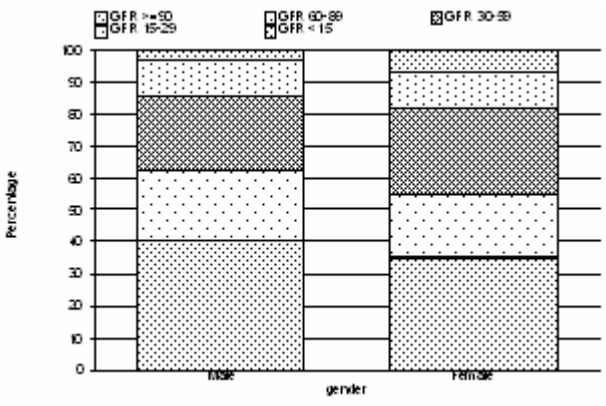
2.3.4.2: Renal function at presentation by gender

There were basically no differences between genders in terms of renal function.

Table 2.3.4.2: Renal function at presentation according to gender for FSGS, 2005-2008

eGFR (ml/min/1.73m^2)	Male		Female	
	n	%	n	%
≥90	82	40	53	35
60-89	46	23	30	20
30-59	46	23	42	27
15-29	23	11	17	11
<15	6	3	10	7
Total	**203**	**100**	**152**	**100**

Figure 2.3.4.2: Renal function at presentation according to gender for FSGS, 2005-2008



2.4: Idiopathic Membranous Nephropathy (IMN)

2.4.1. Introduction

Membranous nephropathy is characterised by subepithelial immune deposits with spikes and thickening of the basement membrane.

2.4.2. Patient population and characteristics

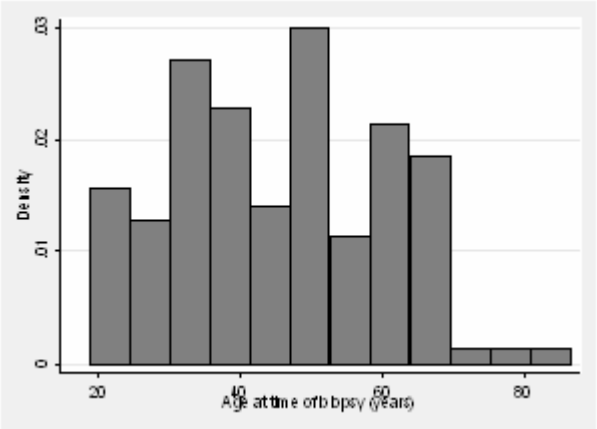
Over the four-year period from 2005-2008, 125 cases of Idiopathic membranous nephropathy (IMN) were reported to the registry. The mean age at biopsy was 45.3 ± 14.7, with a range between 19 and 80.8 years (Table & Figure 2.4.2).

Overall, there were slightly more males than females. The racial distribution was 44% in Malays, 40% in Chinese, 6 % in Indians and 10% in others (Table 2.4.2).

Table 2.4.2: Demographic characteristics for IMN, 2005-2008

Demographic characteristics		n=125	%
Age (years)	45.3 + 14.7 years		
Gender	Male	71	57
	Female	54	43
Race	Malay	55	44
	Chinese	50	40
	Indian	8	6
	Other	12	10

Figure 2.4.2: Age at time of biopsy (years) for IMN, 2005-2008



2.4.3: Clinical presentation

The majority of patients (70%) presented with overt nephrotic syndrome. The median level of proteinuria was 3.5 g/day with a range from 0.3- 19.8 g/day. Asymptomatic urinary abnormalities, nephritic-nephrotic syndrome, and nephritic syndrome were found in 22%, 3% and 2% respectively (Table & Figure 2.4.3(a)). Hypertension was found in 21% of cases (Table 2.4.3 9(c)) and 37% presented with eGFR< 60mls/min (Table 2.4.3(c)).

Table 2.4.3 (a): Clinical presentation for IMN, 2005-2008

Clinical Presentations	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	1	4	8	24	9	27	10	28	28	22
Nephritic syndrome	1	4	1	3	0	0	1	3	3	2
Nephrotic syndrome	20	87	21	64	23	70	23	64	87	70
Nephritic-Nephrotic syndrome	1	4	1	3	0	0	2	6	4	3
Missing	0	0	2	6	1	3	0	0	3	2
Total	**23**	**100**	**33**	**100**	**33**	**100**	**36**	**100**	**125**	**100**

Figure 2.4.3 (a): Clinical presentation for IMN, 2005-2008

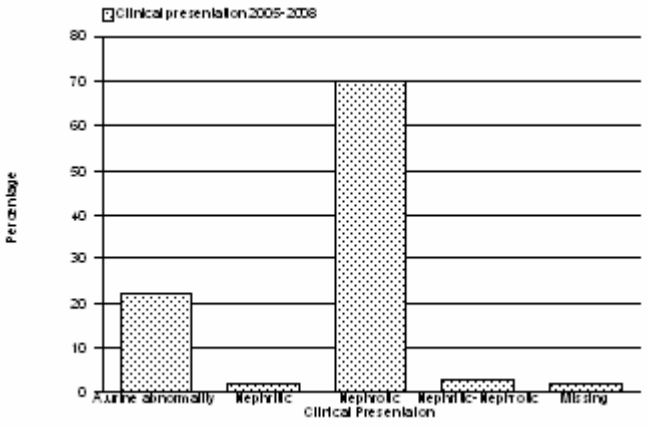


Table 2.4.3 (b): Hypertension in IMN, 2005-2008

Hypertension	n	%
Present	26	21
Absent	97	78
Missing	2	2
Total	**125**	**100**

Table 2.4.3(c): Renal function in IMN, 2005-2008

eGFR (ml/min/1.73m^2)	n	%
≥90	43	34
60-89	35	28
30-59	33	26
15-29	10	8
<15	4	3
Total	**125**	**100**

2.4.3.1: Clinical presentation by age

Nephrotic syndrome remained the commonest clinical presentation across all age groups, and older patients were less likely to be biopsied for asymptomatic urinary abnormalities (Table & Figure 2.4.3.1 (a)). Comparison with respect to incidence of hypertension is limited by the relatively smaller numbers of patients at both extremes of age.

Table 2.4.3.1(a): Clinical presentation by age group for IMN, 2005-2008

Age group (years)	15 ≤ 25		25 ≤ 35		35 ≤ 45		45 ≤ 55		55 ≤ 65		≥ 65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	3	27	6	21	4	18	5	18	10	45	0	0	28	22
Nephritic syndrome	0	0	0	0	0	0	2	7	1	5	0	0	3	2
Nephrotic syndrome	7	64	21	75	17	74	19	68	10	45	13	100	87	70
Nephritic-Nephrotic syndrome	1	9	0	0	1	4	2	7	0	0	0	0	4	4
Missing	0	0	1	4	1	4	0	0	1	5	0	0	3	2
Total	**11**	**100**	**28**	**100**	**23**	**100**	**28**	**100**	**22**	**100**	**13**	**100**	**125**	**100**

Figure 2.4.3.1 (a): Clinical presentation by age group for IMN, 2005-2008

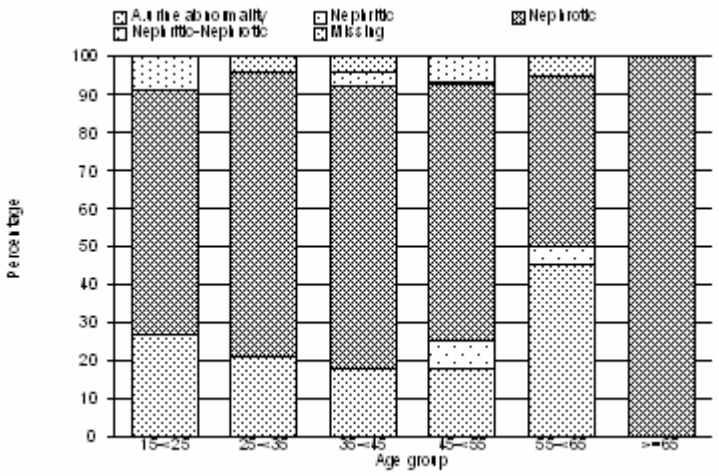


Table 2.4.3.1(b): Hypertension by age group for IMN, 2005-2008

Hypertension	15 ≤ 25		25 ≤ 35		35 ≤ 45		45 ≤ 55		55 ≤ 65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Present	3	27	4	14	4	17	3	11	8	36	4	31	26	21
Absent	8	73	24	86	18	78	24	86	14	64	9	69	97	78
Missing	0	0	0	0	1	4	1	4	0	0	0	0	2	2
Total	**11**	**100**	**28**	**100**	**23**	**100**	**28**	**100**	**22**	**100**	**13**	**100**	**125**	**100**

2.4.3.2: Clinical presentation by gender

There were no significant differences in gender with respect to clinical presentation.

Figure 2.4.3.2 (a): Clinical presentation by gender for IMN, 2005-2008

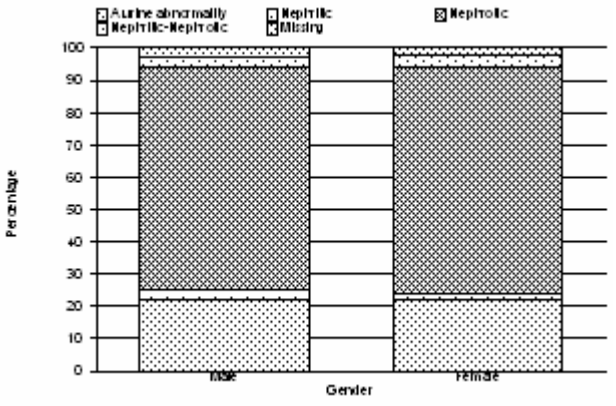


Table 2.4.3.2 (b): Hypertension by gender for IMN, 2005-2008

	Male		Female	
Hypertension	**n**	**%**	**n**	**%**
Present	16	23	10	19
Absent	54	76	43	80
Missing	1	1	1	2
Total	**71**	**100**	**54**	**100**

2.4.4: Renal function at presentation

2.4.4.1: Renal function at presentation by age

Majority of cases (62%) had eGFR > 60 ml/min/1.73m^2 at presentation. There were 27 % of cases with eGFR range of 30-59 ml/min/1.73m^2, 8% in the 15-29 ml/min/1.73m^2 and 3% in the < 15 ml/min/1.73m^2 (Table & Figure 2.4.4.1 (a)). The proportion of patients with eGFR < 60 ml/min/1.73m^2. Increase with age (Figure 2.4.4.1 (b)).

Table 2.4.4.1(a): Renal function at presentation by age group for IMN, 2005-2008

eGFR (ml/min/1.73m^2)	**15 ≤ 25**		**25 ≤ 35**		**35 ≤ 45**		**45 ≤ 55**		**55 ≤ 65**		**≥ 65**		**Total**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
≥90	10	91	13	46	9	39	7	25	3	14	1	8	43	34
60-89	0	0	8	28	8	35	11	39	7	32	1	8	35	28
30-59	1	9	5	18	4	18	7	25	8	36	8	61	33	27
15-29	0	0	1	4	1	4	3	11	2	9	3	23	10	8
<15	0	0	1	4	1	4	0	0	2	9	0	0	4	3
Total	**11**	**100**	**28**	**100**	**23**	**100**	**28**	**100**	**22**	**100**	**13**	**100**	**125**	**100**

Figure 2.4.4.1 (a): Renal function at presentation by age group for IMN, 2005-2008

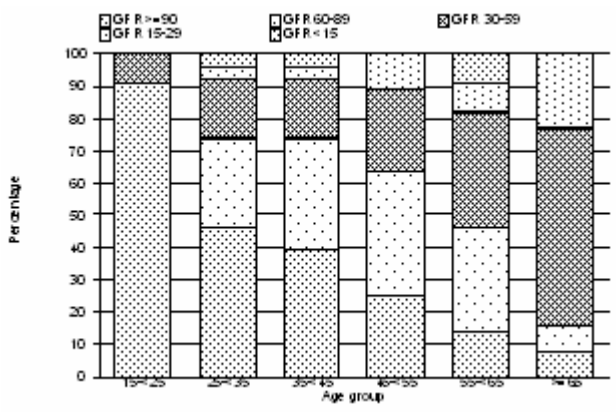
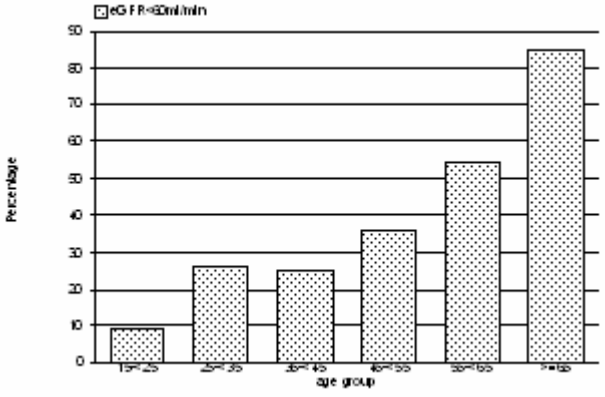


Figure 2.4.4.1 (b): Impaired renal function by age group for IMN, 2005-2008



2.4.4.2: Renal function at presentation by gender

Males appear to have worse renal function. Up to 44% of male vs. 31% of females has eGFR < 60 ml/ min/1.73m^2 at presentation (Table 2.4.4.2).

Table 2.4.4.2: Renal function at presentation according to gender for IMN, 2005-2008

eGFR (ml/min/1.73m^2)	Male		Female	
	n	%	n	%
≥90	17	24	26	48
60-89	23	32	12	21
30-59	23	32	10	19
15-29	7	11	3	6
<15	1	1	3	6
Total	**71**	**100**	**54**	**100**

2.5: Ig A Nephropathy (IgAN)

2.5.1: Introduction

IgAN is defined by the predominant deposition of IgA in the glomerular mesangium although light microscopic appearances and clinical features can vary considerably due to the various patterns of histopathologic injury found in this glomerulonephritis.

2.5.2: Patient population and characteristics

Two hundred and twenty-three cases of IgA nephropathy were reported to the registry over the 3-year period of data collection. The mean age at biopsy was 33.8 ± 12.5 years and majority of the cases (81%) were between ages 15 to 45 years (Table & Figure 2.5.2 (b)). As suggested in the previous report, there is slight female preponderance in our cohort (53% vs. 47%), which is contrary to what has been reported in the literature. The ethnic distribution was Malays (51%), followed by Chinese (28%) and Indians (8%) (Table 2.5.2(a)).

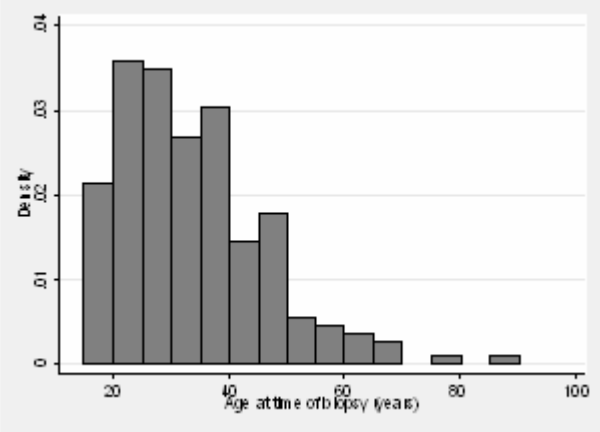
Table 2.5.2(a): Demographic characteristics of patients with IgA nephropathy, 2005-2008

Demographic Characteristics		n=223	%
Age (years)		33.8 ± 12.5	
Gender	Male	104	47
	Female	119	53
Race	Malay	114	51
	Chinese	62	28
	Indian	18	8
	Others	29	13

Table 2.5.2 (b): Age group at time of biopsy (years) for IgA nephropathy, 2005-2008

Age group (years)	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
15-<25	5	16	15	29	15	29	29	33	64	29
25-<35	10	32	14	27	21	40	23	26	68	30
35-<45	10	32	11	22	8	15	21	24	50	22
45-<55	2	6	8	16	6	12	10	11	26	12
55-<65	3	10	2	4	2	4	3	3	10	4
≤65	1	3	1	2	0	0	3	3	5	2
Total	**31**	**100**	**51**	**100**	**52**	**100**	**89**	**100**	**223**	**100**

Figure 2.5.2 (b): Age at time of biopsy (years) for IgA nephropathy, 2005-2008



2.5.3: Clinical presentation

Asymptomatic urine abnormalities remains the most common presentation of IgAN (55%). Up to 25% of those who were biopsied had nephrotic syndrome (Table 2.5.3 (a)). This figure was much higher than the 5% quoted the literature and this may reflect relatively conservative local practices with regards to investigation of asymptomatic urine abnormalities. However, it might not be reflective of the true picture due to the small patient numbers in this age group (5 patients). Up to 32% of patients were hypertensive at presentation (Table 2.5.3 (b)).

Table 2.5.3 (a): Clinical presentation for IgA nephropathy, 2005-2008

Clinical Presentations	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	19	61	20	39	28	54	56	63	123	55
Nephritic syndrome	1	3	3	6	4	8	8	9	16	7
Nephrotic syndrome	8	26	16	31	10	19	21	24	55	25
Nephritic-Nephrotic syndrome	0	0	3	6	4	8	3	3	10	4
Missing	3	10	9	18	6	12	1	1	19	9
Total	**31**	**100**	**51**	**100**	**52**	**100**	**89**	**100**	**223**	**100**

Figure 2.5.3 (a): Clinical presentation for IgA nephropathy, 2005-2008

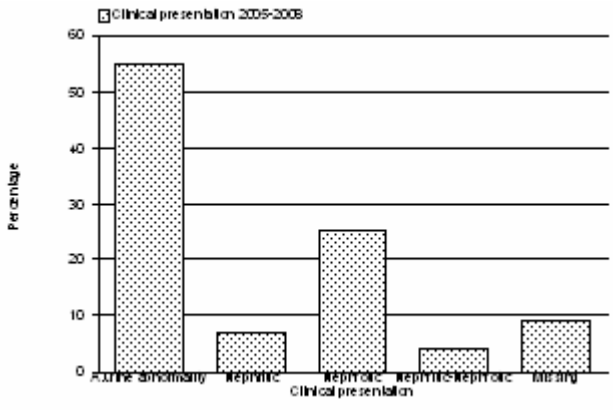


Table 2.5.3 (b): Hypertension in IgA nephropathy, 2005-2008

Hypertension	n	%
Present	71	32
Absent	142	64
Missing	10	4
Total	**223**	**100**

2.5.3.1: Clinical presentation by age

Asymptomatic urine abnormalities is the most common clinical presentation of IgAN in all age groups except in those above the age of 65 years old. This was followed by nephrotic syndrome.

Table 2.5.3.1: Clinical presentation by age group for IgA nephropathy, 2005-2008

Age group (years)	15- <25		25-<35		35-<45		45-<55		55-<65		≤65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	30	47	39	57	31	62	15	57	7	70	1	20	123	55
Nephritic syndrome	8	13	5	7	2	4	1	4	0	0	0	0	16	7
Nephrotic syndrome	19	29	14	22	13	26	6	23	1	10	2	40	55	25
Nephritic-Nephrotic syndrome	3	5	3	4	1	2	2	8	1	10	0	0	10	4
Missing	4	6	7	10	3	6	2	8	1	10	2	40	19	9
Total	**64**	**100**	**68**	**100**	**50**	**100**	**26**	**100**	**10**	**100**	**5**	**100**	**223**	**100**

2.5.3.2 Clinical presentation by gender

More females (58%) than male (51%) presented with asymptomatic urine abnormality.

Table 2.5.3.2: Clinical presentation by gender for IgA nephropathy, 2005-2008

Clinical Presentations	Male		Female	
	n	%	n	%
Asymptomatic urine abnormality	54	51	69	58
Nephritic syndrome	9	9	7	6
Nephrotic syndrome	26	25	29	24
Nephritic-Nephrotic syndrome	4	4	6	5
Missing	11	11	8	7
Total	**104**	**100**	**119**	**100**

2.5.4: Renal function at presentation

2.5.4.1: Renal function at presentation by age

Most of the younger patients (age less than 45 years) have preserved renal function at presentation. As expected, older patients have greater degree of renal impairment (Table & Figure 2.5.4.1).

Table 2.5.4.1: Renal function at presentation by age group for IgA nephropathy, 2005-2008

eGFR (ml/min/1.73m^2)	15 ≤ 25		25 ≤ 35		35 ≤ 45		45 ≤ 55		55 ≤ 65		≥ 65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
≥90	29	46	19	28	12	24	2	8	2	20	0	0	64	29
60-89	13	20	18	26	15	30	6	23	3	30	0	0	55	25
30-59	13	20	18	26	18	36	8	30	1	10	1	20	59	26
15-29	5	8	7	11	4	8	3	12	3	30	3	60	25	11
<15	4	6	6	9	1	2	7	27	1	10	1	20	20	9
Total	**64**	**100**	**68**	**100**	**50**	**100**	**26**	**100**	**10**	**100**	**5**	**100**	**223**	**100**

Figure 2.5.4.1: Renal function at presentation by age group for IgA nephropathy, 2005-2008

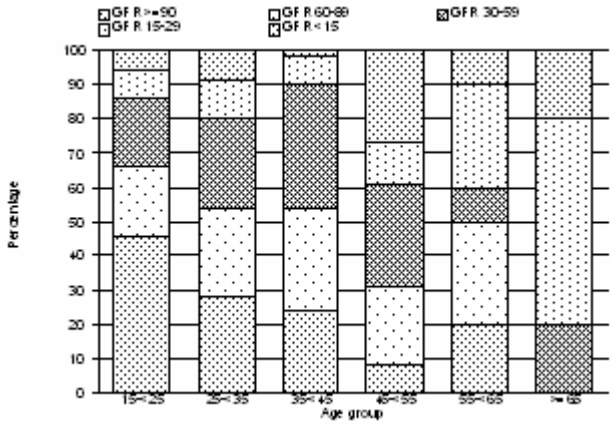
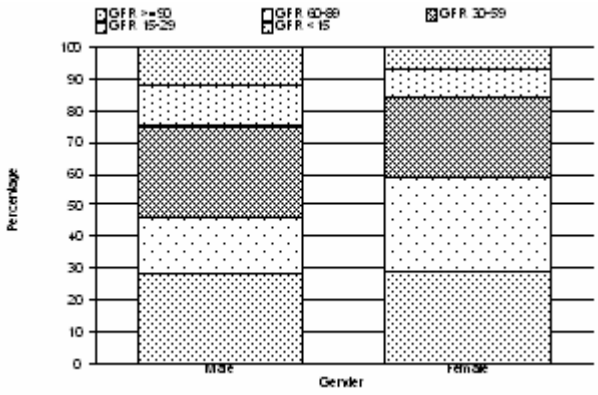


Figure 2.5.4.2: Renal function at presentation according to gender for IgA nephropathy, 2005-2008



2.5.4.2: Renal function at presentation by gender

Male tend to have worse renal function compared to female (54% vs. 41%) have eGFR less than 60 ml/min/1.73m^2 (Table & Figure 2.5.4.2).

Table 2.5.4.2: Renal function at presentation according to gender for IgA nephropathy, 2005-2008

eGFR (ml/min/1.73m^2)	Male		Female	
	n	%	n	%
≥90	29	28	35	29
60-89	19	18	36	30
30-59	30	29	29	25
15-29	14	13	11	9
<15	12	12	8	7
Total	104	100	119	100

CHAPTER 3

Secondary Glomerulonephritis

Rosnawati Yahya
Liew Yew Foong

3.1 Introduction

This chapter covers the main secondary glomerulonephritis that were reported to the MRRB from the years 2005-2008.

Lupus nephritis is the commonest secondary glomerulonephritis in adult contributing to almost 90% of all total secondary glomerulonephritis in Malaysia. Diabetic nephropathy contributed about 10%. Other causes of secondary glomerulonephritis is relatively uncommon (Table 3.1).

Table 3.1: Causes of secondary glomerulonephritis in adult, 2005-2008

Type of secondary GN	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Lupus nephritis	238	94	274	87	269	83	272	83	1053	86
Diabetic nephropathy	8	3	27	9	40	12	37	10	112	9
Post infectious GN	5	2	4	1	8	2	5	1	22	2
Systemic vasculitis	1	0	7	2	2	0	2	1	8	1
Unknown-Secondary	0	0	0	0	3	1	5	1	8	1
Other infection	0	0	1	0	1	0	5	1	7	1
HUS/TTP*	0	0	0	0	0	0	5	1	5	0
Multiple myeloma	0	0	1	0	2	1	1	0	4	0
Malignancy	0	0	0	0	1	0	1	0	2	0
Light/heavy chain disease	0	0	0	0	1	0	1	0	2	0
Henoch Schoenlein Purpura	0	0	0	0	0	0	0	0	0	0
Amyloidosis	0	0	0	0	0	0	0	0	0	0
Polyarteritis nodosa	0	0	0	0	0	0	0	0	0	0
Anti-GBM antibody disease	0	0	0	0	0	0	0	0	0	0
Immunotactoid glomerulopathy	0	0	0	0	0	0	0	0	0	0
Total	**253**	**100**	**314**	**100**	**327**	**100**	**334**	**100**	**1228**	**100**

* Hemolytic uraemic syndrome/Thrombotic thrombocytopenic purpura

3.2: Lupus Nephritis

3.2.1: Introduction

Lupus nephritis is the commonest secondary glomerulonephritis in Malaysia. This section dealt with lupus nephritis in adult population (defined as more than 15 years of age).

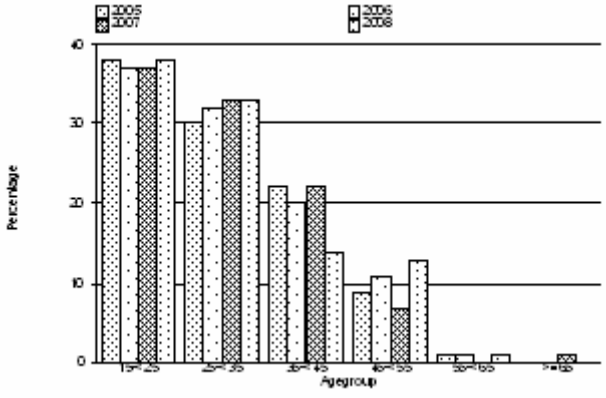
3.2.2: Patient population and characteristics

In the period of 1st January 2005 and 31st December 2008, there was a total of 1053 biopsy-proven lupus nephritis in 1004 patients were reported.

3.2.2.1: Age at time of biopsy

The mean age of adult patients with lupus nephritis at the time of biopsy was 30.3 ± 10.4 years (range: 15-70.4 years). The most predominant age group was between 15 to 25 years old, which accounted for 38% of cases. The onset of lupus above the age of 45 was uncommon and constituted about 10% of cases.

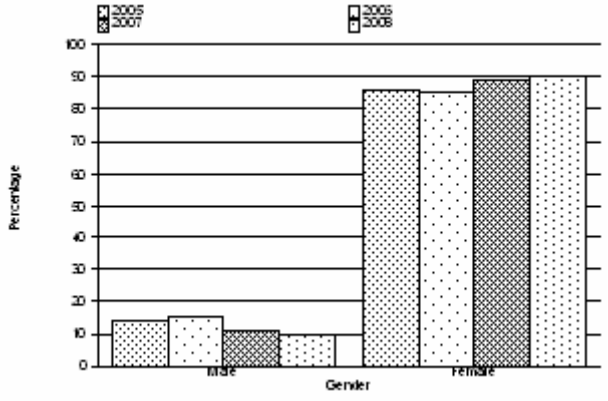
Figure 3.2.2.1: Age group at time of biopsy (years) in lupus nephriitis, 2005-2008.



3.2.2.2: Gender distribution

Lupus nephritis predominantly affects female with female: male ratio of 6.9:1.

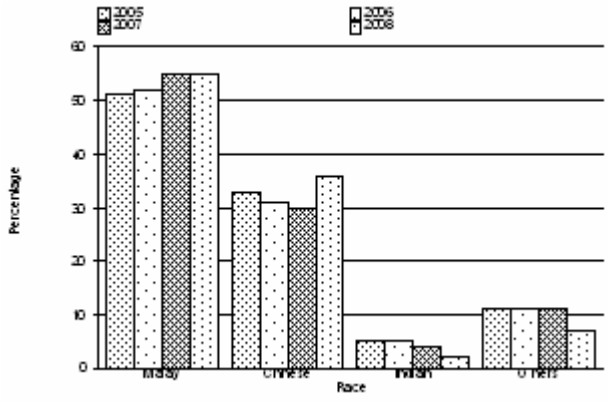
Figure 3.2.2.2: Gender distribution in lupus nephritis, 2005-2008



3.2.2.3: Racial prevalence

Fifty-three percent of patients with lupus nephritis were Malays, 32% were Chinese, 4% were Indian and 10% were of other races (mainly indigenous population of Malaysia).

Figure 3.2.2.3: Racial distribution in lupus nephriitis, 2005-2008



3.2.3: Clinical presentation

In adult patients with lupus nephritis, 38% presented with urine abnormalities, 11% with nephritic syndrome, 30% with nephrotic syndrome and 9% presented with a combination of nephritic and nephrotic picture. There has been an increased in incidence in the latter presentation in recent years. Data were missing in about 12% of cases (Table 3.2.3). At the time of presentation, 30-40 % had impaired renal function (defined by e-GFR by modified MDRD of less than 60 ml/min/1.72m^2). The incidence of hypertension increased almost two fold from 2007 to 2008 (Figure 3.2.3 (a) & (b)).

Table 3.2.3: Clinical presentation by year in lupus nephriitis, 2005-2008

Clinical Presentation	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Urine abnormality	98	41	114	42	97	36	92	34	401	38
Nephritic syndrome	26	11	27	10	29	11	29	11	111	11
Nephrotic syndrome	66	28	76	28	89	33	90	33	321	30
Nephrotic-nephritic syndrome	9	4	15	5	26	10	45	17	95	9
Missing	39	16	42	15	28	10	16	6	125	12
Total	**238**	**100**	**274**	**100**	**269**	**100**	**272**	**100**	**1053**	**100**

Figure 3.2.3 (a): Hypertension by year in lupus nephritis, 2005-2008

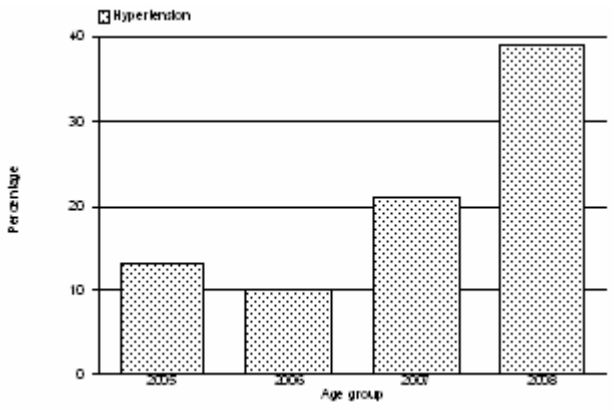
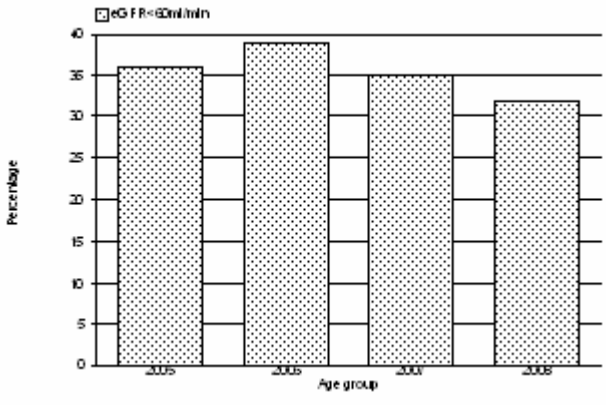


Figure 3.2.3 (b) Impaired renal function by year



3.2.3.1: Clinical Presentation by age

Urine abnormalities were the commonest clinical presentation of lupus nephritis in all age group. This was followed by nephrotic syndrome (Table & Figure 3.2.3.1(a)). The prevalence of hypertension was between 20-25% across all age groups (Figure 3.2.3.1(b)). The prevalence of impaired kidney function (e-GFR of < 60ml/min/1.73 m^2) was higher in older age groups (Figure 3.2.3.1(c)).

Table 3.2.3.1(a): Clinical presentation by age group, 2005-2008

Age group (years)	15- <25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Urine abnormality	137	35	133	39	86	42	38	37	5	72	2	50	401	38
Nephritic syndrome	42	10	41	12	20	10	6	6	1	14	1	25	111	11
Nephrotic syndrome	122	31	107	32	60	29	31	30	1	14	0	0	321	30
Nephrotic-nephritic	36	9	31	9	16	8	12	11	0	0	0	0	95	9
Missing	58	15	27	8	22	11	17	16	0	0	1	25	125	12
TOTAL	**395**	**100**	**339**	**100**	**204**	**100**	**104**	**100**	**7**	**100**	**4**	**100**	**1053**	**100**

Figure 3.2.3.1(a): Clinical presentation by age group, 2005-2008

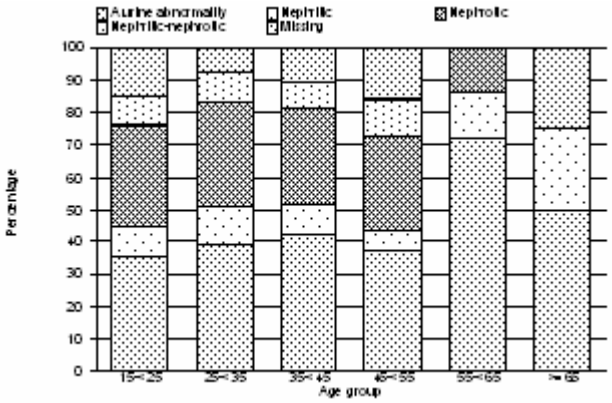


Figure 3.2.3.1(b): Hypertension by age group 2005-2008

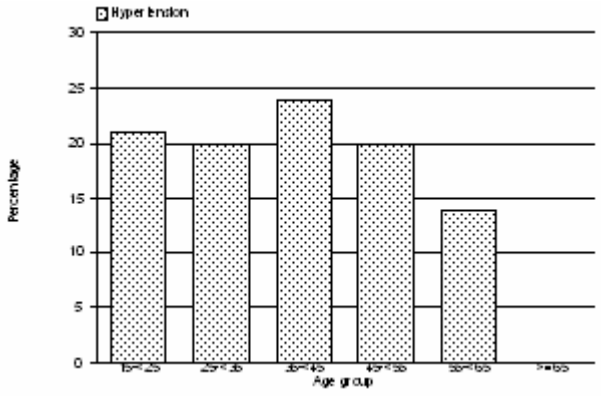
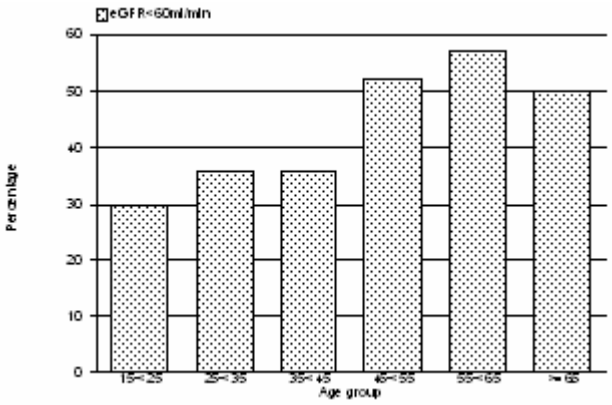


Figure 3.2.3.1(c): Impaired renal function by age group, 2005-2008



3.2.3.2: Clinical presentation by gender

There were no difference in the clinical presentation and proportion of patients with impaired renal function between the two genders (Figure 3.2.3.2 (a & c)). However, the prevalence of hypertension was higher in female (22%) than male (17%) (Figure 3.2.3.2 (b)).

Figure 3.2.3.2 (a): Clinical presentation by gender, 2005-2008.

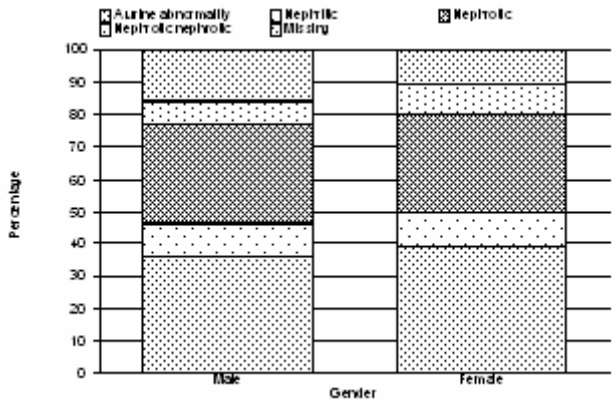


Figure 3.2.3.2(b): Hypertension by gender, 2005-2008.

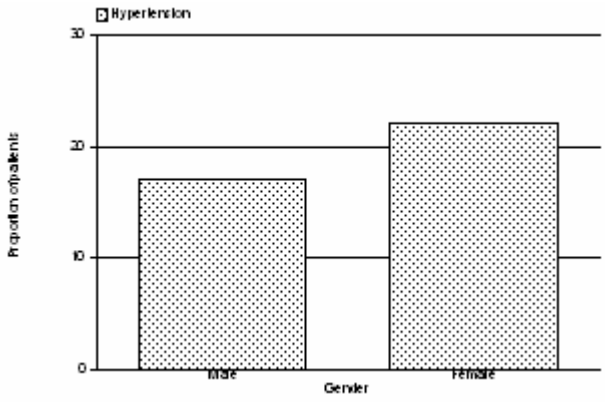
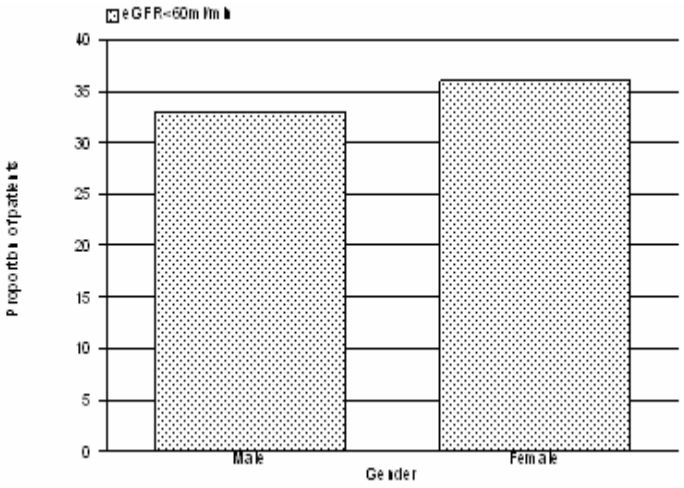


Figure 3.2.3.2(c): Impaired renal function by gender, 2005-2008.



3.2.3.3: Clinical Presentation by histopathology.

There were no clear correlation between histopathological findings and clinical presentation. However, class IV, class IV+V were more likely to present with symptomatic renal disease, with 57% had symptomatic renal disease at presentation. In comparison, those with class II, only 39% had symptomatic renal disease (Table & Figure 3.2.3.3 (a)). The prevalence of hypertension was higher in class IV & IV+V lupus nephritis (Figure 3.2.3.3(b)). The prevalence of impaired kidney function correlated with histopathological findings. The proportion of patients with e-GFR < 60 ml/min/1.72 m^2 were 44%, 22%, 25% and 9% in class IV or IV+V, class III or V+III, class V and class II respectively (Figure 3.2.3.3(c)).

Table 3.2.3.3 (a): Clinical presentation by histopathology in lupus nephritis, 2005-2008

Clinical Presentations	I		II		III & V+III		IV & IV+V		V & V+II		VI		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Urine abnormality	3	60	52	58	94	46	188	30	54	46	3	60	394	38
Nephritic syndrome	0	0	11	12	22	11	71	12	5	4	0	0	109	11
Nephrotic syndrome	2	40	17	19	55	27	206	33	39	33	1	20	320	31
Nephrotic–nephritic syndrome	0	0	7	8	9	4	71	12	5	4	0	0	92	9
Missing	0	0	3	3	25	12	77	13	14	13	1	20	120	11
Total	**5**	**100**	**90**	**100**	**205**	**100**	**613**	**100**	**117**	**100**	**5**	**100**	**1035**	**100**

* 18 cases are missing on lupus subclass

Figure 3.2.3.3 (a): Clinical presentation by histopathology in lupus nephritis, 2005-2008

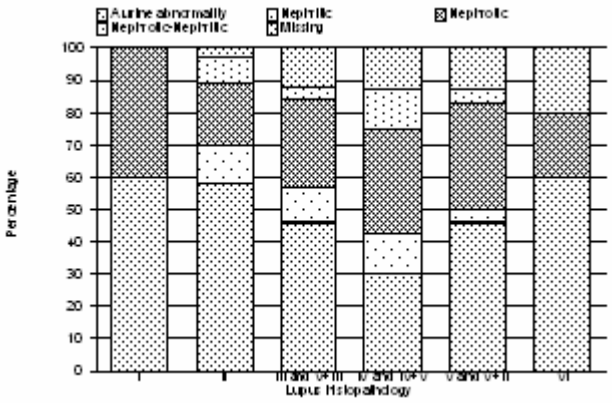


Figure 3.2.3.3(b) Hypertension by histopathology in lupus nephritis, 2005-2008

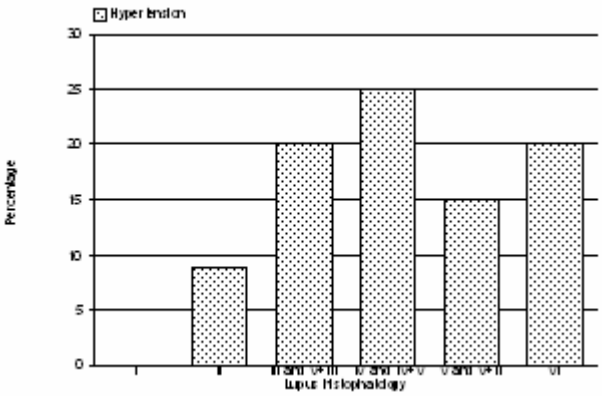
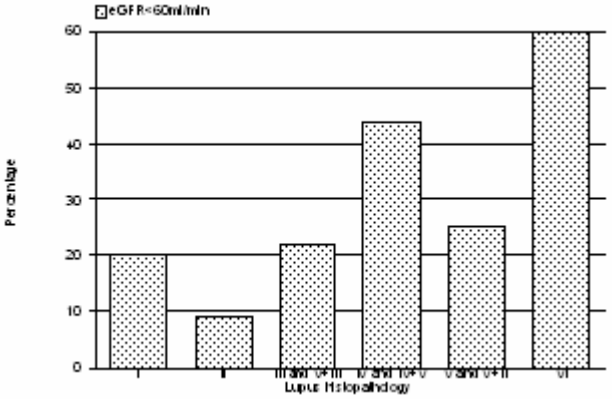


Figure 3.2.3.3(c): Impaired renal function by histopathology in lupus nephritis, 2005-2008



3.2.4: Renal function at presentation.

Thirty-six percent of all patients have impaired renal function (defined as e-GFR < 60ml/min/1.73 m^2) at the time of presentation. Five percent had e-GFR < than 15 ml/min (Table 3.2.4.1).

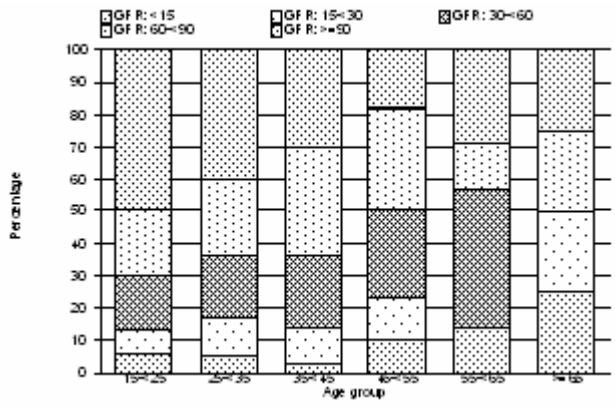
3.2.4.1: Renal function at presentation by age group

The frequency of impaired renal function increases after the age of 35. Between 36-39% has eGFR less than 60 ml/min below the age of 35 and rises to 43% in the age group of 35 to 45 and 53% in age group of 45 to 55 (Table & Figure 3.2.4.1).

Table 3.2.4.1: Renal function by age group in lupus nephritis, 2005-2008

e-GFR (ml/min/1.73m^2)	15 ≤ 25		25 ≤ 35		35 ≤ 45		45 ≤ 55		55 ≤ 65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<15	22	6	17	5	6	3	10	10	1	14	1	25	57	5
15 to < 30	29	7	40	12	22	11	13	13	0	0	1	25	105	10
30 to < 60	67	17	65	19	45	22	30	28	3	43	0	0	210	21
60 to < 90	81	21	82	24	69	34	32	31	1	14	1	25	266	25
> 90	196	49	135	40	62	30	19	18	2	29	1	25	415	39
Total	**395**	**100**	**339**	**100**	**204**	**100**	**104**	**100**	**7**	**100**	**4**	**100**	**1053**	**100**

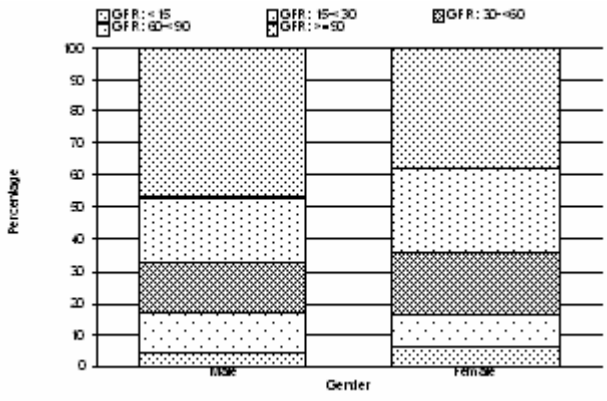
Figure 3.2.4.1: Renal function by age group in lupus nephritis, 2005-2008



3.2.4.2: Renal function at presentation by gender

There were no differences in the renal function at presentation between the two genders (Figure 3.2.4.2).

Figure 3.2.4.2: Renal function at presentation by gender in lupus nephritis, 2005-2008



3.2.4.3: Renal function at presentation by histopathology

In the proliferative lupus nephritis (class III, IV, V+III and V+IV), class IV and V+IV have worse renal function than class III or class V+III (Table 3.2.4.3).

Table 3.2.4.3: Renal function at presentation in lupus nephritis by histopathology, 2005-2008

e-GFR (ml/min/1.73m^2)	I		II		III and V+III		IV and IV+V		V and V+II		VI		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<15	0	0	0	0	5	2	39	6	3	3	1	20	48	5
15 to <30	0	0	2	2	11	5	80	13	9	8	1	20	103	10
30 to <60	1	20	6	7	30	15	155	25	16	14	1	20	209	20
60 to <90	0	0	28	31	60	30	146	25	30	25	1	20	265	26
> 90	4	80	54	60	99	48	193	31	59	50	1	20	410	39
Total	**5**	**100**	**90**	**100**	**205**	**100**	**613**	**100**	**117**	**100**	**5**	**100**	**1035**	**100**

18 cases are missing on lupus subclass

3.2.5: Histopathological diagnosis

There were a total of 1053 adult biopsies with a diagnosis of lupus nephritis. Data on the lupus subclass were incomplete in 18 cases. The distribution of histopathological class based on WHO or ISN/RPS classification is summarized in table 3.2.5. Class IV and IV+V are the predominant biopsy findings accounting for 59% of patients diagnosed with lupus nephritis, followed by class III and III+V which contributes about 20%. There were very few class I and VI lupus nephritis reported to the registry.

Table 3.2.5.: Histopathological diagnosis in lupus nephritis by year, 2005-2008

WHO or ISN/ RPS classification	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
Class I	1	0	1	0	1	0	2	1	5	0
Class II	27	12	14	5	29	11	20	7	90	9
Class III and V+III	38	16	59	22	51	19	57	21	205	20
Class IV and IV+V	135	58	165	62	149	56	164	61	613	59
Class V and V+II	32	14	30	11	32	13	23	9	117	12
Class VI	1	0	0	0	2	1	2	1	5	0
Total	**234**	**100**	**269**	**100**	**264**	**100**	**268**	**100**	**1035**	**100**

* 18 cases are missing on lupus subclass

3.2.5.1: Histopathological diagnosis by age

In adults, class IV or V+IV were the most predominant lesion in all age groups. However, the frequency of class IV and IV+V were less with increasing age (Table 3.2.5.1).

Table 3.2.5.1: Histopathological diagnosis by age group in lupus nephritis, 2005-2008

Histopathology	15 to <25		25 to <35		35 to <45		45 to <55		55 to <65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Class I	3	1	0	0	0	0	1	1	1	13	0	0	5	0
Class II	38	10	31	9	15	7	6	6	0	0	0	0	90	9
Class III or V+III	72	19	74	22	40	20	16	16	2	29	1	33	205	20
Class IV or IV+V	237	60	202	60	120	59	50	50	2	29	2	67	613	60
Class V and V+II	34	9	29	9	25	13	27	27	2	29	0	0	117	11
Class VI	2	1	1	0	2	1	0	0	0	0	0	0	5	0
Total	**386**	**100**	**337**	**100**	**202**	**100**	**100**	**100**	**7**	**100**	**3**	**100**	**1035**	**100**

* 18 cases are missing on lupus subclass

3.2.5.2: Histopathological diagnosis by gender

Class IV and IV+V was the commonest histopathological finding in both genders. Class IV or IV+V occurred in higher frequency in females, whereas class V occurred in higher frequency in males (Table 3.2.5.2).

Table 3.2.5.2: Histopathological diagnosis by gender in lupus nephritis, 2005-2008

Histopathology	Male		Female		Total	
	n	%	n	%	n	%
Class I	1	1	4	0	5	0
Class II	9	7	81	9	90	9
Class III or V+III	31	22	174	19	205	20
Class IV or IV+V	69	52	544	60	613	59
Class V or V+II	22	17	95	12	117	12
Class VI	1	1	4	0	5	0
Total	**133**	**100**	**902**	**100**	**1035**	**100**

*18 cases are missing on lupus subclass

3.2.5.3: Histopathological diagnosis by clinical presentation

Urine abnormalities were the most common clinical presentation, followed by nephrotic syndrome. Seventy-seven percent with nephritic-nephrotic, 64% with nephrotic syndrome and 63% with nephritic syndrome had class IV or class V+IV lupus nephritis. However, 48% with urine abnormalities alone also had class IV or class V+IV (Table 3.2.5.3).

Table 3.2.5.3: Histopathological diagnosis by clinical presentation in lupus nephritis, 2005-2008

Histopathology	Urine abnormality		Nephritic		Nephrotic		Nephritic-nephrotic		Missing		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
I	3	1	0	0	2	1	0	0	0	0	5	0
II	52	13	11	10	17	6	7	8	3	3	90	9
III and III + V	94	23	22	20	55	17	9	10	25	20	205	20
IV and IV+V	188	48	71	65	206	64	71	77	77	64	613	59
V and V+II	54	14	5	5	39	12	5	5	14	12	117	12
Class VI	3	1	0	0	1	0	0	0	1	1	5	0
Total	**394**	**100**	**109**	**100**	**320**	**100**	**92**	**100**	**120**	**100**	**1035**	**100**

*18 cases are missing on lupus subclass

3.2.6: Extra-renal involvement

3.2.6.1: American Rheumatological Association (ARA) criteria in lupus nephritis.

About 2/3 of cases of lupus nephritis fulfilled 4 or more ARA criteria at the time of presentation (Table 3.2.6.1).

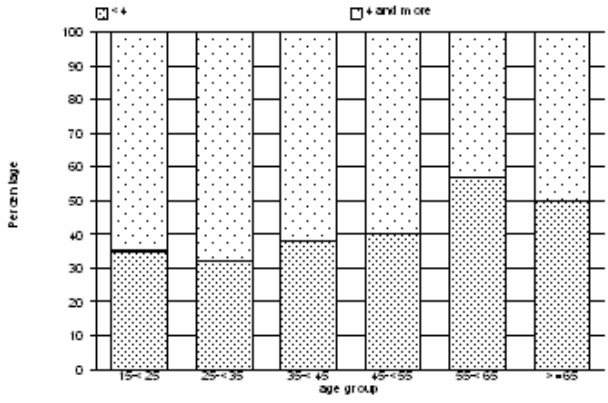
Table 3.2.6.1: ARA criteria in lupus nephritis, 2005-2008

Number of ARA criteria	2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%
<4	81	34	93	34	100	37	97	36	371	35
4 and more	157	66	181	66	169	63	175	64	682	65
Total	**238**	**100**	**274**	**100**	**269**	**100**	**272**	**100**	**1053**	**100**

3.2.6.2: ARA criteria in lupus nephritis by age

In patients less than 55 years of age, about 2/3 satisfied the ARA criteria for the diagnosis of SLE. There were only 11 patients aged 55 years and above (Figure 3.2.6.2).

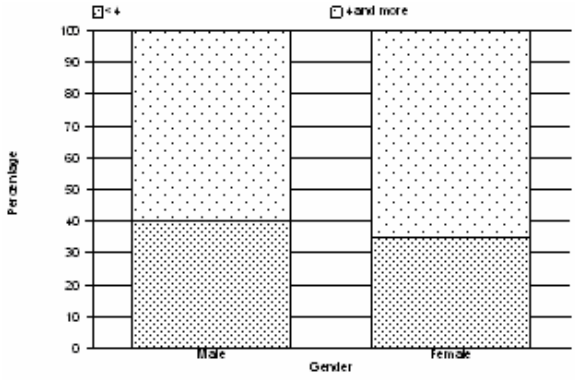
Figure 3.2.6.2: ARA criteria by age group in lupus



3.2.6.3: ARA criteria by gender

The proportion of patients that fulfilled 4 or more ARA criteria at the time of presentation is slightly more in female than male (65% versus 60%) (Figure 3.2.6.3).

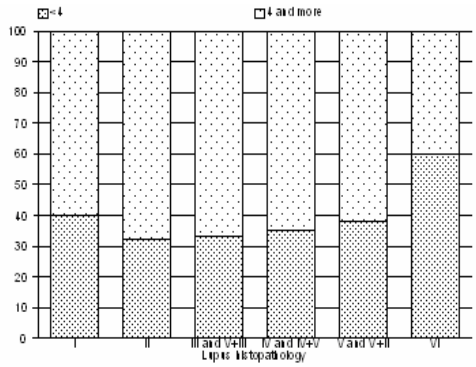
Figure 3.2.6.3: ARA criteria by gender in lupus



3.2.6.4: ARA criteria by histopathological findings

Fulfilling ARA criteria does not predict the severity of renal lesion in lupus nephritis.

Figure 3.2.6.4: ARA criteria by histopathology in lupus



3.2.6.5: Extra-renal involvement

In patients with lupus nephritis, 56% had mucocutaneous involvement, 35% had arthritis, 9% had serositis, 12% had cerebral involvements and 43% had haematological involvements (Table 3.2.6.5(a)). Mucocutaneous involvement, serositis and especially arthritis were more common in females than in males. Neurological and haematological involvements were slightly more common in males (Table & Figure 3.2.6.5 (a)).

Of those with mucocutaneous involvement, the frequency of discoid rash was higher in male and there was no difference in the frequency of malar rash, photosensitivity or oral ulcers between the two genders (Table & Figure 3.2.6.5 (b)).

Table 3.2.6.5 (a): Extra-renal involvement by gender in lupus nephritis, 2005-2008

Other organ involvement	Male (n=134)		Female (n=919)		Total (n=1053)	
	n	%	n	%	n	%
Mucocutaneous	71	53	518	56	589	56
Arthritis	28	21	345	38	373	35
Serositis	11	8	88	10	99	9
Cerebral	22	16	109	12	131	12
Haematological	61	46	391	43	452	43
Total	**193**		**1451**		**1644**	

* Patients may have 1 or more "other organ involvements"

Figure 3.2.6.5 (a): Extra-renal involvement by gender in lupus nephritis, 2005-2008

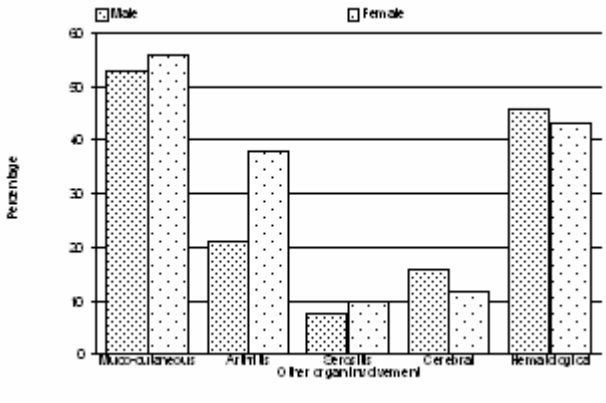
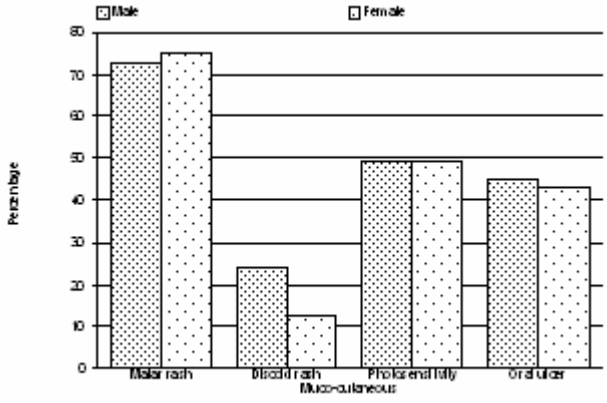


Table 3.2.6.5 (b): Mucocutaneous involvement by gender in lupus nephritis, 2005-2008

Mucocutaneous involvements	Male (n=71)		Female (n=518)		Total (n=589)	
	n	%	n	%	n	%
Malar rash	52	73	387	75	439	75
Discoid rash	17	24	64	12	81	14
Photosensitivity	35	49	256	50	291	50
Oral ulcer	32	45	221	43	253	43
Total	**136**		**928**		**1064**	

Figure 3.2.6.5 (b): Mucocutaneous involvement by gender in lupus nephritis, 2005-2008



3.2.7 Survival in lupus nephritis

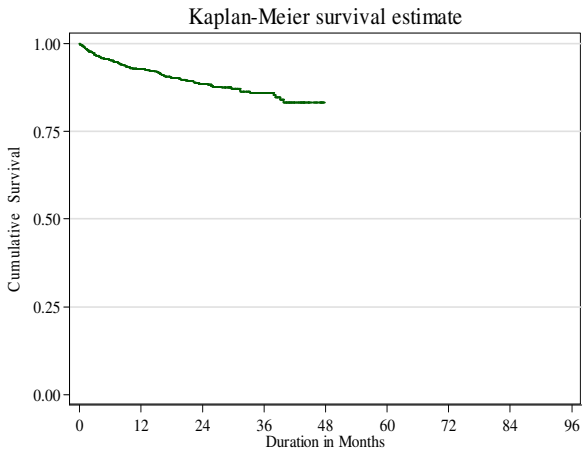
3.2.7.1 Patient survival in lupus nephritis

Table & Figure 3.2.7.1 shows that patient survival was 92.8% at 1 year and 85.9% at 3 years from the time of renal biopsy.

Table 3.2.7.1: Patient survival in lupus nephritis, 2005-2007

Interval (months)	SLE patients survival		
	n	% survival	SE
0	991	100	-
12	642	92.8	0.01
24	381	88.5	0.01
36	173	85.9	0.01
48	2	.	.
60	2	.	.
72	2	.	.
84	2	.	.
96	2	.	.

Figure 3.2.7.1: Patient survival in lupus nephritis, 2005-2007



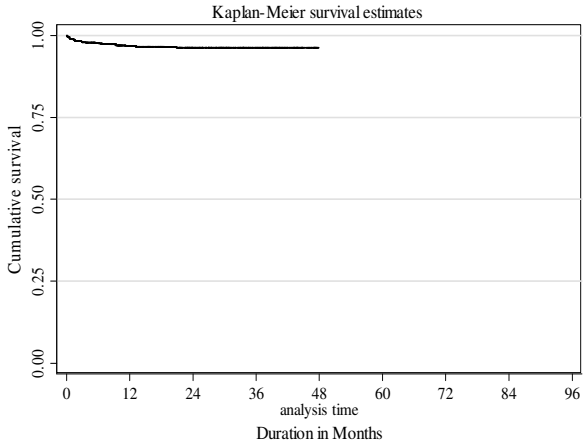
3.2.7.2: Renal survival in lupus nephritis

Table & Figure 3.2.7.2 shows that renal survival was 96.8% at 1 year and 96.2% at 3 years from the time of renal biopsy.

Table 3.2.7.2: Renal survival **in lupus nephritis** , 2005-2007

Interval (months)	Renal survival		
	n	% survival	SE
0	829	100	-
12	578	96.8	0.01
24	354	96.2	0.01
36	163	96.2	0.01
48	2	.	.
60	2	.	.
72	2	.	.
84	2	.	.
96	2	.	.

Figure 3.2.7.2: Renal survival **in lupus nephritis** , 2005-2007



CHAPTER 4

Paediatric Renal Biopsies

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4.1 Introduction

This chapter reports on renal biopsies done in children less than 15 years of age in Malaysia. Data on native kidney biopsies was collected from 1999 to 2008 in Department of Paediatric Hospital Kuala Lumpur and from 2005 to 2008 for other hospitals.

4.2: Number of patients and renal biopsies

4.2.1: Total number of patients and native renal biopsies

The Registry recorded the diagnosis and clinical data of 809 renal biopsies in 755 children.

4.2.2: Number of patients from various hospitals

The majority of renal biopsies were performed in the Ministry of Health hospitals (Table 4.2.2).

Table 4.2.2: Number of patients from various hospitals

Hospitals	n	%
Hospital Kuala Lumpur	350	46
Other MOH Hospitals	398	53
University Hospital	4	1
Army Hospital	1	0
Private Hospital	2	0
Total number of patients	**755**	**100**

4.2.3: Number of native renal biopsies

With the establishment of Malaysia Renal Biopsies Registry (MRRB) in 2005, more data on renal biopsies were submitted. A total of 164 renal biopsies were performed in 2008 (Table 4.2.3).

Table 4.2.3: Number of renal biopsies

Year	n
1999	44
2000	34
2001	31
2002	31
2003	57
2004	39
2005	128
2006	135
2007	146
2008	164
Total	**809**

4.2.4: Number of renal biopsy done on each individual patient

In the paediatric biopsy group, from 1999-2008, 755 patients had renal biopsy done. 666 patients had renal biopsy for the first time, 69 patients had biopsy done twice, 19 patients had biopsy done thrice and 1 patient had four or more biopsy. Therefore about 12% of patients had a repeat native biopsy done (Table 4.2.4).

Table 4.2.4: Distribution of native renal biopsy in patients by number of attempts

Total number of biopsy per patient	n	%
1st episode	666	88
2nd episode	69	9
3rd episode	19	3
>4th episode	1	0
Total no of Patient	**755**	**100**

4.3 Outcome of renal biopsies

4.3.1: Adequacy of renal biopsy for diagnosis

Altogether 770 (95.2%) renal biopsies were assessed to be adequate for diagnosis upon review by nephrologists and histopathologists. A total of 39 (4.8%) biopsies were not conclusive (Table 4.3.1). Thailand, United Kingdom and Japan reported success rates of between 93.4% and 98.7 [1,2,3] . Thus the success rate in the present report is comparable with figures reported by other centers.

Table 4.3.1: Conclusive report

Year	Total number of biopsies	Report conclusive		Report not conclusive	
		n	%	n	%
1999 -2008	809	770	95.2	39	4.8

4.3.2: Number of glomeruli obtained at each biopsy

621 (77.2%) of the biopsies yielded 10 or more glomeruli. The remaining 22.8% reported less than 10 glomeruli (Table 4.3.2).

Table 4.3.2: Number of glomeruli obtained at each biopsy

Year	Total number of biopsies	≥ 10 Glomeruli		< 10 Glomeruli	
		n	%	n	%
1999 -2008	804	621	77.2	183	22.8

* 5 cases with missing number of glomeruli

4.4: Patient characteristics

Table 4.4.1 shows that renal biopsies were performed on 363 (48.1%) boys and 392 (51.9%) girls. The higher number in girls was probably attributed to biopsies among children with systemic lupus erythematous. The mean age at biopsy was 9.4 ± 3.9 years. The racial distribution of the patients was Malay 61.7%, Chinese 19.2%, Indian 7.7% and other ethnic groups 11.4%.

Table 4.4.1: Gender and racial distribution

		n	%
Gender	Male	363	48.1
	Female	392	51.9
	Total	**755**	**100**
Race	Malay	466	61.7
	Chinese	145	19.2
	Indian	58	7.7
	Others	86	11.4
	Total	**755**	**100**

4.5: Clinical presentation

4.5.1: Clinical presentation at biopsy

Nephrotic syndrome was the most frequent clinical presentation accounting for 52.9%. The second commonest indication for performing renal biopsy was nephritic syndrome, which contributed to 14% of cases (Table 4.5.1).

Table 4.5.1: Clinical presentation at biopsy

Clinical presentation	n	%
Asymptomatic urine abnormalities	107	13.2
Nephritic syndrome	113	14
Nephrotic syndrome	428	52.9
Nephritic nephrotic syndrome	69	8.5
Unknown	86	10.6
Missing	6	0.7
Total	**809**	**100**

4.5.2: Renal function at biopsy

Thirty percent of biopsies were performed in the setting of impaired renal function (Table 4.5.2 (a)). Majority of these children had acute kidney injury (59.2%) (Table 4.5.2 (b)).

Table 4.5.2 (a): Renal function at biopsy

Renal function at biopsy	n	%
Impaired	245	30.3
Normal	514	63.5
Not available or missing data	50	6.2
Total	**809**	**100**

Table 4.5.2 (b): Renal impairment at biopsy

Impaired renal function	n	%
Acute	145	59.2
Chronic	96	39.2
Unknown	4	1.6
Total	**245**	**100**

4.5.3 Hypertension at biopsy

About 29% of patients were hypertensive. The most frequent use antihypertensive drug was calcium channel blocker.

Table 4.5.3: Hypertension at biopsy

Hypertension At biopsy	n	%
Present	234	28.9
Absent	565	69.8
Not available or missing data	10	1.2
Total	**809**	**100**
Drug [a]		
ACEI	46	15
Alpha Blocker	18	6
ARB	3	1
B Blocker	22	7
Calcium Channel Blocker	76	25
No drug available	138	46
Total	**303**	**100**

[a] A patient may have more than 1 type of drug

4.6: Diagnosis of paediatric renal biopsies

Lupus nephritis contributed the largest group at 24.8%. This was followed by focal segmental glomerulosclerosis (FSGS) (24.6%). Minimal change disease (MCD) was diagnosed in 17.2% of cases and post-infectious glomerulonephritis (GN) in 9.1%. IgA nephropathy accounted for 4.8% and Henoch Schonlein Purpura 3.1% (Table 4.6).

Table 4.6: Diagnosis of paediatric renal biopsies

	Diagnosis	n	%
1	Lupus nephritis	201	24.8
2	FSGS	199	24.6
3	MCD	139	17.2
4	Post-infectious GN	74	9.1
5	IgA nephropathy	39	4.8
6	Henoch Schonlein Purpura	25	3.1
7	Mesangial proliferative GN non-IgA	18	2.2
8	Advanced glomerulosclerosis	17	2.1
9	HUS/TTP	6	0.7
10	Membranoproliferative GN	8	1
11	Acute tubular necrosis	8	1
12	Vasculitis	5	0.6
13	Membranous nephropathy	6	0.7
14	Chronic interstitial nephritis	3	0.4
15	Acute interstitial nephritis	2	0.2
16	Alport's syndrome	2	0.2
17	Hereditary(others)	1	0.1
18	Malignancy	1	0.1
19	Crescentic GN	1	0.1
20	Idiopathic crescentic ANCA	4	0.5
21	Others	2	0.2
22	Unknown	48	5.9
	Total	**809**	**100**

4.7: Nephrotic syndrome

4.7.1: Renal histopathology diagnosis of children presenting with nephrotic syndrome

Nephrotic syndrome was the clinical diagnosis in 428 biopsies. As shown in Table 4.7.1, FSGS was found in 41.8% and MCD in 28.7%.

Table 4.7.1: Renal histopathology diagnosis of children presenting with nephrotic syndrome

Diagnosis	n	%
FSGS	179	41.8
MCD	123	28.7
Lupus nephritis	64	15
IgA nephropathy	10	2.3
Mesangial proliferative GN non-IgA	11	2.6
Post-infectious GN	6	1.4
Others*	19	4.4
Unknown	16	3.7
Total	**428**	**100**

* (membranous nephropathy, membranoproliferative GN, Henoch Schonlein Purpura, HUS/TTP, vasculitis, hereditary renal disease, acute interstitial nephritis, chronic interstitial nephritis, advance glomerulosclerosis)

4.7.2: The histopathological profile in different steroid response categories

At biopsy, the clinical response to steroid treatment in children with nephrotic syndrome was recorded. 24.1% (47/ 195) were steroid responsive. Majority of patient with steroid responsive nephrotic syndrome had MCD (44.7%). This was followed by FSGS (31.9%). Among children with steroid resistant syndrome, FSGS was the most common underlying renal pathology (Table 4.7.2).

Table 4.7.2: The histopathological profile in different steroid response categories

Diagnosis	Steroid responsive		Steroid resistant	
	n	%	n	%
FSGS	15	31.9	85	57.4
MCD	21	44.7	28	18.9
Lupus nephritis	4	8.5	6	4.1
IgA nephropathy	0	0.0	2	1.4
Mesangial proliferative GN non-IgA	1	2.1	6	4.1
Post-infectious GN	6	12.8	6	4.1
Others*	0	0.0	9	6.1
Unknown	0	0.0	6	4.1
Total	**47**	**100.0**	**148**	**100.0**

* (membranous nephropathy, membranoproliferative GN, crecentic GN, Henoch Schonlein Purpura, HUS/TTP, vasculitis, hereditary renal disease, acute interstitial nephritis, chronic interstitial nephritis, advanced glomerulosclerosis)

4.8: Renal histopathology diagnosis of children presenting with nephritic syndrome

Renal biopsy was performed in 113 children with nephritic syndrome. The majority demonstrated post-infectious GN (36.3%), while the others had lupus nephritis (30.1%), IgA nephropathy (6.2%) and Henoch Schonlein Purpura (5.3%) (Table 4.8).

Table 4.8: Renal histopathology diagnosis of children presenting with nephritic syndrome

Diagnosis	n	%
Post-infectious GN	41	36.3
Lupus nephritis	34	30.1
IgA nephropathy	7	6.2
Henoch Schonlein Purpura	6	5.3
FSGS	5	4.4
MCD	3	2.7
Messangial proliferative	3	2.7
Acute tubular necrosis	3	2.7
Others*	3	2.7
Unknown	8	7.1
Total	**113**	**100**

* (Systemic vasculitis, Idiopathic crescentic, Alport's syndrome)

4.9: Causes of acute renal failure

The causes of acute renal failure were post-infectious GN (26.2%), lupus nephritis (26.2%) and FSGS (9.7%). 4.8% of children thought to have acute renal failure were found to have advanced glomerulosclerosis on biopsy (Table 4.9).

Table 4.9: Causes of acute renal failure in children who underwent renal biopsy

Diagnosis	n	%
Post-infectious GN	38	26.2
Lupus nephritis	38	26.2
FSGS	14	9.7
Advanced glomerulosclerosis	7	4.8
HUS/TTP	6	4.1
Acute tubular necrosis	6	4.1
MCD	5	3.4
Acute interstitial nephritis	3	2.1
IgA nephropathy	3	2.1
Others*	12	8.3
Unknown	13	9
Total	**145**	**100**

*(membranoproliferative GN, mesangial proliferative GN non-IgA, crescentic, Idiopathic crescentic GN, Henoch scholein purpura, vasculitis, malignancy)

4.10: Paediatric focal segmental glomerulosclerosis and minimal change disease

4.10.1: Characteristics of paediatric focal segmental glomerulosclerosis and minimal change disease among children with steroid resistant nephrotic syndrome

There was no difference in terms of age at presentation, race and gender in children with FSGS or MCD. The urine albumin excretion and creatinine clearance at biopsy was similar (Table 4.10.1).

Table 4.10.1: Clinical characteristics of children with steroid resistant nephrotic syndrome

Clinical characteristics	FSGS	MCD	p value
n	85 (75.22%)	28 (24.78%)	0.4311
Mean age (year)	7.4	6.7	0.4311
Median age (year)	7.5	6.2	
Race			
Malay	59(69.41%)	16(57.14%)	
Chinese	8(9.41%)	6(21.43%)	
Indian	9(10.59%)	3(10.71%)	
Others	9(10.59%)	3(10.7%)	
Total	85	28	0.3883
Gender			
Boy	48(56.47%)	20(71.43%)	
Girl	38(28.57%)	8(28.57%)	0.1612
Gross haematuria			
Present	1(1.18%)	1(3.57%)	
Absent	36(42.35%)	14(50%)	
Not available	48(56.47%)	13(46.43%)	0.3563
Hypertension			
Present	25(29.41%)	6(21.43%)	
Absent	60(70.59%)	22(78.57%)	0.4122
Family history			
Yes	2(2.35%)	1(3.57%)	
No	79(92.94%)	26(92.86%)	
Unknown/ missing	4(4.71%)	1(3.57%)	0.2583
eGFR ml/min/1.73m²			
GFR <30	4(4.71%)	0 (0%)	
GFR 30-60	14(16.47%)	2(7.14%)	
GFRl 60-90	8(9.41%)	4(14.29%)	
GFR > 90	59(69.41%)	22(78.57%)	0.344
Dialysis required			
Yes	1(1.18%)	0(0%)	
No	80(94.12%)	26(92.86%)	
Unknown	4(4.71%)	2(7.14%)	0.7283

Table 4.10.1: Clinical characteristics of children with steroid resistant nephrotic syndrome (cont.)

Clinical characteristics	FSGS	MCD	p value
24HUP g (n, mean)	n=26, 3.73	n=5, 1.75	
Urine albumin mg /m²/H (n, mean)	n=23, 197.7	N=4, 145.1	0.6355
Albumin g/L (n, mean)	n=81, 21.04	n=27,25.56	0.4575
Histology			
Tubulointerstitial disease			
Yes	4 (4.71%)	1(3.57%)	
No	81(95.29%)	27(96.43%)	0.8002

1 Mann Whitney test , 2 Pearson Chi^2, 3 Fisher Exact , 4 Test of proportion
** Calculated Glomerular filtration rate (ml/min/1.73m²) base on Schwartz Formula

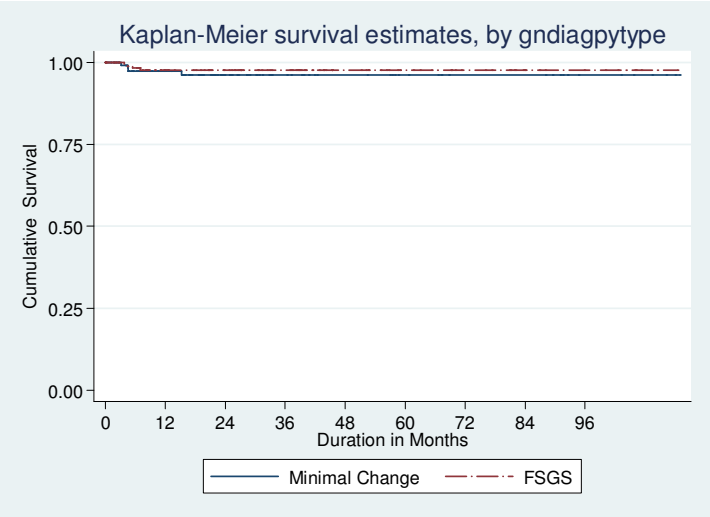
4.10.2: Patient survival in focal segmental glomerulosclerosis and minimal change disease

Table & Figure 4.10.2 shows that patient survival was similar for both MCD and FSGS; 96-97% at 3 years and 5 years from the time of renal biopsy.

Table 4.10.2: Patient survival for focal segmental glomerulosclerosis and minimal change disease

Interval (months)	Minimal change disease			FSGS		
	n	% survival	SE	n	% survival	SE
0	127	100	-	190	100	-
12	92	97.4	0.02	141	97.6	0.01
24	47	96.1	0.02	108	97.6	0.01
36	31	96.1	0.02	78	97.6	0.01
48	23	96.1	0.02	52	97.6	0.01
60	18	96.1	0.02	40	97.6	0.01
72	13	96.1	0.02	30	97.6	0.01
84	13	96.1	0.02	18	97.6	0.01
96	7	96.1	0.02	14	97.6	0.01

Figure 4.10.2: Patient survival by focal segmental glomerulosclerosis and minimal change disease



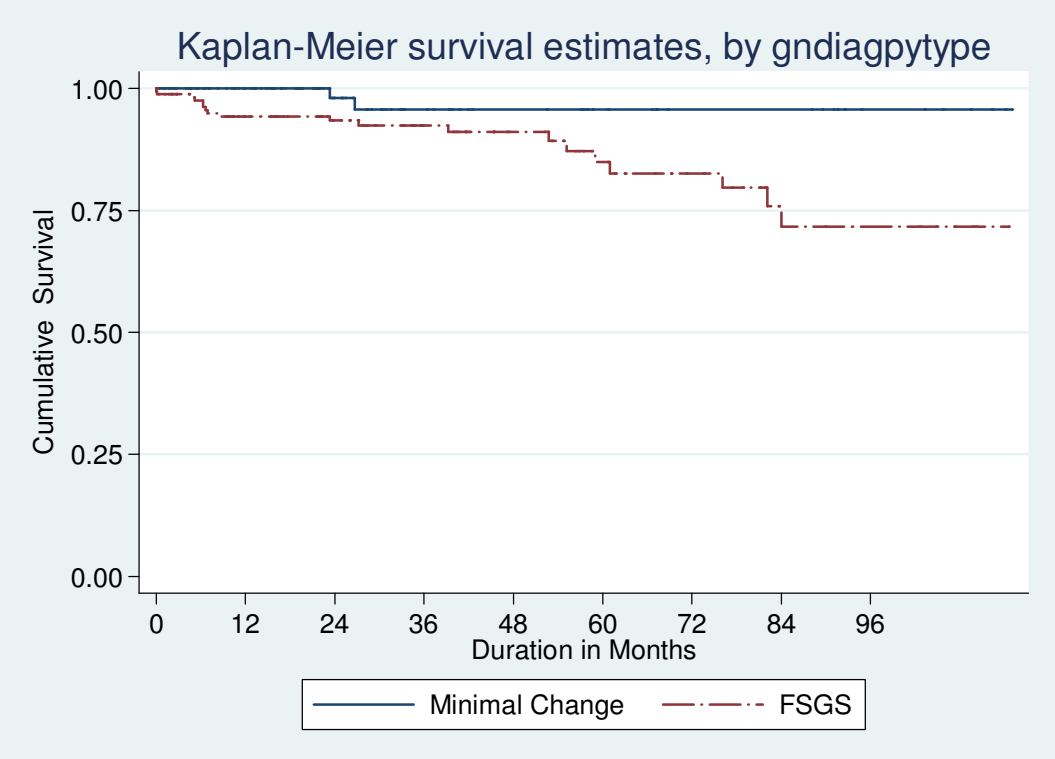
4.10.3: Renal survival of patient with focal segmental glomerulosclerosis and minimal change disease

The renal survival data was extracted from the Malaysia Dialysis Transplant Registry. Table 4.10.3 and Figure 4.10.3 show that FSGS has poorer renal survival; 92.4% and 84.6% at 3 years and 5 years respectively. Renal survival for MCD at 3 years and 5 years remained at 95.7%.

Table 4.10.3: Renal survival of patient with focal segmental glomerulosclerosis and minimal change disease

Interval (days)	Minimal change disease			FSGS			
	n	% survival	SE	n	% survival	SE	p-value
0	115	100	-	170	100	-	0.012
12	86	100	-	131	94.3	0.89	
24	47	98.0	0.02	103	93.4	0.88	
36	31	95.7	0.03	75	92.4	0.87	
48	23	95.7	0.03	49	91.0	0.84	
60	18	95.7	0.03	38	84.6	0.74	
72	13	95.7	0.03	29	82.3	0.70	
84	13	95.7	0.03	17	70.8	0.53	
96	7	95.7	0.03	14	70.8	0.53	

Figure 4.10.3: Renal survival by focal segmental glomerulosclerosis and minimal change



4.11: Paediatric Lupus Nephritis

4.11.1: Total number of patients and renal biopsies

There were 204 renal biopsies performed for 182 children with lupus.

4.11.2: Number of renal biopsy done on each individual patient with lupus

154 patients had renal biopsy for the first time. About 15% of patients had a repeat native biopsy done (Table 4.11.2).

Table 4.11.2: Distribution of renal biopsy in patient with lupus by number of episodes / attempts

Total number of biopsy per patient	n	%
1st episode	154	85
2nd episode	24	13
3rd episode	4	2
>4th episode	0	0
Total Patient	**182**	**100**

4.11.3: Patient characteristics of paediatric lupus nephritis

The female: male ratio was 6.3:1 reflecting the preponderance of lupus in females. The racial distribution for paediatric lupus nephritis was Malay (61%), Chinese (26.4%), Indian (4.9%) and others (7.7%). The mean age of children with lupus nephritis at the time of biopsy was 11.5 ± 2.8 years.

4.11.4: Extra renal manifestation of paediatric SLE

The most common extra renal manifestations among 180 children were cutaneous involvement (malar rash in 63.3%, photosensitivity in 38.9%, oral ulcers in 28.9% and discoid rash in 5%. This was followed by haematological involvement in 60.6%, joint involvement in 26.7%, serositis in 13.3% and cerebral involvement in 13.3% (Table 4.11.4(a)).

In Hong Kong, prolonged fever was the most common extrarenal manifestation (55%). Fever was unfortunately not captured in our database. The other common features were malar rash, polyarthritis and haematological involvement [4]. 160 cases (78%) fulfilled 4 or more ARA criteria at presentation (Table 4.11.4(b)).

Table 4.11.4(a): Clinical presentation of paediatric lupus

Clinical presentation	n	%
Total number of patient	180	100
Malar rash	114	63.3
Discoid rash	9	5
Photosensitivity	70	38.9
Oral ulcers	52	28.9
Arthritis	48	26.7
Serositis	24	13.3
Cerebral	24	13.3
Hematological	**109**	**60.6**

Table 4.11.4(b): ARA criteria at presentation

Number of ARA criteria	n	%
<4	44	22
≥ 4	160	78
Total	**204**	**100**

4.11.5: Classification of paediatric lupus nephritis

All renal biopsies were reviewed and classified according to WHO or ISN/RPS Classification. Class-IV or V+IV lupus Nephritis was found in 131 (64.2%) patients. Less frequent findings were class-III or V+III (16.7%), II (7.4%), V or V+II (6.4%) and VI (1%) lupus nephritis. (Table 4.11.5)

Hong Kong reported 54% in class IV.[4] Thailand reported 48.8% in class IV and 30.5% in class II. [5]

Table 4.11.5: Classification of paediatric lupus nephritis

WHO/ISN /RPS Class	n	%
Class I	0	0
Class II	15	7.4
Class III or V+III	34	16.7
Class IV or V+IV	131	64.2
Class V or V+II	13	6.4
Class VI	2	1
Unknown	9	4.4
Total	204	100

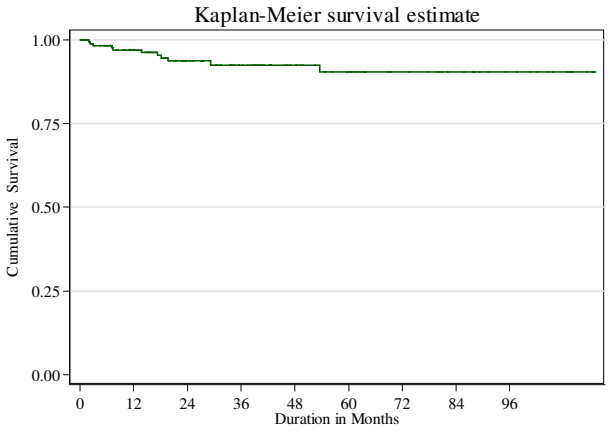
4.11.6: Patient survival in lupus nephritis

Table & Figure 4.11.6 shows that patient survival was 92.6% at 3 years and 90.5% at 5 years from the time of renal biopsy.

Table 4.11.6: Patients survival in lupus nephritis

Interval (months)	Lupus Nephritis patients		
	n	% survival	SE
0	184	100	-
12	135	97.0	0.01
24	92	93.7	0.02
36	68	92.6	0.02
48	50	92.6	0.02
60	38	90.5	0.03
72	27	90.5	0.03
84	21	90.5	0.03
96	**15**	**90.5**	**0.03**

Figure 4.11.6: Patient survival in lupus nephritis



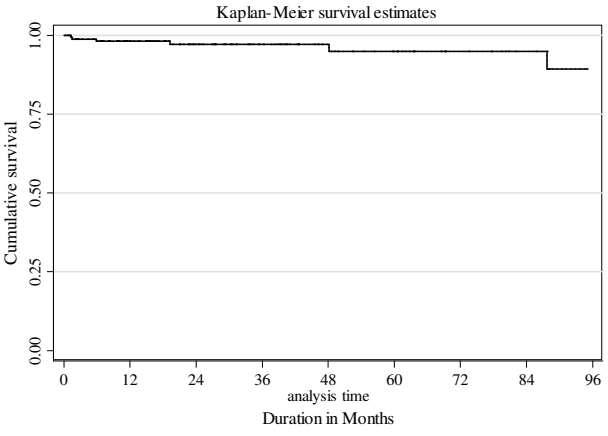
4.11.7: Renal survival of patient with lupus nephritis

Table & Figure 4.10.7 shows that renal survival was 97.1% at 3 years and 5 years from the time of renal biopsy.

Table 4.11.7: Renal survival of patient with lupus nephritis

Interval (months)	Lupus Nephritis patients		
	n	% survival	SE
0	164	100	-
12	122	98.0	0.01
24	88	97.1	0.01
36	64	97.1	0.01
48	46	97.1	0.01
60	36	97.1	0.03
72	25	94.9	0.03
84	19	94.9	0.03
96	15	89.4	0.06

Figure 4.11.7: Renal survival of patient with lupus nephritis



4.12: Renal outcome

Of the 755 patients biopsied, 61 children were reported to the Malaysian Dialysis and Transplant Registry with end stage renal disease[6] .FSGS is the most common known cause of end stage renal disease accounting for 37.7%. This was followed by lupus nephritis (13.1%), advanced glomerulosclerosis (9.8%), post-infectious GN (6.6%) and IgA nephropathy (6.6%). Two patients with minimal change and one patient with acute tubular necrosis progressed to end stage renal disease

Table 4.12: Causes of end stage renal disease in children who underwent renal biopsy

Causes	n	%
FSGS	23	37.7
Lupus nephritis	8	13.1
Advance gloemrulosclerosis	6	9.8
Post-infectious GN	4	6.6
IgA nephropathy	4	6.6
Systemic vasculitis	3	4.9
Membranoproliferative GN	2	3.3
Chronic interstitial nephritis	2	3.3
Minimal change	2	3.3
Mesangial proliferative GN non-IgA	1	1.6
HUS/TTP	1	1.6
Acute tubular necrosis	1	1.6
Idiopathic crescentic	1	1.6
Unknown	3	4.9
Total	**61**	**100**

4.13: Biopsy failure and complications

4.13.1: Risk factors for biopsy failure

The definition of biopsy failure is biopsy which yields less than 10 glomeruli. There was no significant difference in success of renal biopsy with regards to age, real time ultrasound guidance and previous failed biopsy. This is probably because of the small number of data reported and small number of failed renal biopsies (Table 4.13.1).

Table 4.13.1: Risk factors for biopsy failure

Factors	n	Number of failure	Risk ratio	95% CI	p value
Age (years)					
≤2	35	0	-		
>2-≤5	107	1	1.19	(0.40, 3.57)	0.759
>5-≤10	236	0	0.63	(0.32, 1.26)	0.192
>10 (ref*)	431	8	-		
No real-time guided ultrasound	74	2	0.56	(0.21, 1.49)	0.243
Real-time guided ultrasound (ref*)	20	7	-	-	-
Unknown	2	0	-	-	-
Previous failed biopsy	9	8	0.47	(0.05, 4.54)	0.514
Successful biopsy (ref*)	90	85			
Uncooperative patient**	6	1	-	-	-
Cooperative patient (ref*)	93	8			

4.13.2: Complications

As shown in Table 4.13.2, complications were reported in 5.4% of biopsies. The most common complication was bleeding, which occurred in 4.1% biopsies. Seven patients had perirenal haematoma. Blood transfusion was needed in 7 patients. There was one reported case of arteriovenous fistula post biopsy. None of the patients needed either surgical or radiological intervention. There were no cases of loss of kidney or death in association with biopsy procedure.

United Kingdom reported complications rate of 12%.[(2)] Macroscopic haematuria was recorded in 7%. One patient required a single blood transfusion. The overall complication rate in Japan was 5.8%. Gross haematuria occurred in 2.7% and large perirenal hematoma in 0.9% of cases. [(3)]

Table 4.13.2: Frequency of complications

	n	**%**
Total number of biopsies	809	
Total number of complications	44	5.4
Type of complication		
Bleeding	33	70.2
- Gross haematuria	31	93.9
- Haematoma	1	3
Perirenal collection	7	14.9
Infection	0	0
Arteriovenous malformation	1	2.1
Hypotension	1	2.1
Others	3	6.4
Unknown	2	4.3

4.13.3: Risk factors for complication

The risk of complication post renal biopsy was higher in those who had lower GFR and renal failure requiring dialysis. The risk is lower in those who had less than 2 passes of the biopsy needle. Age, hemoglobin level and lupus nephritis were not found to have significant impact on complication rate (Table 4.13.3).

Table 4.13.3: Risk factors for complication

Factors	n	Number of complication	Hazard ratio	95% CI	p value
Age (years)					
≤2	35	3	1.86	(0.51, 6.76)	0.348
>2-≤5	107	10	2.13	(0.95, 4.77)	0.065
>5-≤10	236	10	0.90	(0.41, 1.97)	0.799
>10 (ref*)	431	21	-	-	-
Renal failure					
needed dialysis	64	10	2.39	(1.12, 5.12)	0.025
not needed dialysis (ref*)	632	34	-	-	-
Unknown[a]	113	0	-	-	-
Calculated GFR					
<15 ml/min/1.73m²	56	9	3.28	(1.38, 7.78)	0.007
15-<30 ml/min/1.73m²	42	2	0.90	(0.28, 1.80)	0.888
30-<60 ml/min/1.73m²	162	6	0.71	(0.20, 4.04)	0.468
60-<90 ml/min/1.73m²	122	6	0.96	(0.37, 2.47)	0.931
≥90 ml/min/1.73m² (ref*)	427	21	-	-	-
Hemoglobin (Hb) level					
Hgb ≤8g/dL	21	1	1.05	(0.13, 8.40)	0.963
Hgb >8-≤10g/dL	150	11	1.37	(0.66, 2.82)	0.399
Hgb ≥11g/dL (ref*)	610	31	-	-	-
Unknown[b]	28	1	-	-	-
Not realtime ultrasound guided	359	26	0.63	(0.32, 1.25)	0.184
Ultrasound – Realtime guided (ref*)	125	14	-	-	-
Unknown[c]	30	2	-	-	-
Plug biopsy **	4	0	-	-	-
Not plug biopsy (ref*)	452	36			
Unknown[d]	58	6	-	-	-
SLE	130	9	0.77	(0.36, 1.66)	0.505
Non SLE (ref*)	384	33			
Needle size					
14G	23	2	0.90	(0.20, 4.00)	0.895
16G (ref*)	411	38	-	-	-
18G	75	1	0.13	(0.02, 0.95)	0.044
Unknown[e]	5	1	-	-	-

Table 4.13.3: Risk factors for complication (cont.)

Factors	n	Number of complication	Hazard ratio	95% CI	p value
Number of passes					
≤2	293	18	0.49	(0.26, 0.96)	0.036
3 ≤ 4 (ref)	181	21	-	-	-
≥ 5	14	2	1.23	(0.26, 5.88)	0.795
Unknown[f]	26	1	-	-	-

** Not able to do analysis due to the small sample size
a No information on renal failure needed dialysis for biopsy procedure data
b No information on haemoglobin (Hgb) level for biopsy procedure data
c No information ultrasound biopsy for biopsy procedure data
d No information on plug biopsy for biopsy procedure data
e No information on needle size for biopsy procedure data
f No information on number of passes for biopsy procedure data

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CHAPTER 5

Renal Allograft Biopsy

Wong Hin Seng

5.1 Introduction

The systematic collection of renal allograft biopsy data was first started in the Department of Nephrology, Hospital Kuala Lumpur in 2004 and by 2005, has involved all the Ministry of Health hospitals in the country. The university hospitals joined in 2007 and the private hospitals began submitting data in 2008.

5.2: Number of renal allograft biopsy

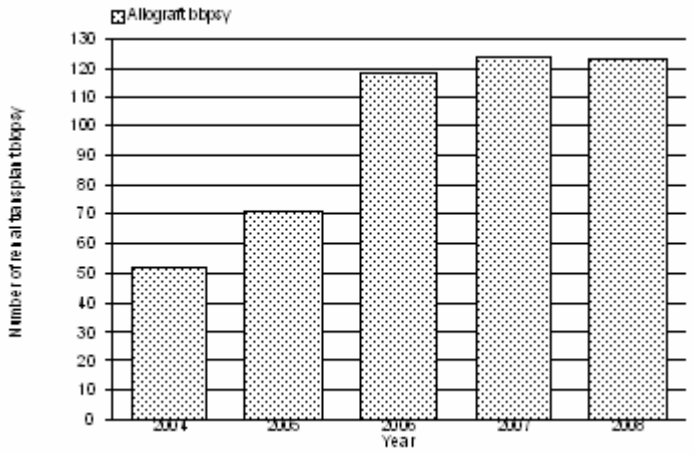
5.2.1: Number of renal allograft biopsy by year

There is an increasing trend in the number of renal allograft biopsy reported and the number has doubled over the last 5 years despite a decreased in the number of new transplant recipients (190 new transplant recipients in 2004 compared to 88 in 2008) and only a marginal increase in the number of functioning renal allograft (1595 functioning allograft in 2004 compared to 1730 in 2008) during the same period (Table & Figure 5.2.1). This marked increased in the number of renal allograft biopsies reported in recent years may be largely contributed by the marked increased in the number of participating centres (21 participating centres in 2005 compared to 43 centres in 2008) in the Malaysian Registry of Renal Biopsy.

Table 5.2.1: Number of renal allograft biopsy, 2004-2008

Year	2004	2005	2006	2007	2008	Total
Number of renal transplant biopsy	52	71	118	124	123	488

Figure 5.2.1: Number of renal allograft biopsy, 2004-2008



5.2.2: Number of renal allograft biopsy by year and site

In 2008, of the 43 participating centres, renal allograft biopsies were performed in only 12 centres with 90% of the biopsies performed in 5 centres (centre 1,7,19,20 & 24) in the Klang Valley (Table 5.2.2). These five centres have a very large number of renal transplant recipients and four of these centres are active renal transplant centres; performing most of the renal transplantation in this country.

Table 5.2.2: Number of renal allograft biopsy by centre, 2004-2008

Centre	2004 n	2004 %	2005 n	2005 %	2006 n	2006 %	2007 n	2007 %	2008 n	2008 %	Total n	Total %
1	47	90	28	39	50	42	43	35	37	30	205	42
2	0	0	0	0	0	0	0	0	3	2	3	1
3	0	0	12	17	11	9	2	2	4	3	29	6
4	0	0	0	0	1	1	0	0	0	0	1	0
5	0	0	1	1	2	2	2	2	0	0	5	1
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	5	7	11	9	12	10	10	8	38	8
8	0	0	0	0	1	1	1	1	1	1	3	1
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	2	2	1	1	1	1	4	1
11	0	0	0	0	2	2	0	0	1	1	3	1
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	6	8	5	4	2	2	5	4	18	4
18	0	0	0	0	0	0	0	0	0	0	0	0
19	4	8	1	1	13	11	9	7	17	14	44	9
20	1	2	18	25	19	16	22	18	14	11	74	15
21	0	0	0	0	1	1	0	0	0	0	1	0
22	0	0	0	0	0	0	0	0	2	2	2	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	30	24	27	22	57	12
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	1	1	1	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

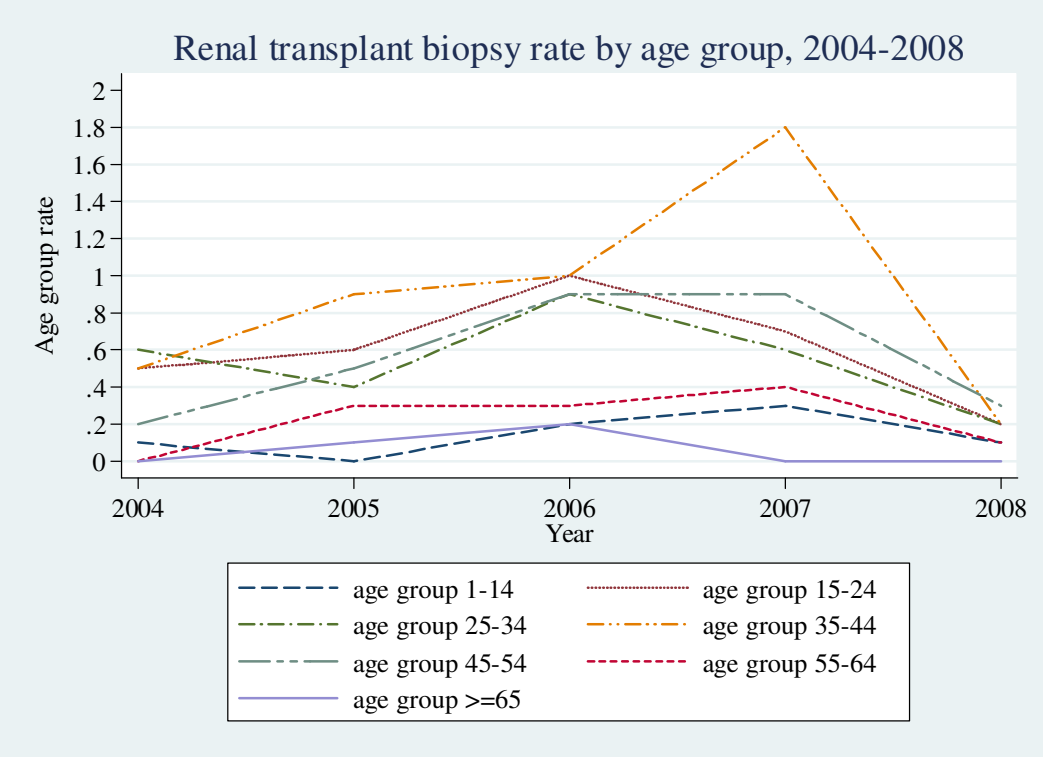
5.2.3: Number of renal allograft biopsy by year and age

Majority of the allograft renal biopsies were performed in the age group of 15 to 54 years and this pattern remained relatively unchanged over the last 5 years (Table 5.2.3). This probably reflects the transplant recipients' demography in this country. However in recent years, there is an increasing trend in the number of allograft biopsies performed in older transplant recipients. Allograft biopsies performed in the older age group (older than 54 years) has increased from 2% (2004) to 10% in 2008 (Table & Figure 5.2.3).

Table 5.2.3: Renal allograft biopsy by year and age group, rate per million population 2004-2008

Age group	2004			2005			2006			2007			2008			Total		
	n	%	Rate	n	%	Rate	n	%	Rate	n	%	Rate	n	%	Rate	n	%	Rate
<15	3	6	0.1	0	0	0	5	4	0.2	7	6	0.3	9	7	0.3	24	5	0.2
15-<25	14	27	0.5	15	21	0.6	26	22	1	19	15	0.7	22	18	0.8	96	20	0.7
25-<35	15	29	0.6	11	15	0.4	25	21	0.9	15	12	0.6	20	16	0.7	86	18	0.6
35-<45	14	27	0.5	23	32	0.9	26	22	1	49	40	1.8	25	20	0.9	137	28	1
45-<55	5	10	0.2	12	17	0.5	24	20	0.9	24	19	0.9	34	28	1.2	99	20	0.7
55-<65	1	2	0	8	11	0.3	8	7	0.3	10	8	0.4	9	7	0.3	36	7	0.3
≥65	0	0	0	2	3	0.1	4	3	0.2	0	0	0	4	3	0.1	10	2	0.1
Total	**52**	**101**	**1.9**	**71**	**99**	**2.8**	**118**	**99**	**4.5**	**124**	**100**	**4.7**	**123**	**99**	**4.3**	**488**	**100**	**3.6**

Figure 5.2.3 Renal allograft biopsy by year and age group, rate per million population 2004-2008



5.3: Clinical presentation at biopsy

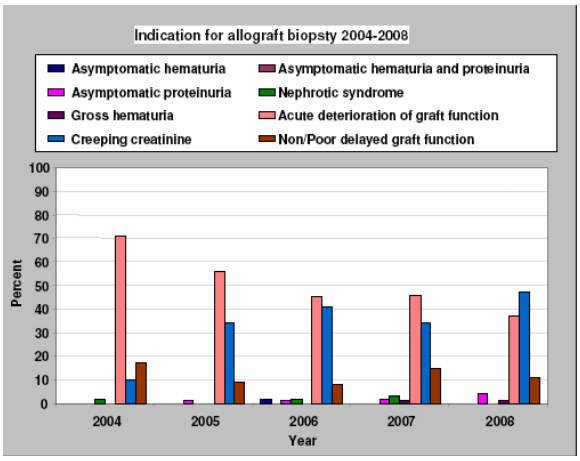
The most common indications for renal allograft biopsy were acute and chronic allograft dysfunction. This remained unchanged over the last 5 years and in 2008 accounted for 95% of the total number of renal allograft biopsies performed (Table 5.3). However there is a reversal in the pattern where the number of allograft biopsies performed for acute graft dysfunction has declined (71% in 2004 to 37% in 2008) by 50% while the number of allograft biopsies performed for chronic allograft dysfunction (creeping serum creatinine) has increased by nearly 5 folds (10% in 2004 to 47% in 2008).

Table 5.3: Indications for renal allograft biopsy, 2004-2008

Current clinical presentation	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic hematuria	0	0	0	0	2	2	0	0	0	0	2	0
Asymptomatic hematuria and proteinuria	0	0	0	0	0	0	0	0	0	0	5	1
Asymptomatic proteinuria	0	0	1	1	1	1	2	2	4	4	8	2
Nephrotic syndrome	1	2	0	0	3	2	3	3	0	0	7	1
Gross hematuria	0	0	0	0	0	0	1	1	1	1	2	0
Acute deterioration of graft function	34	71	39	56	55	45	55	46	42	37	225	47
Creeping creatinine	5	10	24	34	50	41	41	34	54	47	174	36
Non/Poor delayed graft function	8	17	6	9	10	8	18	15	13	11	55	12
Total	**48**	**100**	**70**	**100**	**121**	**100**	**120**	**100**	**114**	**100**	**478**	**100**

*** Patients may have one or more clinical presentation**

* 23 patients have no information on clinical presentation
For 2004, 1 patient has 2 indications
For 2006, 4 patients have 2 indications
For 2007, 2 patients have 2 indications
For 2008, 6 patients have 2 indications



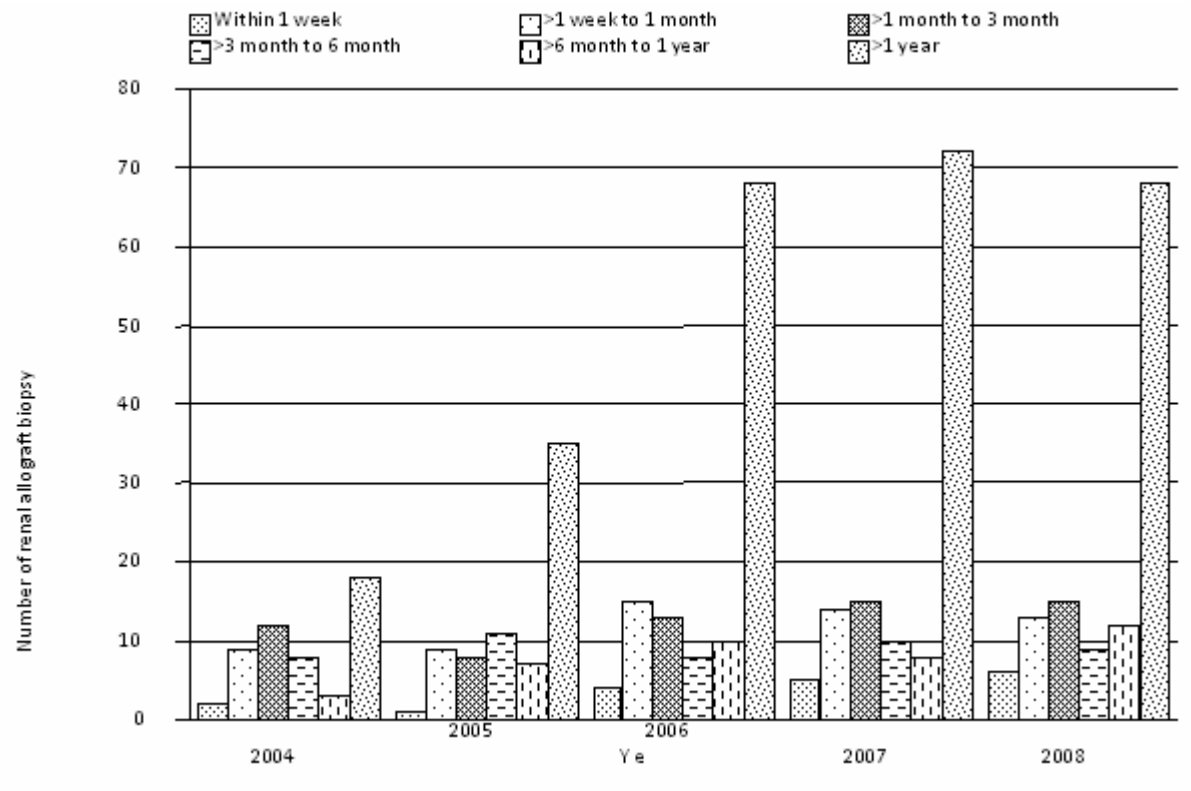
5.4: Timing of renal allograft biopsy

The number of renal allograft biopsies performed within the first six months post renal transplantation remained relatively unchanged over the last 5 years (Table & Figure 5.4). However in recent years, there has been a marked increased in the number of renal allograft biopsies performed in recipients after 1 year post transplant (35% in 2004 to 55% in 2008). This reflects the increasing importance of chronic allograft nephropathy among renal transplant recipients.

Table 5.4: Timing of renal allograft biopsy, 2004-2008

Timing of renal transplant biopsy	Within 1 week		>1 week to 1month		> 1month to 3 months		> 3 months to 6 months		> 6months to 1 year		>1 yr post transplant		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
2004	2	4	9	17	12	23	8	15	3	6	18	35	52	100
2005	1	1	9	13	8	11	11	15	7	10	35	49	71	100
2006	4	3	15	13	13	11	8	7	10	8	68	58	118	100
2007	5	4	14	11	15	12	10	8	8	6	72	58	124	100
2008	6	5	13	11	15	12	9	7	12	10	68	55	123	100
Total	**18**	**4**	**60**	**12**	**63**	**13**	**46**	**9**	**40**	**8**	**261**	**53**	**488**	**100**

Figure 5.4: Timing of renal allograft biopsy, 2004-2008



5.5: Renal allograft biopsy procedure

5.5.1: Renal allograft biopsy method

Over the last 5 years, nearly all renal allograft biopsies were performed under ultrasonographic guidance with real-time guidance accounting for at least 65% in 2008 (Table 5.5.1). When missing data are censored, ultrasonographic guidance with real-time renal allograft biopsy accounted for 96% in 2008 (Figure 5.5.1) and ultrasonography was used in all allograft biopsies.

Table 5.5.1: Biopsy method, 2004-2008

Method	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Blind (not US guided)	0	0	1	1	0	0	1	1	0	0	2	0
US guided: real-time	48	92	27	38	62	53	65	52	80	65	282	58
US guided: not real-time	3	6	32	46	33	28	5	4	3	2	76	16
Missing*	1	2	11	15	23	19	53	43	40	33	128	26
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

* Missing means no data on biopsy technique

Figure 5.5.1: Biopsy method, 2004-2008

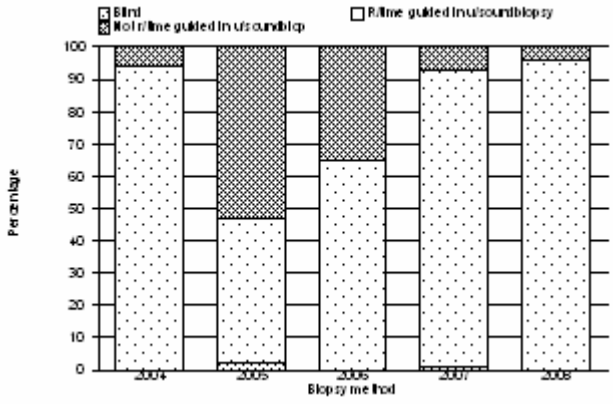
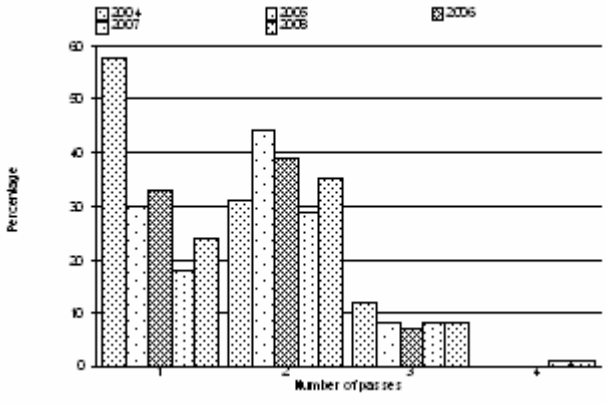


Figure 5.5.2: Number of passes, 2004-2008



5.5.2: Number of passes

The average number of passes for renal allograft biopsy remained unchanged over the last 5 years where majority had one or two passes only. In 2008, the average number of passes made during allograft biopsy was 1.78 (after censoring incomplete data) with only 1 allograft biopsy required more than 3 passes (Table & Figure 5.4.2).

Table 5.5.2: Number of passes, 2004-2008

Number of passes	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
1	30	58	21	30	39	33	22	18	30	24	142	29
2	16	31	31	44	46	39	36	29	43	35	172	35
3	6	12	6	8	8	7	10	8	10	8	40	8
4	0	0	0	0	0	0	1	1	1	1	2	0
Missing*	0	0	13	18	25	21	55	44	39	32	132	27
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

* No data information on number of passes

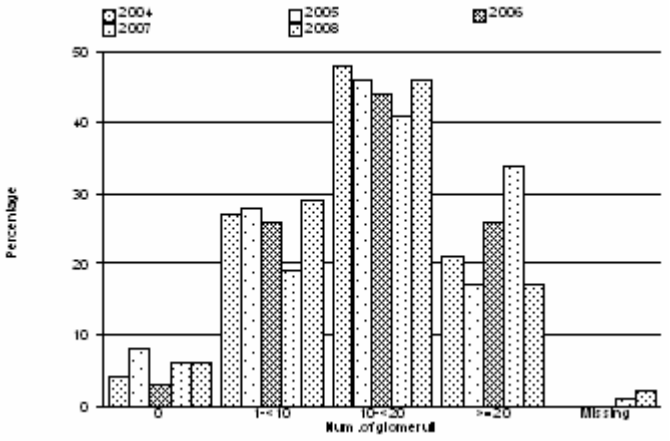
5.5.3: Number of glomeruli obtained on biopsy

With an average of 1.76 passes made during allograft biopsy, 69% of the renal allograft biopsies performed over the last 5 years yield at least 10 glomeruli (Table & Figure 5.4.3). Renal allograft biopsies that did not yield any glomerulus were uncommon and accounted for only 5%. This pattern remained unchanged over the last 5 years

Table 5.5.3: Number of glomeruli obtained on biopsy, 2004-2008.

Number of glomeruli obtained	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
0	2	4	6	8	4	3	7	6	7	6	26	5
1-9	14	27	20	28	31	26	23	19	36	29	124	25
10-19	25	48	33	46	52	44	51	41	57	46	218	45
>20	11	21	12	17	31	26	42	34	21	17	117	24
Missing/Unknown*	0	0	0	0	0	0	1	1	2	2	3	1
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

Figure 5.5.3: Number of glomeruli obtained on biopsy, 2004-2008



5.5.4: Type of complications

Over the last 5 years, complications from renal allograft biopsy were uncommon. In 2008 (after censoring missing data), 97% of all biopsies do not have any complications while a major complication was only reported in 1 allograft biopsy (Table 5.5.4).

Table 5.5.4: Type of complications, 2004-2008

Type of complications	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
No complication	49	94	53	75	95	81	68	55	88	72	353	72
Mild complication[a]	1	2	1	1	1	1	3	2	2	2	8	2
Severe complication[b]	0	0	1	1	0	0	1	1	1	1	3	1
Missing / Unknown[c]	2	4	16	23	22	19	52	42	32	26	124	25
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

[a] Mild complication is defined as presence of gross hematuria, perirenal collection, hematoma, or AVM that do not require intervention

[b] Severe complication is defined as presence of hypotension or complications requiring intervention.

[c] No data information for complications

5.6: Histological diagnosis

Acute rejection has remained the most common histological diagnosis (Table 5.6) and in 2008 accounted for 49% of all allograft biopsies. The number of allograft biopsies with histological diagnosis of acute rejection has increased over the last 5 years with a corresponding decrease in the number of allograft biopsies with the histological diagnosis of calcineurin inhibitor toxicity and chronic allograft nephropathy (Figure 5.6). This may be a result of the changing pattern in the calcineurin inhibitors usage among nephrologists in recent years.

Furthermore, the numbers of allograft biopsies with histological diagnosis of acute rejection continue to increase despite a decreased in the number of allograft biopsies performed for acute graft dysfunction (37% in 2008), suggesting that in recent years, acute rejection in renal allograft may not present with the classical acute rise in serum creatinine and may instead manifest as chronic graft dysfunction.

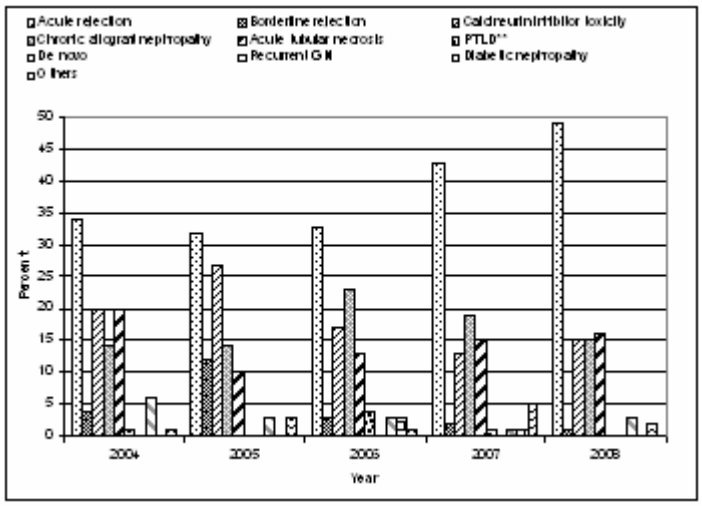
Chronic allograft nephropathy, calcineurin inhibitor toxicity and acute tubular necrosis remained the next three commonest histological diagnosis and in 2008 accounted for 46% of all allograft biopsies.

Table 5.6: Histological diagnosis, 2004-2008

Histological diagnosis	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Acute rejection	24	34	25	32	55	33	57	43	52	49	213	38
Borderline rejection	3	4	9	12	5	3	3	2	1	1	21	4
Calcineurin inhibitor toxicity	14	20	21	27	29	17	18	13	16	15	98	18
Chronic allograft nephropathy	10	14	11	14	39	23	26	19	16	15	102	18
Acute tubular necrosis	14	20	8	10	21	13	20	15	17	16	80	14
PTLD**	1	1	0	0	6	4	1	1	0	0	8	1
De novo	0	0	0	0	0	0	0	0	0	0	0	0
Recurrent GN	4	6	2	3	5	3	1	1	3	3	15	3
Diabetic nephropathy	0	0	0	0	5	3	1	1	0	0	6	1
Others	1	1	2	3	2	1	7	5	2	2	14	3
Total	**71**	**100**	**78**	**100**	**167**	**100**	**134**	**100**	**107**	**100**	**557**	**100**

* Patients may have more than 1 diagnosis classification
**Post Transplant Lymphoproliferative disease

Figure 5.6: Histological diagnosis, 2004-2008



APPENDIX I:

Data Management

Lim Jie Ying
Lee Day Guat

Data Management

The Malaysian Registry of Renal Biopsy (MRRB) was established on the 1st January 2005. It started off as a pilot project involving centers with Nephrology services within the Ministry of Health Malaysia. In its infancy, this registry was called Glomerulonephritis (GN) Registry but subsequently changed to MRRB as it was deemed to be more appropriate.

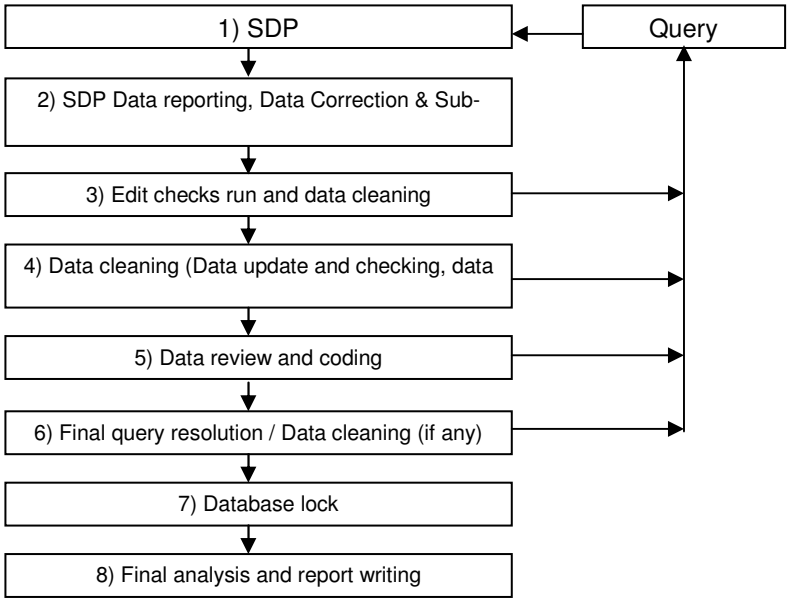
The MRRB has gone through several enhancements in the data collection format in order to make it user friendly.

The operations of the MRRB are supported by an extensive ICT infrastructure to ensure operational efficiency and effectiveness. The MRRB data is stored in SQL Server and has a web-based application.

Data sources
Before the setting up of the MRRB, there were two separated databases in MOH related to renal biopsy. They are the paediatric (Institute Paediatric, HKL) renal biopsy database (1993 – 2004) and adult Department of Nephrology HKL renal biopsy database (2004-2005). The data from these databases had been mapped and incorporated into MRRB in 2005.

MRRB intends to be a national population-based registry and the participation is opened to all hospitals with nephrology services for renal biopsy throughout Malaysia.

Data flow process
This section describes the data management flow process of the Malaysian Registry of Renal Biopsy.



SDP
Nephrologist or renal physician who provides renal biopsy services in Malaysia.

SDP Data reporting, Data Correction and Submission tracking

Primary source data is reported by SDP via web applications e-Case Report Forms:

- MRRB Patient Notification form (Native Kidney Biopsy)
- MRRB Patient Notification form (Graft Kidney Biopsy)
- MRRB Biopsy Procedure form
- MRRB Outcome Notification form

The secondary data source is to determine both renal and mortality outcomes. Verification of both renal and mortality outcomes can be done through the Malaysian Dialysis and Transplant Registry and National Vital Registration System respectively.

Edit checks run and Data cleaning

Edit checks identify missing compulsory data, out of range values, inconsistent data, invalid values and error with de-duplication. Data cleaning is then performed based on the results of edit checks.

Data review and coding

Expert panels and registry manager performed data coding of free text description to its predetermined coding table or dictionary. The expert panel comprises of members with expertise and knowledge in the relevant area. They also perform Quality Control function on the assessment of coding. They ensure that complex medical data are reviewed and assessed to detect clinical nuances.

Final query resolution / data cleaning / database lock

A final edit check was performed to ensure that data is clean. All queries were resolved before database is locked to ensure data quality and integrity. Final dataset is subsequently locked and exported to statistician for analysis.

Data release and publication policy

The MRRB is part of the National Renal Registry (NRR), which is owned by the Malaysian Society of Nephrology (MSN). One of the primary objectives of the Registry is to make data available to the renal community. The registry's published report is available on the website http://www.msn.org.my/nrr or https://www.macr.org.my/emrrb. The report is copyrighted. However it may be freely reproduced without the permission of the National Renal Registry, Malaysia. Acknowledgement would be appreciated. Suggested citation is: Rosnawati Y, Wan Jazilah WI (Eds), Second Report of the Malaysian Registry of Renal Biopsy 2008 Kuala Lumpur 2010.

The Registry encourages original research and publication using MRRB data in part or full. Any request for raw data or aggregated data must be made in writing (by e-mail, fax, or registered mail). The researcher is required to submit a completed Data Release Application Form and signed Data Release Agreement Form, accompanied with a study proposal / mock tables. Such request will require approval from NRR Advisory Board.

NRR position as follows:

- The NRR does not envisage independent individual publication based entirely on NRR published results, without further analyses or additional data collection.
- NRR however agrees that investigator shall have the right to publish any information or material arising in part out of NRR work. In other words, there must be additional original contribution by the investigator in the work intended for publication.
- NRR encourages the use of its data for research purpose. Any proposed publication or presentation (e.g. manuscript, abstract or poster) for submission to journal or scientific meeting that is based in part or entirely on NRR data should be sent to the NRR prior to submission. NRR will undertake to comment on such documents within 4 weeks. Acknowledgement of the source of the data would also be appreciated.
- Any formal publication of a research based in part or entirely on NRR data in which the input of NRR exceeded that of conventional data management and provision will be considered as a joint publication by investigator and the appropriate NRR personnel.

The Malaysian Society of Nephrology has made a grant towards the cost of running the registry and the report printing to allow distribution to all members of the association and the source data producers. The report will also be distributed to relevant Health Authorities and international registries.

Further copies of the report can be made available with donation of RM60.00 to defray the cost of printing. The full report is also available in the registry web site *www.msn.org.my/nrr*.

APPENDIX II:

Analysis Criteria and Statistical Methodology

Lena Yeap

ANALYSIS SETS

This refers to the sets of cases whose data are to be included in the analysis for this report.

1. All biopsies from 2005-2008
   The analysis set in Chapter 1 includes all patients who underwent native and graft kidney biopsies from 2005-2008.
   The analysis set consists of biopsy number where it is defined as number of episodes of distribution of renal biopsy in patients. Biopsy number was taken for the highest episode only for each patient. This analysis set was used for analysis in Chapter 1.

2. All native renal biopsy, 2005-2008
   The analysis set in Chapter 1 includes patients who underwent native renal biopsy from 2005-2008.

3. Primary glomerulonephritis patients
   Patients described in Chapter 2 are those whose age is more or equal to 15 years old with primary glomerulonephritis on renal biopsies performed 2005-2008

4. Lupus nephritis patients
   Patients described in Chapter 3 are those whose age are more or equal to 15 years old, were ticked YES on SLE and were diagnosed lupus nephritis on renal biopsies from 2005-2008.

5. Paediatric native renal biopsy, 1999-2007
   Patients described in Chapter 4 were aged less than 15 years old at the time that native kidney biopsies were performed during the period 1999-2007.

6. Renal Allograft biopsy
   The analysis set is confined to all graft biopsies from 2004-2008.

STATISTICAL METHOD

Patient's characteristics
These sections included the patient's age at biopsy, gender, and ethnic group in every chapter of this report. In statistics, imputation is the substitution of some value for a missing data point. Therefore, missing of patient's age has been considered to replace with technique imputation for chapter 1, 2 and 3. Then we used the imputation values for the analysis set. For ethnic group other than Malay, Chinese or Indian, will be classified as Others. Patient's centre state was used to describe the reported renal biopsy by state and is used for the analysis in chapter 1.

Clinical presentation
These sections described the current clinical presentation. All chapters are considered for clinical syndrome. However, apart from clinical syndrome, chapter 2 and chapter 3 are also considered for Hypertension and Renal function.

Biopsy procedure data
For biopsy data, hotdeck imputation is considered for variable biopsy technique when data is not available or missing.

Laboratory data
Few variables in this dataset were missing. Those variables are GFR, urine protein, 24hrs urine protein and urine RBC. Therefore, imputation was done to these variables.

Histological diagnosis
In this section, analysis was confined to available data only and no imputation was done.

Centre survey data
Centre survey data were used to determine the numbers of unreported native renal biopsy in participating centers. This is only applying for Chapter 1.

Hazard ratio
The hazard ratio in survival analysis is the effect of an explanatory variable on the hazard or risk of an event. The hazard ratio compares groups differing in risk factors. If the hazard ratio is 2.0, then the rate failure in one group is twice the rate in other group. This was used for analysis in Chapter 4.

Risk ratio
The risk ratio is the risk of an event (diagnosis) relative to exposure. The risk ratio takes on values between zero and infinity. One is the neutral value and means that there is no difference between the groups compared. This was used for analysis in Chapter 4.

Survival analysis
The unadjusted survival probabilities were calculated using the Kaplan-Meier method. Survival analysis involves the modelling of time to event data, in this context, death is considered an event.
Survival rate is a part of survival analysis, indicating the percentage of people in this group who are alive for a given period of time after diagnosis with the minimal change disease and focal segmental glomerulosclerosis. This was used for analysis in Chapter 4.

Renal allograft biopsy rates
Renal transplant biopsy rate is calculated by the ratio of the count of number of patients in a given year (according to its age group) to the mid-year population of Malaysia in that year, and expressed as in per million populations. This was used for analysis in Chapter 5.

American Rheumatological Association (ARA) Criteria
An ARA criterion is defined as YES on SLE clinical presentation and SLE lab data. Eleven criteria have been considered for ARA. Nine criteria are from SLE clinical presentation with presentation of malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal, cerebral, and hematological. However, the other two are from SLE lab data where patient should have positive on ANF, and at least 1 is Positive on dsDNA, ssDNA, Anti-cardiolipin antibody, Anti-phospholipid antibody, Histone, Nucleo, Ro, La or Sm. This was used for analysis in Chapter 3.

Extra renal involvement criteria
Patient who have at least one of the followings: malar rash, siscoid rash, photosensitivity or oral ulcers will be grouped as Muco-cutaneous for other organ involvement criteria. This was used for analysis in Chapter 3.

Density of histogram
Density scales the height of the bars so that the sum of their areas equals 1. The density scale is calculated by the probability of the patients in the interval that concerned and divides with that interval. This figure was considered in Chapter 2.

APPENDIX III:

Abbreviations

Abbreviations

ADMAN	Association of Dialysis Medical Assistants and Nurses
ANCA	Antineutrophilic Cytoplasmic Antibody
ARA	American Rheumatological Association
AVM	Arterio-venous malformation
CRC	Clinical Research Centre
CrCl	Creatinine Clearance
CRM	Clinical Registry Manager
eGFR	Calculated Creatinine Clearance based on Schwartz Formula
ESRD	End Stage Renal Disease
MCD	Minimal Change Disease
FSGS	Focal Segmental Glomerulosclerosis
IMN	Idiopathic Membranous Nephropathy
GFR	Glomerular Filtration Rate
GN	Glomerulonephritis
GNreg	GN Registry
Hgb	Hemoglobin
HPE	Histopathology examination
HSP	Henoch Schonlein Purpura
HUS/TTP	Haemolytic uremic syndrome / Thrombotic Thrombocytopenic Purpura
IgAN	IgA Nephropathy
ISN/RPS	International Society Nephrology/ Renal Pathology Society
LN	Lupus Nephritis
MCD	Minimal Change Disease
MOH	Ministry of Health, Malaysia
MOSS	Malaysian Organ Sharing System
MRRB	Malaysian Registry of Renal Biopsy
MSN	Malaysian Society of Nephrology
NRR	National Renal Registry
Ref*	References
RRT	Renal replacement therapy
SDP	Source Data Producer
SLE	Systemic Lupus Erythromatosis
WHO	World Health Organization

APPENDIX IV:

Formula

e-GFR formula

This formula is used in Chapter 4 Paediatric Renal Biopsy

Calculated Creatinine Clearance base on Schwartz Formula:

$$\text{Schwartz Formula} = \frac{\text{*K x Height (cm)}}{\text{Serum Creatinine (umol/L)}}$$

**K for infant less than 1 year is 35,*
**K for child >1year is 40*

Adult

Male : $175 \times (\text{creatinine(umol/l)} / 88.4)^{-1.154} \times (\text{age})^{-0.203} \times 1.0$

Female : $175 \times (\text{creatinine (umol/l)} / 88.4)^{-1.154} \times (\text{age})^{-0.203} \times 0.742$