

**1st REPORT OF  
THE MALAYSIAN REGISTRY  
of**

**RENAL BIOPSY**



*Editors:*  
**Rosnawati Yahya  
Wan Jazilah Wan Ismail**

*With contribution by:*  
Wan Shaariah, Sunita B, Yap Y C, Wong H S, Lee DG, Lim JY, Hoo LP



Malaysian Society of Nephrology



Ministry of Health Malaysia

**1<sup>st</sup> REPORT OF  
THE MALAYSIAN REGISTRY  
of  
RENAL BIOPSY**

*Sponsors:*

**Malaysian Society of Nephrology**

The National Renal Registry is funded with grants from:

**The Ministry of Health Malaysia**

**Ain Medicare**

**Baxter Healthcare**

**Fresenius Medical Care**

**Roche**

Prelim Report Awaiting Approval from KKM

December 2008  
© National Renal Registry, Malaysia  
ISSN 1985-6989



***Published by:***

**The National Renal Registry**  
Malaysian Society of Nephrology  
2<sup>nd</sup> Floor, MMA House  
124, Jalan Pahang  
50286 Kuala Lumpur  
Malaysia

Telephone. : (603) 4045 8636  
Direct Fax : (603) 4042 7694  
e-mail : [nrr@msn.org.my](mailto:nrr@msn.org.my)  
Web site : <http://www.msn.org.my/nrr>

Cover illustration by Dr. Nik Hasimah Nik Yahya HKL

***Important information:***

This report is copyrighted. However it may be freely reproduced without the permission of the National Renal Registry. Acknowledgment would be appreciated. Suggested citation is:

Rosnawati Yahya, Wan Jazilah W I (Eds) First Report of the Malaysian Registry of Renal Biopsy. Kuala Lumpur 2008

This report is also published electronically on these websites <http://www.msn.org.my/nrr> or <https://www.macr.org.my/emrrb> .

## ACKNOWLEDGEMENTS

**The National Renal Registry would like to thank the following:**

*All the nephrologists and staff of the participating hospitals  
for their hard work and contribution,*

**The Ministry of Health, Malaysia for support seen and unseen,**

**For their generous support -**

**Ain Medicare**

**Baxter Healthcare**

**Fresenius Medical Care**

**Roche**

*The staff of the Clinical Research Centre particularly Lim Jie Ying,  
Hoo Ling Ping and Azizah Alimat*

**&**

*All who have in one way or another supported the National Renal  
Registry.*

Prelim Report Awaiting Approval from KKM

## **NRR ADVISORY COMMITTEE MEMBERS 2008 to 2010**

### **MSN Nominees**

<b>Chairman</b>	Dato' Dr. Zaki Morad B Mohd Zaher
<b>Members</b>	Dr. Lim Teck Onn Dr. Lim Yam Ngo Dr. T. Thiruventhiran Dr. Tan Hee Wu Dr. Wong Hin Seng

### **ADMAN Nominees**

<b>Members</b>	Tam Chong Chiang Fauziah Nizamudin
<b>Secretariat</b>	Lee Day Guat

### **NRR Office Staff**

<b>Clinical Registry Manager</b>	Lee Day Guat
<b>Clinical Research Assistant</b>	Suhazelini Ali Choo Cheh Loo Anis Aizza Zainudin Nur Hasliana Abdul Halit

## MRRB SREERING COMMITTEE MEMBERS

### MSN Nominees

<b>Chairperson</b>	Dato' Dr Wan Shaariah Md Yusuf
<b>Members</b>	Dr Lim Soo Kun
	Dr Rosnawati Yahya
	Dr Sunita Bavanandan
	Dr Wan Jazilah Wan Ismail
	Dr Wong Hin Seng
	Dr Yap Yoke Chin

### CRC Technical Support Staff

<b>Director</b>	Dr. Lim Teck Onn
<b>Epidemiologist</b>	Dr. Jamaiyah Haniff
<b>IT Manager</b>	Celine Tsai Pao Chien
<b>Database Administrator</b>	Lim Jie Ying
<b>Network Administrator</b>	Kevin Ng Hong Heng
	Adlan Ab Rahman
	Scott Huang Li Surin
<b>Statistician</b>	Hoo Ling Ping
	Siti Haryanie Abdul Aziz
<b>Webmaster</b>	Patrick Lum See Kai
<b>Desktop Publisher</b>	Azizah Alimat

## **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.

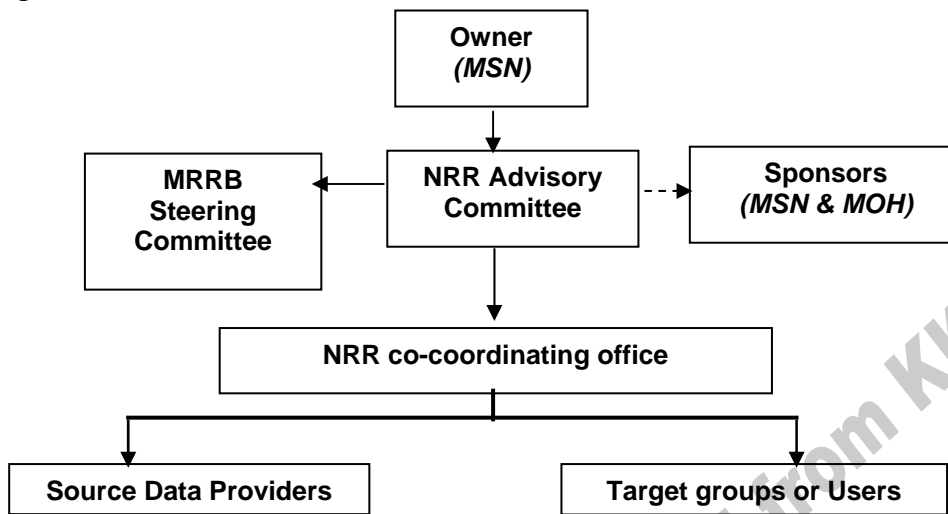
### **Objectives**

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. This year (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](mailto: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.

Prelim Report Awaiting Approval from KKM

## PARTICIPATING CENTRES AT DECEMBER 2007

SDP Name	Adult Nephrology	Paediatric Nephrology
Kuala Lumpur Hospital	√	√
Sultanah Bahiyah Hospital, Alor Star	√	
Pulau Pinang Hospital	√	√
Raja Permaisuri Bainun Hospital, Ipoh	√	
Tengku Ampuan Rahimah Hospital, Kelang	√	
Tuanku Ja'afar Hospital, Seremban	√	√
Melaka Hospital	√	
Sultanah Aminah Hospital, Johor Bharu	√	
Tengku Ampuan Afzan Hospital, Kuantan	√	√
Sultanah Nur Zahirah Hospital, Kuala Terengganu	√	
Raja Perempuan Zainab II Hospital, Kota Bharu	√	
Queen Elizabeth Hospital, Kota Kinabalu	√	
Sarawak General Hospital	√	
Selayang Hospital	√	√
Sultan Ismail Hospital, Pandan		√
Likas Hospital		√

Prelim Report Awaiting Approval from KKM

## CONTRIBUTING EDITORS

Chapter	Title	Authors	Institutions
1	Overview of Renal Biopsy in Malaysia	Wan Shaariah Md Yusuf	Tuanku Jaafar Hospital
		Lee Ming Lee	Tuanku Jaafar Hospital
		Lee Day Guat	National Renal Registry
2	Primary Glomerulonephritis	Sunita Bavanandan	Kuala Lumpur Hospital
		Lee Han Wai	Queen Elizabeth Hospital
		Lim Soo Kun	University Malaya Medical Centre
3	Secondary Glomerulonephritis	Rosnawati Yahya	Kuala Lumpur Hospital
		Liew Yew Fong	Penang Hospital
4	Paediatric Renal Biopsy	Lee Ming Lee	Tuanku Jaafar Hospital, Seremban
		Lim Yam Ngo	Kuala Lumpur Hospital
		Lynster Liaw	Pulau Pinang Hospital
		Susan Pee	Sultan Ismail Hospital, Johor
		Wan Jazilah Wan Ismail	Selayang Hospital
		Yap Yoke Chin	Kuala Lumpur Hospital
5	Renal Allograft Biopsy	Wong Hin Seng	Selayang Hospital

### Report Editors

Rosnawati Yahya

Wan Jazilah Wan Ismail

## PREFACE

**Prelim Report Awaiting Approval from KKM**

## FOREWORD

**Prelim Report Awaiting Approval from KKM**

# CONTENTS

<b>CHAPTER 1</b>	<b>OVERVIEW OF RENAL BIOPSY IN MALAYSIA</b>	<b>1</b>
1.1	Introduction	2
1.2	<b>Renal biopsies from the participating centres</b>	<b>2</b>
1.2.1	Ascertainment rate of total biopsy performed	2
1.2.2	Type of renal biopsy performed	3
1.2.3	Number of renal biopsy done on each individual patient	4
1.2.4	Demographic distribution of renal biopsy (Native and Graft)	5
1.2.4.1	Age distribution	5
1.2.4.2	Gender distribution	7
1.2.4.3	Racial distribution	7
1.2.5	Renal Biopsy Report Analysis	8
1.2.6	Histopathology specimen distribution to histopathology laboratories	9
1.3	<b>Native kidney biopsy</b>	<b>10</b>
1.3.1	Clinical Indications of renal biopsy	10
1.3.2	Histopathological Diagnosis	11
1.3.3	Histopathology findings in common clinical presentation	12
1.3.3.1	Histopathological diagnosis in patients with nephrotic syndrome	12
1.3.3.2	Histopathological diagnosis in patients with urinary abnormalities	12
1.3.3.3	Histopathological diagnosis in patients with nephritic-nephrotic syndrome	13
1.3.3.4	Histopathological diagnosis in patients with nephritic syndrome	13
1.3.3.5	Primary GN according to various age group	14
<b>CHAPTER 2</b>	<b>PRIMARY GLOMERULONEPHRITIS</b>	<b>15</b>
2.1	Introduction	16
2.2	<b>Minimal Change Disease</b>	<b>16</b>
2.2.1	Introduction	16
2.2.2	Patient population and characteristics	16
2.2.3	Clinical presentation	17
2.2.3.1	Clinical presentation by age	17
2.2.3.2	Clinical presentation by gender	18
2.2.4	Renal function at presentation	18
2.3	<b>Focal Segmental Glomerulosclerosis</b>	<b>19</b>
2.3.1	Introduction	19
2.3.2	Patient population and characteristics	19
2.3.3	Clinical Presentation	20
2.3.3.1	Clinical presentation by age	21
2.3.3.2	Clinical presentation by gender	21
2.3.4	Renal function at presentation	22
2.3.4.1	Renal function at presentation by age	22
2.3.4.2	Renal function at presentation by gender	23
2.4	<b>Idiopathic Membranous Nephropathy</b>	<b>24</b>
2.4.1	Introduction	24
2.4.2	Patient population and characteristics	24
2.4.3	Clinical presentation	25
2.4.3.1	Clinical Presentation by age	26
2.4.3.2	Clinical presentation by gender	26
2.4.4	Renal function at presentation	27

## CONTENT (con't)

2.5	<b>IgA Nephropathy (IgAN)</b>	28
2.5.1	Introduction	28
2.5.2	Patient population and characteristics	28
2.5.3	Clinical presentation	29
2.5.3.1	Clinical presentation by age	30
2.5.3.2	Clinical presentation by gender	30
2.5.4	Renal function at presentation	31
	<i>References</i>	32
<b>CHAPTER 3</b>	<b>SECONDARY GLOMERULONEPHRITIS</b>	33
3.1	<b>Lupus Nephritis</b>	34
3.1.1	Introduction	34
3.1.2	<b>Patient population and characteristics</b>	34
3.1.2.1	Age at time of biopsy	34
3.1.2.2	Gender distribution	34
3.1.2.3	Racial prevalence	34
3.1.3	<b>Clinical presentation</b>	35
3.1.3.1	Clinical Presentation by age	36
3.1.3.2	Clinical presentation by gender	37
3.1.3.3	Clinical Presentations by histopathology	38
3.1.4	<b>Renal function at presentation</b>	39
3.1.4.1	Renal function at presentation by age group	39
3.1.4.2	Renal function at presentation by gender	40
3.1.4.3	Renal function at presentation by histopathology	40
3.1.5	<b>Histopathological diagnosis</b>	41
3.1.5.1	Histopathological diagnosis by age	42
3.1.5.2	Histopathological diagnosis by gender	43
3.1.5.3	Histopathological diagnosis by clinical presentation	43
3.1.6	<b>Extra-renal involvement</b>	44
3.1.6.1	American Rheumatological Association (ARA) criteria in lupus nephritis.	44
3.1.6.2	ARA criteria in lupus nephritis by age	44
3.1.6.3	ARA criteria in lupus nephritis by gender	44
3.1.6.4	ARA criteria in lupus nephritis by histopathological findings	44
3.1.6.5	Extra-renal involvement.	45
<b>CHAPTER 4</b>	<b>PAEDIATRIC RENAL BIOPSY</b>	46
4.1	Introduction	47
4.2	<b>Number of patients and renal biopsies</b>	47
4.2.1	Total number of patients and native renal biopsies	47
4.2.2	Number of native renal biopsies from various hospitals	47
4.3	Outcome of renal biopsies	47
4.4	Patient characteristics	47
4.5	<b>Clinical presentation</b>	48
4.5.1	Clinical presentation at biopsy	48
4.5.2	Renal function at biopsy	48
4.6	Diagnosis of paediatric renal biopsies	48
4.7	Renal histopathology diagnosis of children presenting with nephrotic syndrome	49
4.8	Renal histopathology diagnosis of children presenting with nephritic syndrome.	49
4.9	Causes of acute renal failure	50

## CONTENT (con't)

4.10	<b>Paediatric focal segmental glomerulosclerosis and minimal change disease</b>	50
4.10.1	Characteristics of paediatric focal segmental glomerulosclerosis and minimal change disease	50
4.10.2	Patient survival in focal segmental glomerulosclerosis and minimal change disease	51
4.10.3	Renal survival of patient with focal segmental glomerulosclerosis and minimal change disease	52
4.11	<b>Paediatric lupus nephritis</b>	53
4.11.1	Patient characteristics of paediatric lupus nephritis	53
4.11.2	Extra renal manifestation of paediatric SLE	53
4.11.3	Classification of paediatric lupus nephritis	53
4.12	Renal outcome	53
4.13	<b>Biopsy failure and complication</b>	54
4.13.1	Risk factors for biopsy failure	54
4.13.2	Complications	54
4.13.3	Risk factors for complication	55
	<i>References</i>	56
<b>CHAPTER 5</b>	<b>RENAL ALLOGRAFT BIOPSY</b>	57
5.1	Introduction	58
5.2	<b>Number of renal allograft biopsy</b>	58
5.2.1	Number of renal allograft biopsy by year	58
5.2.2	Number of renal allograft biopsy by year and site	58
5.2.3	Number of renal allograft biopsy by year and age group.	59
5.3	Clinical presentation at biopsy	59
5.4	Timing of renal allograft biopsy	60
5.5	<b>Biopsy Procedure</b>	61
5.5.1	Biopsy method	61
5.5.2	Number of passes	61
5.5.3	Number of glomeruli obtained on biopsy	62
5.5.4	Type of complications	62
5.6	Histological diagnosis	63
	Appendix I	II
	Appendix II	IV
	Appendix III	VII
	Appendix IV	VIII

## LIST OF TABLES

		Page
Table 1.2.1	Total number of reported and unreported renal biopsies by centres, 2005 - 2007	2
Table 1.2.2	Distribution of reported native and graft renal biopsies by centres, 2005-2007	3
Table 1.2.3 (a)	Distribution of native renal biopsy in patients by number of episodes / attempts	4
Table 1.2.3 (b)	Distribution of renal allograft biopsy in patients by number of episodes / attempts	4
Table 1.2.4.1 (a)	Age distribution of native renal biopsy, 2005-2007	5
Table 1.2.4.1 (b)	Age distribution of renal allograft biopsy, 2005-2007	5
Table 1.2.4.1 (c)	Age group distribution of reported renal biopsies by state, 2005-2007	6
Table 1.2.4.2 (a)	Gender distribution of native renal biopsy, 2005-2007	7
Table 1.2.4.2 (b)	Gender distribution of renal allograft biopsy, 2005-2007	7
Table 1.2.4.3 (a)	Racial distribution of native renal biopsy, 2005-2007	7
Table 1.2.4.3 (b)	Racial distribution of renal allograft biopsy, 2005-2007	7
Table 1.2.5	Number of glomeruli obtained at each biopsy by centres, 2005-2007	8
Table 1.2.6 (a)	Distribution of biopsy specimens to histopathology laboratories by participating centres, 2005-2007	9
Table 1.2.6 (b)	Histopathology laboratories receiving renal biopsy specimens, 2005-2007	10
Table 1.3.1 (a)	Indications for native renal biopsies, 2005-2007.	10
Table 1.3.1 (b)	Renal function at time of biopsy	10
Table 1.3.2	Histopathology of all native renal biopsies, 2005-2007	11
Table 1.3.3.1	Histopathological diagnosis in patients presenting with nephrotic syndrome	12
Table 1.3.3.2	Histopathological diagnosis in patients presenting with urine abnormalities, 2005-2007	12
Table 1.3.3.3	HPE diagnosis in patients presenting with nephritic-nephrotic syndrome, 2005-2007	13
Table 1.3.3.4	Histopathological diagnosis in patients presenting with nephritic syndrome, 2005-2007	13
Table 1.3.3.5	Primary GN according to the various age group, 2005 -2007	14
Table 2.2.2 (a)	Demographic characteristics for minimal change disease, 2005-2007	16
Table 2.2.2 (b)	Age group at time of biopsy (years) for minimal change disease, 2005-2007	16
Table 2.2.3 (a)	Overall clinical presentation for minimal change disease, 2005-2007	17
Table 2.2.3 (b)	Presence of hypertension in minimal change disease, 2005-2007	17
Table 2.2.3.1	Clinical presentation by age group for minimal change disease, 2005-2007	17
Table 2.2.3.2	Clinical presentation by gender for minimal change disease, 2005-2007	18
Table 2.2.4	Renal function at presentation by age group for minimal change disease, 2005-2007	18
Table 2.3.2 (a)	Demographic characteristics for FSGS, 2005-2007	19
Table 2.3.2 (b)	Age group at time of biopsy (years) for FSGS, 2005-2007	19
Table 2.3.3 (a)	Overall clinical presentation for FSGS, 2005-2007	20
Table 2.3.3 (b)	Presence of hypertension in FSGS, 2005-2007	20
Table 2.3.3.1	Clinical presentation by age group for FSGS, 2005-2007	21
Table 2.3.3.2	Clinical presentation by gender for FSGS, 2005-2007	21

## LIST OF TABLES *(con't)*

Table 2.3.4 (a)	Impaired renal function in FSGS by year, 2005-2007	22
Table 2.3.4.1	Renal function at presentation by age group for FSGS, 2005-2007	22
Table 2.3.4.2	Renal function at presentation according to gender for FSGS, 2005-2007	23
Table 2.4.2	Demographic characteristics for idiopathic membranous nephropathy, 2005-2007	24
Table 2.4.3 (a)	Overall clinical presentation for idiopathic membranous nephropathy, 2005-2007	25
Table 2.4.3 (b)	Presence of hypertension in idiopathic membranous nephropathy, 2005-2007	25
Table 2.4.3.1	Clinical presentation by age group for idiopathic membranous nephropathy, 2005-2007	26
Table 2.4.3.2	Clinical presentation by gender for idiopathic membranous nephropathy, 2005-2007	26
Table 2.4.4 (a)	Renal function at presentation by age group for idiopathic membranous nephropathy, 2005-2007	27
Table 2.4.4 (b)	Renal function at presentation according to gender for idiopathic membranous nephropathy, 2005-2007	27
Table 2.5.2 (a)	Demographic characteristics of patients with IgA nephropathy, 2005-2007	28
Table 2.5.2 (b)	Age group at time of biopsy (years) for IgA nephropathy, 2005-2007	28
Table 2.5.3 (a)	Overall clinical presentation for IgA nephropathy, 2005-2007	29
Table 2.5.3 (b)	Presence of hypertension in IgA nephropathy, 2005-2007	29
Table 2.5.3.1	Clinical presentation by age group for IgA nephropathy, 2005-2007	30
Table 2.5.3.2	Clinical presentation by gender for IgA nephropathy, 2005-2007	30
Table 2.5.4 (b)	Renal function at presentation by age group for IgA nephropathy, 2005-2007	31
Table 2.5.4 (c)	Renal function at presentation according to gender for IgA nephropathy, 2005-2007	32
Table 3.1.3	Clinical presentation by year, 2005-2007	35
Table 3.1.3.1 (a)	Clinical presentation by age group, 2005-2007	36
Table 3.1.3.3 (a)	Clinical presentations by histopathology, 2005-2007	38
Table 3.1.4.1	Renal function by age group, 2005-2007	39
Table 3.1.4.3	Renal function at presentation by histopathology, 2005-2007	40
Table 3.1.5	Histopathological diagnosis, 2005-2007	41
Table 3.1.5.1	Histopathological diagnosis by age group, 2005-2007	42
Table 3.1.5.2	Histopathological diagnosis by gender, 2005-2007	43
Table 3.1.5.3	Histopathological diagnosis by clinical presentation, 2005-2007	43
Table 3.1.6.1	ARA criteria in lupus nephritis, 2005-2007	44
Table 3.1.6.5 (a)	Extra-renal involvement by gender, 2005-2007	45
Table 3.1.6.5 (b)	Mucocutaneous involvement by gender, 2005-2007	45
Table 4.2.2	Number of renal biopsies	47
Table 4.4	Gender and racial distribution	47
Table 4.5.1	Clinical presentation at biopsy	48
Table 4.5.2	Renal function at biopsy	48
Table 4.6	Diagnosis of paediatric renal biopsies	48
Table 4.7	Renal histopathology diagnosis of children presenting with nephrotic syndrome	49
Table 4.8	Renal histopathology diagnosis of children presenting with nephritic syndrome	49
Table 4.9	Causes of acute renal failure in children who underwent renal biopsy	50

## LIST OF TABLES *(con't)*

Table 4.10.1	Characteristic of paediatric focal segmental glomerulosclerosis and minimal change disease	50
Table 4.10.2	Patient survival for focal segmental glomerulosclerosis and minimal change disease	51
Table 4.10.3	Renal survival of patient with focal segmental glomerulosclerosis and minimal change disease	52
Table 4.11.3	Classification of paediatric lupus nephritis	53
Table 4.12	Causes of end stage renal disease in children who underwent renal biopsy	53
Table 4.13.1	Risk factors for biopsy failure	54
Table 4.13.2	Frequency of complication	54
Table 4.13.3	Risk factors for complication	55
Table 5.2.1	Number of renal allograft biopsy, 2004-2007	58
Table 5.2.2	Number of renal allograft biopsy by year and SDP, 2004-2007	58
Table 5.2.3	Renal allograft biopsy by year and age group, rate (per million population), 2004-2007	59
Table 5.3	Indications for renal allograft biopsy, 2004-2007	59
Table 5.4	Timing of renal allograft biopsy, 2004-2007	60
Table 5.5.1	Biopsy method, 2004-2007	61
Table 5.5.2	Number of passes, 2004-2007	61
Table 5.5.3	Number of glomeruli obtained on biopsy, 2004-2007	62
Table 5.5.4	Type of complications, 2004-2007	62
Table 5.6	Histological diagnosis, 2004-2007	63

## LIST OF FIGURES

	Page
Figure 1.3.3.5	14
Figure 2.2.2 (b)	16
Figure 2.2.4	18
Figure 2.3.2 (b)	19
Figure 2.3.3 (a)	20
Figure 2.3.3.2	21
Figure 2.3.4.1 (a)	22
Figure 2.3.4.1 (b)	22
Figure 2.3.4.2	23
Figure 2.4.2	24
Figure 2.4.3 (a)	25
Figure 2.4.3.2	26
Figure 2.4.4 (a)	27
Figure 2.5.2 (b)	28
Figure 2.5.3 (a)	29
Figure 2.5.4 (a)	31
Figure 2.5.4 (b)	31
Figure 3.1.2.1	34
Figure 3.1.2.2	34
Figure 3.1.2.3	34
Figure 3.1.3 (a)	35
Figure 3.1.3 (b)	35
Figure 3.1.3.1 (a)	36
Figure 3.1.3.1 (b)	36
Figure 3.1.3.1 (c)	36
Figure 3.1.3.2 (a)	37
Figure 3.1.3.2 (b)	37
Figure 3.1.3.2 (c)	37
Figure 3.1.3.3 (a)	38
Figure 3.1.3.3 (b)	38
Figure 3.1.3.3 (c)	38
Figure 3.1.4.1	39
Figure 3.1.4.2	40
Figure 3.1.4.3	41
Figure 3.1.5.1	42
Figure 3.1.6.2	44

## LIST OF FIGURES *(con't)*

Figure 3.1.6.3	ARA criteria in lupus nephritis by gender, 2005-2007	44
Figure 3.1.6.4	ARA criteria in lupus nephritis by histopathology, 2005-2007	44
Figure 3.1.6.5 (a)	Extra-renal involvement by gender, 2005-2007	45
Figure 3.1.6.5 (b)	Mucocutaneous involvement by gender, 2005-2007	45
Figure 4.10.2	Patient survival by focal segmental glomerulosclerosis and minimal change disease	51
Figure 4.10.3	Renal survival by focal segmental glomerulosclerosis and minimal change	52
Figure 5.2.1	Number of renal allograft biopsy, 2004-2007	58
Figure 5.4	Timing of renal allograft biopsy, 2004-2007	60
Figure 5.5.1	Biopsy method (censored for missing data), 2004-2007	61
Figure 5.5.2	Number of passes, 2004-2007	61
Figure 5.5.3	Number of glomeruli obtained on biopsy, 2004-2007	62

Prelim Report Awaiting Approval from KKM

# REPORT SUMMARY

## Chapter 1: Overview of Renal Biopsy in Malaysia

- A total of 2419 renal biopsies were done over 3 years (2005-2007). Twenty-one MOH centers contributed data and these were analyzed in this first MRRB report.
- However Paediatric Institute, HKL started data collection from 1999 and the Nephrology department HKL started data collection on renal allograft biopsies from 2004. This will be discussed in their respective chapters.
- The average ascertainment rate for 2005-2007 was 93.3%.
- 281(11.6%) of these were graft biopsies.
- About a fifth (19%) was done in children under 15 years of age. Majority (75%) was done in patients between 15 – 55 years of age. Only 4% was done in patients older than 55 years of age.
- 21.3% of the biopsies yielded less than 10 glomeruli; the cutoff number for an adequate biopsy.
- More than half (55%) of the biopsies done were sent out to another (tertiary) centre for processing and reporting.
- The main indications for biopsy were nephrotic syndrome (46%) and asymptomatic urinary abnormalities (26%).
- FSGS (26.1%) and minimal change disease (25.8%) were the commonest histopathological diagnosis in patients presenting with nephrotic syndrome.
- Lupus nephritis (52%) was the commonest histopathological diagnosis in patients who presented with acute nephritic syndrome.
- The commonest primary GN reported was FSGS (36%) followed by minimal change (32%) and IgA nephropathy (15%).
- The commonest secondary GN was lupus nephritis (87%).

## Chapter 2: Primary Glomerulonephritis

- The commonest primary GN reported was focal segmental glomerulosclerosis (FSGS), followed by minimal change.

### Minimal change disease

- Mean age at the time of biopsy was 28.6 + 12.5 years
- Male to female ratio was 2:1
- Nephrotic syndrome was the commonest clinical presentation.
- 22% had e-GFR <60 ml/min at time of biopsy.
- There is a higher risk of renal impairment with increasing age

### Focal Segmental Glomerulosclerosis (FSGS)

- Mean age at the time of biopsy was 32.1 + 13.5 years.
- Male to female ratio was 1.3:1
- Nephrotic syndrome was the commonest clinical presentation
- 43% had e-GFR < 60 ml/min at time of biopsy
- There is a higher risk of renal impairment with increasing age

## REPORT SUMMARY (con't)

### **Idiopathic membranous nephropathy**

- Accounts for only 8% of total primary GN
- Mean age at biopsy was 46 + 15.5 years.
- There was bimodal peak in incidence
- Male to female ration was 1.1:1
- 71% presented with nephrotic syndrome
- 38% had e-GFR < 60 ml/min at time of biopsy
- There is a higher risk of renal impairment with increase age and male gender.

### **IgA nephropathy**

- Accountf for 1% of Total primary GN Accounts for only 8% of total primary GN
- Mean age at biopsy was 33.7 + 12.4 years
- There was female prepondence with male to female ration was 0.8 : 1
- 50% presented with asymptomatic urine abnormalities and up to 25% presented with nephrotic syndrome
- 48% had e-GFR < 60 ml/min at time of biopsy
- There is a higher risk of renal impairment with increase age and male gender.

## **Chapter 3: Secondary Glomerulonephritis**

### **Lupus nephritis**

- Lupus nephritis was the commonest secondary GN.
- The mean age of lupus nephritis in adults (>15 years old) was 30.2 + 10.3.
- The female to male ratio was 6.2:1.
- The most common clinical presentation of lupus nephritis was urine abnormalities (39%), followed by nephrotic syndrome (29%).
- The commonest histopathological finding was WHO or ISN/RPS class IV or IV+V. (59%)
- There were 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 (52%),
- 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 are more likely to have impaired function.

## **Chapter 4: Paediatric Renal Biopsy**

- Paediatric Institute Hospital Kuala Lumpur contributed data from 1999. Subsequently 6 other MOH paediatric nephrology centers submitted data following the establishment of MRRB.
- 640 renal biopsies were performed in 579 children. 606 (94.7%) were assessed to be adequate for interpretation.
- More renal biopsies were performed in girls (52.2%) This was attributed to the higher number of biopsies performed on children with lupus nephritis.
- Nephrotic syndrome was the most frequent clinical presentation at biopsy.
- The commonest histopathological diagnoses were FSGS, lupus nephritis and MCD and this accounted for 27.2%, 26.1% and 17.8 % respectively.
- IgA nephropathy accounted for only 4.4%. This may not be an accurate indicator of incidence of IgA in Malaysian children due to differences in biopsy practices.

## REPORT SUMMARY *(con't)*

- Children who presented with acute renal failure at the time of biopsy had histopathological diagnoses of post infectious GN (29.8%), lupus nephritis
- (29.8%) FSGS (8.7%) and HUS/TTP (5.8%). In contrast HUS/TTP is the leading cause of acute renal failure in North America and Europe.
- Children with FSGS had significantly lower creatinine clearance at biopsy. There were also more Indian children in the FSGS group compared to the MCD group.
- Comparing FSGS and MCD groups there were no differences in the patients' 3 and 5 years survival from the time of biopsy. However FSGS had poorer renal survival both at 3 years (92%) and 5 years (82%). Renal survival for the MCD group was 94% at both 3 and 5 years.
- In the paediatric lupus group class IV and V+IV was the commonest histopathological finding on biopsy at 65.7%.
- Complications post-renal biopsy was reported in 5.4%. Gross haematuria was the commonest complication at 4.5%.
- Risk of complication was highest in those who had dialysis dependant renal failure. Age, Hb, lupus nephritis and needle size were not found to have any significant impact.

### **Chapter 5: Renal Allograft Biopsy**

- Department of Nephrology, Hospital Kuala Lumpur contributed data since 2004 and by 2005, submission of data were performed by other MOH hospitals.
- The number of renal allograft biopsy has almost doubled over the last 4 years despite a decreased in the number of new transplants. This was attributed to the changing trend in the management of renal transplant recipients.
- 92% of the renal allograft biopsies were performed in 4 centers in the Klang valley. Three of these centres were actively involved in the care of new recipients in the perioperative and immediate postrenal transplant period. A large number of transplant recipients were also followed up in these centers.
- The commonest indication for renal allograft biopsy was impaired renal allograft dysfunction and acute renal allograft dysfunction.
- There was a marked increased in the number of renal allograft biopsies performed after 1 year post transplant in both 2006 and 2007. This reflected the increasing importance of chronic allograft nephropathy.
- Most renal allograft biopsies were performed under ultrasound guidance and this accounted for 84% in 2007.
- Complications were uncommon and major complications requiring intervention occurred in less than 2%.
- Acute rejection (acute and borderline) has remained the commonest histological diagnosis. This accounted for 31-34% of all renal allograft biopsies.

## **CHAPTER 1**

### **Overview Of Renal Biopsy In Malaysia**

Wan Sha'ariah Md Yusuf

Lee Ming Lee

Lee Day Guat

Prelim Report Awaiting Approval from KKM

## 1.1: Introduction

The Malaysian Registry of Renal Biopsy (MRRB) was first established on the 1st of 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 GN Registry but subsequently changed to MRRB as it was deemed to be more appropriate.

Before MRRB, there were two known existing databases in MOH hospitals related to renal biopsy. They were the paediatric (Paediatric Institute, HKL) renal biopsy database (1993 – 2004) and adult HKL renal biopsy database (2004). This will be elaborated in their respective chapters subsequently.

The MRRB data collection is still on going. In 2008, the participation was opened to non-MOH nephrologists and renal physicians. Thus, the subsequent reports will include data from all the MOH centres, universities and private hospitals.

## 1.2: Renal biopsies from the participating centres

### 1.2.1 Ascertainment rate of total biopsy performed

From 2005 to 2007, a total of 21 centres (15 adult and 6 paediatric) from the Ministry of Health (MOH) submitted data to the MRRB. These participating centres will be identified by their source document provider (SDP) number.

In 2005, a total 749 renal biopsies were performed and of these, 716 were reported. In 2006, 991 renal biopsies were performed and 927 were reported. In 2007, 853 renal biopsies were performed and of these 776 were reported. This gives an ascertainment rate of 95.6% for 2005, 93.5% for 2006 and 91% in 2007. The average ascertainment rate for 2005-2007 was 93.3% (Table 1.2.1)

Table 1.2.1: Total number of reported and unreported renal biopsies by centres, 2005 – 2007

Centre	2005		2006		2007		Total			
	Reported	Not reported	Reported	Not reported	Reported	Not reported	Reported	Not reported		
	n	n	n	n	n	n	n	%	n	%
1	97	0	107	0	101	0	305	13	0	0
2	2	0	10	1	24	0	36	1	1	1
3	97	3	104	0	65	0	266	11	3	2
4	13	0	18	0	19	0	50	2	0	0
5	28	0	38	0	44	6	110	5	6	3
6	31	4	44	4	56	0	131	5	8	5
7	27	0	28	0	24	0	79	3	0	0
8	10	3	5	0	11	0	26	1	3	2
9	21	0	27	0	21	0	69	3	0	0
10	68	0	81	0	61	0	210	9	0	0
11	0	11	42	21	4	28	46	2	60	34
12	0	0	2	0	7	1	9	0	1	1
13	18	3	6	27	0	25	24	1	55	32
14	15	0	24	0	27	5	66	3	5	3
15	39	0	51	0	44	0	134	6	0	0
16	74	0	101	10	63	0	238	10	10	6
17	42	0	51	0	42	0	135	6	0	0
18	90	9	140	0	109	12	339	14	21	12
19	16	0	24	1	14	0	54	2	1	1
20	28	0	24	0	37	0	89	4	0	0
21	0	0	0	0	3	0	3	0	0	0
<b>Total</b>	<b>716</b>	<b>33</b>	<b>927</b>	<b>64</b>	<b>776</b>	<b>77</b>	<b>2419</b>	<b>100</b>	<b>174</b>	<b>100</b>

### 1.2.2 Type of renal biopsy performed

As expected, majority of the biopsies reported were from native kidneys: 90.2% in 2005, 87.5% in 2006 and 87.8% in 2007. The rest were from graft kidneys (Table 1.2.2).

Table 1.2.2: Distribution of reported native and graft renal biopsies by centres, 2005-2007

centre	2005		2006		2007		Total			
	Native	Graft	Native	Graft	Native	Graft	Native		Graft	
	n	n	n	n	n	n	n	%	n	%
1	69	28	57	50	58	43	184	9	121	43
2	2	0	10	0	24	0	36	2	0	0
3	85	12	93	11	63	2	241	11	25	9
4	13	0	17	1	19	0	49	2	1	0
5	27	1	36	2	42	2	105	5	5	2
6	26	5	34	10	43	13	103	5	28	10
7	27	0	27	1	23	1	77	4	2	1
8	10	0	5	0	11	0	26	1	0	0
9	21	0	25	2	20	1	66	3	3	1
10	68	0	79	2	61	0	208	10	2	1
11	0	0	42	0	4	0	46	2	0	0
12	0	0	2	0	7	0	9	0	0	0
13	18	0	6	0	0	0	24	1	0	0
14	15	0	24	0	27	0	66	3	0	0
15	35	4	48	3	44	0	127	6	7	3
16	72	2	99	2	61	2	232	11	6	2
17	41	1	38	13	33	9	112	5	23	8
18	73	17	122	18	87	22	282	13	57	20
19	16	0	23	1	14	0	53	3	1	0
20	28	0	24	0	37	0	89	4	0	0
21	0	0	0	0	3	0	3	0	0	0
<b>Total</b>	<b>646</b>	<b>70</b>	<b>811</b>	<b>116</b>	<b>681</b>	<b>95</b>	<b>2138</b>	<b>100</b>	<b>281</b>	<b>100</b>

**1.2.3: Number of renal biopsy done on each individual patient**

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

In the native biopsy group, from 2005 to 2007, 2071 patients had renal biopsy done. 1762 patients had renal biopsy for the first time, 263 patients had biopsy done twice, 43 patients had biopsy done thrice and 3 patients had four or more biopsy done on them. Therefore about 14.9% of patients had a repeat native biopsy done (table 1.2.3(a)).

In the allograft biopsy group; over the same period, 214 patients underwent a graft biopsy. 146 patients had biopsy done once, 46 patients had biopsy done twice, 16 patients had biopsy done thrice and 6 patients had biopsy done four times or more (Table 1.2.3 (b)). As expected, there was a higher rate of repeat graft biopsies (31.8%).

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

Total no of biopsy/ patient	2005		2006		2007		Total n
	n	%	n	%	n	%	
1	523	85	676	86	563	84	1762
2	83	13	98	13	82	12	263
3	9	1	9	1	25	4	43
≥4	0	0	0	0	3	0	3
<b>Total no. of patients</b>	<b>615</b>	<b>100</b>	<b>783</b>	<b>100</b>	<b>673</b>	<b>100</b>	<b>2071</b>

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

Total no of biopsy/ patient	2005		2006		2007		Total N
	N	%	N	%	N	%	
1	36	75	61	70	49	62	146
2	10	21	17	20	19	24	46
3	2	4	7	8	7	9	16
≥4	0	0	2	2	4	5	6
<b>Total no. of patients</b>	<b>48</b>	<b>100</b>	<b>87</b>	<b>100</b>	<b>79</b>	<b>100</b>	<b>214</b>

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

### 1.2.4.1: Age distribution

Eighty one percent of native biopsies were done in patients older than 15 years old and in this group, 93.2% of the biopsies were done in patients less than 55 years age. Very few (6%) biopsies were done in patients older than 55 years old. (Table 1.2.4.1 (a))

In the graft biopsy group, 96.1% were done in patients older than 15 years old and of these, 85.4% were in the age group of 15 to less than 55 years. Only 10.7% 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 Selangor (23%), followed by WP Kuala Lumpur (16%) and Penang (13%). In the paediatric group (age < 15 years old), the highest number of renal biopsy were reported in WP Kuala Lumpur (29%), followed by Johor (24%) and Selangor (14%) (Table 1.2.4.1(c)).

Table 1.2.4.1(a): Age distribution of native renal biopsy, 2005-2007

Age group	2005	2006	2007	Total	
	n	n	n	n	%
<15	127	133	145	405	19
15-<25	170	236	189	595	28
25-<35	145	183	152	480	22
35-<45	116	126	99	341	16
45-<55	59	79	61	199	9
55-<65	17	42	24	83	4
≥65	12	12	11	35	2
<b>Total</b>	<b>646</b>	<b>811</b>	<b>681</b>	<b>2138</b>	<b>100</b>

Table 1.2.4.1(b): Age distribution of renal allograft biopsy, 2005-2007

Age group (years)	2005	2006	2007	Total	
	n	n	n	n	%
<15	0	5	6	11	4
15-<25	15	26	16	57	20
25-<35	11	24	12	47	17
35-<45	23	25	32	80	29
45-<55	12	24	20	56	20
55-<65	6	8	9	23	8
≥65	3	4	0	7	2
<b>Total</b>	<b>70</b>	<b>116</b>	<b>95</b>	<b>281</b>	<b>100</b>

Table 1.2.4.1(c): Age group distribution of reported renal biopsies by state, 2005-2007

Year of biopsy State	2005						2006						2007						Total					
	Age < 15		Age ≥ 15		Age < 15		Age ≥ 15		Age < 15		Age ≥ 15		Age < 15		Age ≥ 15		Age < 15		Age ≥ 15		Age < 15		Age ≥ 15	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Johor	29	22	67	11	24	17	81	10	45	30	53	8	98	24	201	10								
Kedah	0	0	2	0	0	0	10	1	4	3	20	3	4	1	32	2								
Kelantan	2	2	13	2	0	0	24	3	3	2	24	4	5	1	61	3								
Melaka	2	2	19	3	1	1	26	3	1	1	20	3	4	1	65	3								
Negeri Sembilan	11	8	26	5	6	4	27	3	10	7	25	4	27	6	78	5								
Pahang	0	0	0	0	6	4	38	5	6	4	5	1	12	3	43	2								
Perak	2	2	26	4	2	1	36	5	0	0	44	7	4	1	106	5								
Perlis	0	0	0	5	0	0	0	0	0	0	0	0	0	0	0	0								
Penang	14	11	96	16	18	14	104	13	19	12	65	10	51	12	265	13								
Sabah	1	1	38	6	5	4	46	6	5	3	42	7	11	3	126	6								
Sarawak	6	5	68	12	6	4	95	12	4	3	59	10	16	4	222	11								
Selangor	17	13	120	20	28	20	180	23	17	11	162	26	62	14	462	23								
Terengganu	2	2	16	3	1	1	5	1	0	0	0	0	3	1	21	1								
WP Kuala Lumpur	41	32	98	17	41	30	117	15	37	24	106	17	119	29	321	16								
<b>Total</b>	<b>127</b>	<b>100</b>	<b>589</b>	<b>104</b>	<b>138</b>	<b>100</b>	<b>789</b>	<b>100</b>	<b>151</b>	<b>100</b>	<b>625</b>	<b>100</b>	<b>416</b>	<b>100</b>	<b>2003</b>	<b>100</b>								

### 1.2.4.2: Gender distribution

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 15<sup>th</sup> Report of The Malaysian Dialysis and Transplant Registry.

Table 1.2.4.2(a): Gender distribution of native renal biopsy, 2005-2007

Gender	2005	2006	2007	Total	
	n	n	n	n	%
Male	231	332	265	828	40
Female	384	451	408	1,243	60
<b>Total</b>	<b>615</b>	<b>783</b>	<b>673</b>	<b>2071</b>	<b>100</b>

Table 1.2.4.2(b): Gender distribution of renal allograft biopsy, 2005-2007

Gender	2005	2006	2007	Total	
	n	n	n	n	%
Male	29	59	49	137	64
Female	19	28	30	77	36
<b>Total</b>	<b>48</b>	<b>87</b>	<b>79</b>	<b>214</b>	<b>100</b>

### 1.2.4.3: Racial distribution

Among the patients who had native kidney biopsy, majority were Malays (57%), followed by Chinese (24%)(Table 1.2.4.3(a)). In the allograft biopsy group, majority of patients were Chinese (56%) followed by Malays (29%) (Table 1.2.4.3(b))

Table 1.2.4.3(a): Racial distribution of native renal biopsy, 2005-2007

Race	2005	2006	2007	Total	
	n	n	n	n	%
Malay	344	442	391	1,177	57
Chinese	150	188	164	502	24
Indian	43	60	38	141	7
Others	78	93	80	251	12
<b>Total</b>	<b>615</b>	<b>783</b>	<b>673</b>	<b>2071</b>	<b>100</b>

Table 1.2.4.3(b): Racial distribution of renal allograft biopsy, 2005-2007

Race	2005	2006	2007	Total	
	n	n	n	n	%
Malay	14	23	26	63	29
Chinese	28	52	39	119	56
Indian	3	9	9	21	10
Others	3	3	5	11	5
<b>Total</b>	<b>48</b>	<b>87</b>	<b>79</b>	<b>214</b>	<b>100</b>

**1.2.5: Renal Biopsy Report Analysis**

A total of 2419 renal biopsies were performed from 2005 to 2007. 515 (21.3%) 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. 58(2.4%) biopsies were classified as missing because the histopathology reports were not submitted to MRRB. The remaining 76.3% reported 10 or more glomeruli.

Table 1.2.5: Number of glomeruli obtained at each biopsy by centres, 2005-2007

Total no. of glomeruli Centre	Less 10		10 & above		Missing		Total	
	n	%	n	%	n	%	n	%
1	54	18	250	82	1	0	305	100
2	7	19	29	81	0	0	36	100
3	37	14	229	86	0	0	266	100
4	4	8	44	88	2	4	50	100
5	22	20	88	80	0	0	110	100
6	32	24	93	71	6	5	131	100
7	13	16	66	84	0	0	79	100
8	9	35	17	65	0	0	26	100
9	30	43	39	57	0	0	69	100
10	67	32	141	67	2	1	210	100
11	4	9	20	43	22	48	46	100
12	2	22	7	78	0	0	9	100
13	8	33	13	54	3	13	24	100
14	28	42	37	56	1	2	66	100
15	11	8	122	91	1	1	134	100
16	69	29	169	71	0	0	238	100
17	15	11	118	87	2	1	135	100
18	53	16	268	79	18	5	339	100
19	9	17	45	83	0	0	54	100
20	41	46	48	54	0	0	89	100
21	0	0	3	100	0	0	3	100
<b>Total</b>	<b>515</b>	<b>21.3</b>	<b>1846</b>	<b>76.3</b>	<b>58</b>	<b>2.4</b>	<b>2419</b>	<b>100</b>

**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 centre for processing and reporting. A total of 44.9% of HPE slides were read locally and 55.1% were sent to another laboratory (Table 1.2.6 (a))

The histopathology laboratories were coded by a number. (Table 1.2.6 (b)).

Table 1.2.6(a): Distribution of biopsy specimens to histopathology laboratories by participating centres, 2005-2007

Centre	Local histopathology laboratories						Outside histopathology laboratories						All				
	2005 n	2005 %	2006 n	2006 %	2007 n	2007 %	Total n	Total %	2005 n	2005 %	2006 n	2006 %	2007 n	2007 %	Total n	Total %	
1	58	19	58	19	98	32	214	70	39	13	49	16	3	1	91	30	100
2	90	34	98	37	31	12	219	82	2	6	10	28	24	67	36	100	100
3	13	26	17	34	11	22	41	82	7	3	6	2	34	13	47	18	100
4	26	24	37	34	44	40	107	97	0	0	1	2	8	16	9	18	100
5	9	11	7	9	8	10	24	30	2	2	1	1	0	0	3	3	100
6	9	11	7	9	8	10	24	30	31	24	44	34	56	43	131	100	100
7	9	35	5	19	8	31	22	85	18	23	21	27	16	20	55	70	100
8	21	30	26	38	21	30	68	99	1	4	0	0	3	12	4	15	100
9	68	32	81	39	60	29	209	100	0	0	1	1	0	0	1	1	100
10	0	0	11	24	0	0	11	24	0	0	31	67	4	9	35	76	100
11	18	75	6	25	0	0	24	100	0	0	2	22	7	78	9	100	100
12	0	0	0	0	9	14	9	14	15	23	24	36	18	27	57	86	100
13	36	27	37	27	41	30	114	84	39	29	51	38	44	33	134	100	100
14	9	3	12	4	0	0	21	6	74	31	101	42	63	26	238	100	100
15	2	4	0	0	0	0	2	4	6	4	14	10	1	1	21	16	100
16	9	3	12	4	0	0	21	6	81	24	128	38	109	32	318	94	100
17	2	4	0	0	0	0	2	4	14	26	24	44	14	26	52	96	100
18	28	31	24	27	37	42	89	100	28	31	24	27	37	42	89	100	100
19	0	0	0	0	0	0	0	0	0	0	0	0	3	100	3	100	100
20	359		395		331		1085		357		532		445		1334		
21																	
<b>Total</b>	<b>359</b>		<b>395</b>		<b>331</b>		<b>1085</b>		<b>357</b>		<b>532</b>		<b>445</b>		<b>1334</b>		<b>2419</b>

Table 1.2.6(b): Histopathology laboratories receiving renal biopsy specimens, 2005-2007

Histopathology Laboratories	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
1	0	0	3	0	1	0	4	0
3	26	4	37	5	44	6	107	4
4	0	0	0	0	9	1	9	0
5	211	29	363	39	428	55	1002	42
6	19	2	6	1	6	1	31	1
7	23	3	26	3	37	5	86	4
8	105	15	125	14	42	5	272	11
10	11	2	12	1	0	0	23	1
11	18	3	13	1	16	2	47	2
12	96	13	105	11	97	13	298	12
13	0	0	11	1	0	0	11	0
16	38	5	69	7	2	0	109	5
17	15	2	25	3	17	2	57	2
18	154	22	132	14	77	10	363	16
<b>Total</b>	<b>716</b>	<b>100</b>	<b>927</b>	<b>100</b>	<b>776</b>	<b>100</b>	<b>2419</b>	<b>100</b>

### 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 (26%) (Table 1.3.1 (a)). A total of 1157 (54%) patients had normal renal function at time of biopsy, 28% 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, 2005-2007

Indications	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
Urinary abnormalities	166	26	215	27	184	27	565	26
Acute Nephritic syndrome	60	9	65	8	55	8	180	8
Nephrotic syndrome	309	48	368	45	317	47	994	46
Nephrotic-nephritic syndrome	21	3	38	5	49	7	108	5
Unknown	90	14	125	15	76	11	291	14
<b>Total</b>	<b>646</b>	<b>100</b>	<b>811</b>	<b>100</b>	<b>681</b>	<b>100</b>	<b>2138</b>	<b>100</b>

Patient may have more than one indication for renal biopsy

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

Renal function	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
Normal	362	56	410	51	385	57	1157	54
Impaired	149	23	236	29	216	32	601	28
Missing / unknown	135	21	165	20	80	12	380	18
<b>Total</b>	<b>646</b>	<b>100</b>	<b>811</b>	<b>100</b>	<b>681</b>	<b>100</b>	<b>2138</b>	<b>100</b>

### 1.3.2: Histopathological Diagnosis

In the native kidney biopsy group, the three most common primary glomerulonephritis (GN) reported were focal segmental glomerulosclerosis (FSGS) (36%), minimal change disease (32%), followed by IgA nephropathy (15%). Membranous nephropathy only comprises 8% of the total primary GN subgroup. (Table 1.3.2).

Lupus nephritis was the commonest secondary GN contributing 87% of cases. (Table 1.3.2 )

The most common tubulointerstitial disease reported was acute tubular necrosis (63%). (Table 1.3.2)

Table 1.3.2: Histopathology of all native renal biopsies, 2005-2007

Type	Histopathological Diagnosis	2005		2006		2007		Total	
		n	%	n	%	n	%	n	%
<b>Primary GN</b> (n=968)	Minimal change	94	33	103	28	110	35	307	32
	FSGS	101	35	144	39	104	33	349	36
	Ig A nephropathy	36	13	62	17	50	16	148	15
	Membranous nephropathy	21	7	32	9	28	9	81	8
	Membrano-proliferative	12	4	10	3	4	1	26	3
	Mesangial Proliferative	16	6	10	3	11	4	37	4
	Crescentic ANCA	1	0	0	0	0	0	1	0
	Idiopathic Crescentic	6	2	9	2	3	1	18	2
	Unknown	0	0	0	0	1	0	1	0
<b>Subtotal</b>	<b>287</b>	<b>100</b>	<b>370</b>	<b>100</b>	<b>311</b>	<b>100</b>	<b>968</b>	<b>100</b>	
<b>Secondary GN</b> (n=954)	Lupus nephritis	270	89	309	86	255	87	834	87
	Other Infection	0	0	1	0	1	0	2	0
	Henoch Schonlein purpura	3	1	2	1	2	1	7	1
	HUS / TTP	2	1	1	0	0	0	3	0
	Amyloidosis	1	0	4	1	1	0	6	1
	Systemic vasculitis	1	0	3	1	2	1	6	1
	Postinfectious GN	17	6	12	3	12	4	41	4
	Malignancy	0	0	1	0	0	0	1	0
	Light/Heavy chain disease	0	0	0	0	1	0	1	0
	Diabetic nephropathy	8	3	26	7	12	4	46	5
	Multiple myeloma	0	0	1	0	1	0	2	0
Unknown	0	0	0	0	5	2	5	1	
<b>Subtotal</b>	<b>302</b>	<b>100</b>	<b>360</b>	<b>100</b>	<b>292</b>	<b>100</b>	<b>954</b>	<b>100</b>	
<b>Tubulointerstitial disease</b> (n=117)	Acute interstitial nephritis	5	24	7	14	6	13	18	15
	Acute tubular necrosis	10	48	33	67	31	66	74	63
	Chronic interstitial nephritis	6	29	9	18	10	21	25	21
	<b>Subtotal</b>	<b>21</b>	<b>100</b>	<b>49</b>	<b>100</b>	<b>47</b>	<b>100</b>	<b>117</b>	<b>100</b>
<b>Vascular</b> (n=17)	Atherosclerosis	0	0	0	100	2	25	2	12
	Benign/malignant hypertension	2	100	7	100	5	63	14	82
	Unknown	0	0	0	0	1	13	1	6
	<b>Subtotal</b>	<b>2</b>	<b>100</b>	<b>7</b>	<b>100</b>	<b>8</b>	<b>100</b>	<b>17</b>	<b>100</b>
<b>Hereditary</b> (n=7)	Alport's syndrome	0	0	2	50	0	0	2	29
	Thin basement membrane disease	1	50	1	25	0	0	2	29
	Others	1	50	1	25	1	100	3	43
	<b>Subtotal</b>	<b>2</b>	<b>100</b>	<b>4</b>	<b>100</b>	<b>1</b>	<b>100</b>	<b>7</b>	<b>100</b>
<b>Advance GN</b>		15	100	18	100	16	100	49	100
<b>Others</b>		0	0	2	100	10	100	12	100

\* Patients may have either one or more histopathology or inconclusive report

**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 focal segmental glomerulosclerosis (26.1%), followed by minimal change (25.7%) and lupus nephritis (23.9%) (Table 1.3.3.1)

Table 1.3.3.1: Histopathological diagnosis in patients presenting with nephrotic syndrome

Histopathological Diagnosis		n	%
Primary GN	Minimal Change	260	25.7
	FSGS	263	26.1
	Ig A nephropathy	40	4.0
	Membranous nephropathy	59	5.9
	Membrano-proliferative	16	1.6
	Mesangial proliferative GN-non IgA	17	1.7
	Crescentic	3	0
	Unknown	1	0
	<b>Sub total</b>	<b>659</b>	<b>65</b>
Secondary GN	Lupus nephritis	241	23.9
	HUS/TTP	1	0.1
	Amyloidosis	4	0.4
	Systemic vasculitis	1	0.1
	Post infectious GN	7	0.7
	Diabetic nephropathy	20	2.0
	Unknown	4	0.4
<b>Sub total</b>	<b>278</b>	<b>28</b>	
Others	71	7	
<b>Total</b>	<b>1008</b>	<b>100</b>	

\* 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 was the commonest histopathology reported in the primary GN group was IgA (13%); while the most common secondary GN was lupus nephritis (59%).(Table 1.3.3.2).

Table 1.3.3.2: Histopathological diagnosis in patients presenting with urine abnormalities, 2005-2007

Histopathological Diagnosis		n	%
Primary GN	Minimal Change	28	5
	FSGS	47	9
	Ig A nephropathy	69	13
	Membranous nephropathy	15	3
	Membrano-proliferative	3	1
	Mesangial Proliferative GN-non IgA	14	2
	Idiopathic Crescentic	2	0
	<b>Sub total</b>	<b>178</b>	<b>33</b>
Secondary GN	Other Infection	2	0
	Lupus Nephritis	315	59
	Henoch Schonlein purpura	2	0
	Amyloidosis	2	0
	Post infectious GN	6	1
	Diabetic nephropathy	5	1
	Multiple myeloma	1	0
<b>Sub total</b>	<b>333</b>	<b>61</b>	
Others	33	6	
<b>Total</b>	<b>544</b>	<b>100</b>	

\* 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 commonest histopathology among the primary GN was IgA (9%) 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-nephrotic syndrome, 2005-2007

Histopathological diagnosis		n	%
<b>Primary GN</b>	Minimal Change	8	6
	FSGS	9	8
	Ig A nephropathy	11	9
	Membranous nephropathy	2	2
	Membrano-proliferative	2	2
	Messangial Proliferative GN-non IgA	2	2
	Idiopathic Crescentic	1	1
<b>Sub total</b>	<b>35</b>	<b>30</b>	
<b>Secondary GN</b>	Lupus Nephritis	58	49
	Henoch Schonlein purpura	2	2
	Systemic vasculitis	1	1
	Post infectious GN	5	4
	Diabetic nephropathy	2	2
<b>Sub total</b>	<b>68</b>	<b>58</b>	
<b>Others</b>		14	12
<b>Total</b>		<b>117</b>	<b>100</b>

\* 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 (Table 1.3.3.4)

Table 1.3.3.4: Histopathological diagnosis in patients presenting with nephritic syndrome, 2005-2007

Histopathological Diagnosis		n	%
<b>Primary GN</b>	Minimal Change	7	4
	FSGS	15	9
	Ig A nephropathy	12	6
	Membranous nephropathy	2	1
	Membrano-proliferative	3	2
	Messangial Proliferative GN-non IgA	3	2
	Idiopathic Crescentic	5	3
<b>Sub total</b>	<b>47</b>	<b>27</b>	
<b>Secondary GN</b>	Lupus Nephritis	91	52
	Henoch Schonlein purpura	1	1
	Systemic vasculitis	2	1
	Post infectious GN	15	9
	Diabetic nephropathy	4	2
<b>Sub total</b>	<b>113</b>	<b>65</b>	
<b>Others</b>		14	8
<b>Total</b>		<b>174</b>	<b>100</b>

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

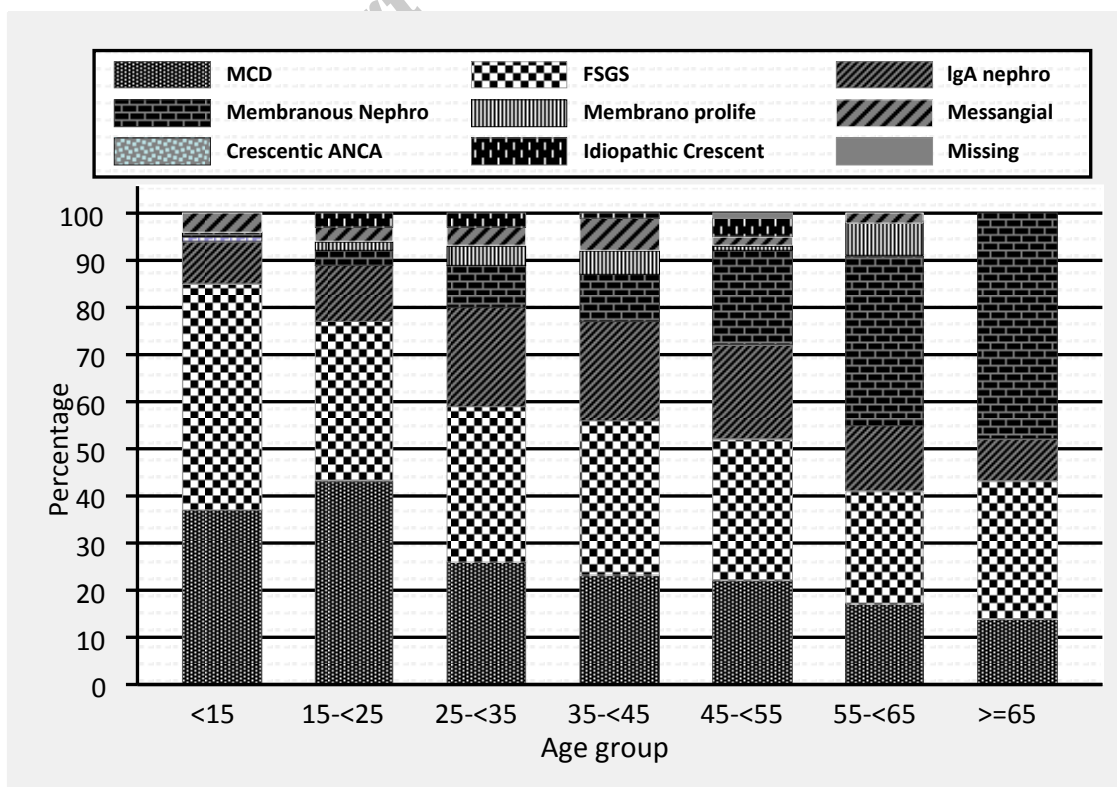
**1.3.3.5 Primary GN according to various age group**

FSGS was the commonest GN in the <15 year age group (48%) and also in adults between 25 - <55 years old(32%). This was followed by minimal change disease; <15 years (36%) and adults age (30.2%). However the commonest GN in the 15- 25 year age group was minimal change disease (43%). In patients above 55 years of age the commonest primary GN was membranous nephropathy (39.7%) (Table 1.3.3.5)

Table 1.3.3.5: Primary GN according to the various age group, 2005 -2007

	<15		15-<25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Minimal change disease	83	37	116	43	49	26	31	23	18	22	7	17	3	14	307	32
FSGS	108	48	92	34	64	33	44	33	25	30	10	24	6	29	349	36
Ig A Nephropathy	21	9	34	12	41	21	28	21	16	20	6	14	2	9	148	15
Membranous nephropathy	2	1	7	3	18	9	13	10	16	20	15	36	10	48	81	8
Membrano proliferative	3	1	5	2	7	4	7	5	1	1	3	7	0	0	26	3
Messangial proliferative	8	4	8	3	8	4	10	7	2	2	1	2	0	0	37	4
Crescentic ANCA	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
Idiopathic crescentic	1	0	8	3	5	3	1	1	3	4	0	0	0	0	18	2
Missing	0	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0
<b>Total</b>	<b>227</b>	<b>100</b>	<b>270</b>	<b>100</b>	<b>192</b>	<b>100</b>	<b>134</b>	<b>100</b>	<b>82</b>	<b>100</b>	<b>42</b>	<b>100</b>	<b>21</b>	<b>100</b>	<b>968</b>	<b>100</b>

Figure 1.3.3.5: Primary GN according to the various age group, 2005 -2007



## **CHAPTER 2**

### **Primary Glomerulonephritis**

Sunita Bavanandan

Lim Soo Kun

Lee Han Wei

Prelim Report Awaiting Approval from KKM

## 2.1: Introduction

This chapter covers the main primary glomerulonephritis that were reported to the MRRB from the years 2005-2007, namely minimal change disease, focal segmental glomerulosclerosis, idiopathic membranous glomerulonephritis and IgA nephropathy.

## 2.2: Minimal Change Disease

### 2.2.1: Introduction

Minimal change disease is defined by absence of histological glomerular abnormality. If electron microscopy were performed evidence of epithelial cell foot process fusion would be present.

### 2.2.2: Patient population and characteristics

A total of 224 cases of minimal change disease were reported in 2005-2007. The mean age of the patients at the time of biopsy was  $28.6 \pm 12.5$  (Table 2.2.2) with a clear predominance in second and third decades of life (Table & Figure 2.2.2 (b)). The frequencies of age groups 15 to <25, and 25 to <35 were 52%, 22% and 14% respectively, which is 88% when combined. The diagnosis of minimal change disease is relatively rare after 55 years of age and our reported frequency was less than 4% in this age group.

There is a higher incidence of minimal change disease in males, with a ratio of 2:1 in the three-year registry data (overall 68% as compared to 32% in the female group. The racial group distribution in Malay, Chinese and Indian was 62%, 14% and 5% respectively.

Table 2.2.2(a): Demographic characteristics for minimal change disease, 2005-2007

Demographic characteristics		n	%
Age		28.6± 12.5 years	
Gender	Male	153	68
	Female	71	32
Race	Malay	139	62
	Chinese	32	14
	Indian	9	5
	Others	44	14

Figure 2.2.2(b): Age at time of biopsy (years) for minimal change disease, 2005-2007

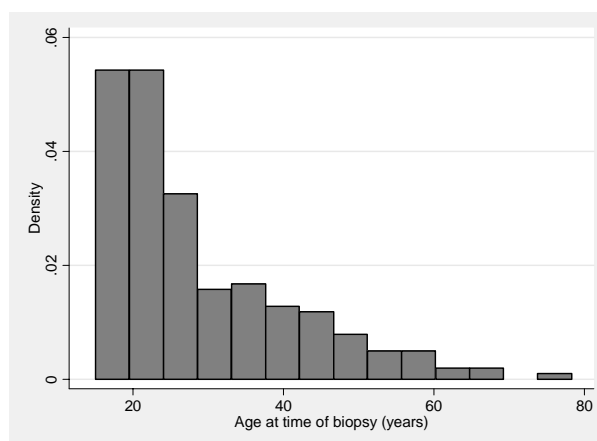


Table 2.2.2(b): Age group at time of biopsy (years) for minimal change disease, 2005-2007

Age group (years)	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
15-<25	32	42	47	58	37	56	116	52
25-<35	21	29	18	22	10	15	49	22
35-<45	11	14	10	12	10	15	31	14
45-<55	10	13	4	5	4	6	18	8
55-<65	1	1	2	2	4	6	7	3
≥65	1	1	1	1	1	2	3	1
<b>Total</b>	<b>76</b>	<b>100</b>	<b>82</b>	<b>100</b>	<b>66</b>	<b>100</b>	<b>224</b>	<b>100</b>

### 2.2.3: Clinical presentation

Nephrotic syndrome, as expected, was the most common presentation (83%). Other presentations were asymptomatic urine abnormality (9%), nephritic syndrome (3%), nephritic-nephrotic syndrome (3%) (Table 2.2.3(a)) Only 6% of patients were hypertensive (Table 2.2.3(b)). The mean level of 24 hours urine protein was  $3.1 \pm 1.1$ g, with a range 0.2-13.4g/day.

Table 2.2.3(a): Overall clinical presentation for minimal change disease, 2005-2007

Clinical Presentation	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	4	5	8	11	8	12	20	9
Nephritic syndrome	2	3	2	2	3	5	7	3
Nephrotic syndrome	69	91	68	83	50	75	187	83
Nephritic-Nephrotic syndrome	1	1	2	2	3	5	6	3
Missing	0	0	2	2	2	3	4	2
<b>Total</b>	<b>76</b>	<b>100</b>	<b>82</b>	<b>100</b>	<b>66</b>	<b>100</b>	<b>224</b>	<b>100</b>

Table 2.2.3 (b): Presence of hypertension in minimal change disease, 2005-2007

Hypertension	Total	
	n	%
Present	14	6
Absent	210	94
Missing	0	0
<b>Total</b>	<b>224</b>	<b>100</b>

#### 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: Clinical presentation by age group for minimal change disease, 2005-2007

Clinical presentations	15- <25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormalities	10	9	4	8	4	13	1	5	1	14	0	0	20	9
Nephritic syndrome	3	3	1	2	1	3	1	5	0	0	1	33	7	3
Nephrotic syndrome	96	82	43	88	25	81	16	90	5	72	2	67	187	83
Nephritic-Nephrotic syndrome	5	4	0	0	1	3	0	0	0	0	0	0	6	3
Missing	2	2	1	2	0	0	0	0	1	14	0	0	4	2
<b>Total</b>	<b>116</b>	<b>100</b>	<b>49</b>	<b>100</b>	<b>31</b>	<b>100</b>	<b>18</b>	<b>100</b>	<b>7</b>	<b>100</b>	<b>3</b>	<b>100</b>	<b>224</b>	<b>100</b>

**2.2.3.2: Clinical presentation by gender**

There are basically no differences between genders in terms of clinical presentation.

Table 2.2.3.2: Clinical presentation by gender for minimal change disease, 2005-2007

	2005		2006		2007		Total									
	Male	Female	Male	Female	Male	Female	Male	Female								
	n.	%	n	%	n	%	n	%								
Asymp.urine abnormality	2	4	2	8	3	5	5	22	7	16	1	5	12	8	8	11
Nephritic syndrome	0	0	2	8	2	3	0	0	2	5	1	5	4	3	3	4
Nephrotic syndrome	47	94	22	84	51	87	17	74	31	70	19	85	129	84	58	82
Nephritic-nephrotic syndr	1	2	0	0	2	3	0	0	3	7	0	0	6	4	0	0
Missing	0	0	0	0	1	2	1	4	1	2	1	5	2	1	2	3
<b>Total</b>	<b>50</b>	<b>100</b>	<b>26</b>	<b>100</b>	<b>59</b>	<b>100</b>	<b>23</b>	<b>100</b>	<b>44</b>	<b>100</b>	<b>22</b>	<b>100</b>	<b>153</b>	<b>100</b>	<b>71</b>	<b>100</b>

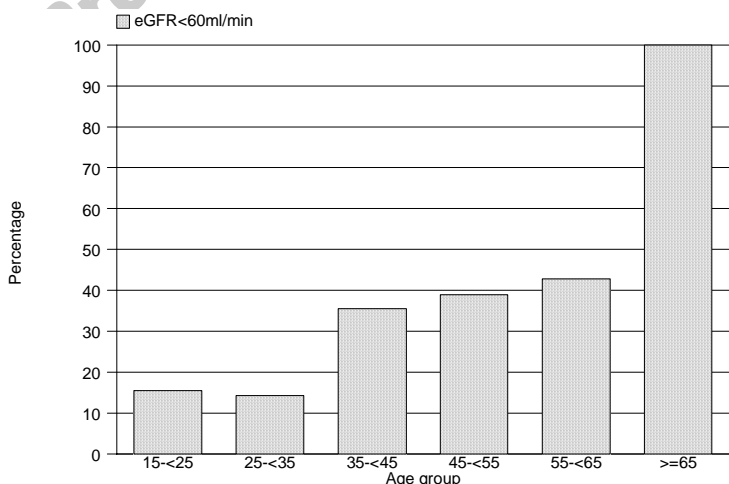
**2.2.4: Renal function at presentation**

The majority (78%) of subjects had eGFR>60: 41% with eGFR>90 ml/min/1.73m<sup>2</sup> and 37% with eGFR 60-89 ml/min/1.73m<sup>2</sup>. About a fifth of the subjects had eGFR < 60 ml/min/1.73m<sup>2</sup> but the majority of these patients (17%) were in the region of estimated eGFR 30-59 ml/min/1.73m<sup>2</sup> (Tables 2.2.4). However, we need to bear in mind the proportion with renal impairment is higher than expected for MCD, as one of the main indications for biopsy would have been renal impairment. In general, the older the patient the higher risk of renal impairment at presentation (Figure 2.2.4).

Table 2.2.4: Renal function at presentation by age group for minimal change disease, 2005-2007

eGFR (ml/min/1.73m <sup>2</sup> )	15- <25		25- <35		35- <45		45- <55		55- <65		≥ 65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
≥90	61	53	22	45	5	17	3	17	2	29	0	0	93	41
60-89	37	32	20	41	15	48	8	44	2	29	0	0	82	37
30-59	13	11	5	10	10	32	7	39	1	13	2	67	38	17
15-29	5	4	2	4	0	0	0	0	0	0	0	0	7	3
<15	0	0	0	0	1	3	0	0	2	29	1	33	4	2
<b>Total</b>	<b>116</b>	<b>100</b>	<b>49</b>	<b>100</b>	<b>31</b>	<b>100</b>	<b>18</b>	<b>100</b>	<b>7</b>	<b>100</b>	<b>3</b>	<b>100</b>	<b>224</b>	<b>100</b>

Figure 2.2.4: Impaired renal function by age group for minimal change disease, 2005-2007



## 2.3: Focal Segmental Glomerulosclerosis

### 2.3.1: Introduction

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

### 2.3.2: Patient population and characteristics

A total of 241 cases of FSGS were reported. The mean age at the time of biopsy was  $32.1 \pm 13.5$ . The first three decades of life were the predominant age groups in this type of renal disease. (Table 2.3.2 (b)). After the age of 55, the frequency rate was only 6% compared to other age groups (Table 2.3.2(b))

FSGS was slightly more common in males (56%) compared to females (44%). The distribution according to ethnicity was 61% in Malay, 14% in Chinese, 7% in Indian and 18% in others.

Table 2.3.2(a): Demographic characteristics for FSGS, 2005-2007

Demographic characteristics	n	%
Age	32.1 ± 13.5	
Gender		
Male	136	56
Female	105	44
Race		
Malay	147	61
Chinese	34	14
Indian	16	7
Others	44	18

Figure 2.3.2(b): Age at time of biopsy (years) for FSGS, 2005-2007

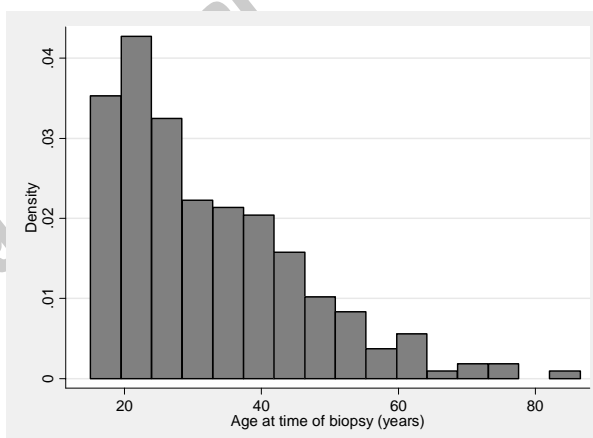


Table 2.3.2(b): Age group at time of biopsy (years) for FSGS, 2005-2007

Age group (years)	2005		2006		2007		Total	
	n	%	n.	%	n	%	n	%
15-<25	18	31	45	42	29	38	92	38
25-<35	16	27	23	22	25	32	64	27
35-<45	13	21	18	17	13	17	44	19
45-<55	8	14	9	9	8	10	25	10
55-<65	3	5	5	5	2	3	10	4
≥65	1	2	5	5	0	0	6	2
<b>Total</b>	<b>59</b>	<b>100</b>	<b>105</b>	<b>100</b>	<b>77</b>	<b>100</b>	<b>241</b>	<b>100</b>

**2.3.3: Clinical Presentation**

Nephrotic syndrome was the most common reported clinical presentation (69%). Other reported presentations were asymptomatic urine abnormality (18%), nephritic syndrome (5%), nephritic-nephrotic syndrome (3%) (Table & Figure 2.3.3(a)). Hypertension was present in 8% (Table 2.3.3 (b)) with a higher likelihood in older age groups. The mean level of 24 hours urine protein was  $3.9 \pm 1.0$  with a range of 2.8 to 8.4g/day.

Table 2.3.3 (a): Overall clinical presentation for FSGS, 2005-2007

Clinical Presentation	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	10	17	19	18	15	19	44	18
Nephritic syndrome	3	5	5	5	4	5	12	5
Nephrotic syndrome	42	71	75	71	50	65	167	69
Nephritic-Nephrotic syndrome	1	2	0	0	6	8	7	3
Missing	3	5	6	6	2	3	11	5
<b>Total</b>	<b>59</b>	<b>100</b>	<b>105</b>	<b>100</b>	<b>77</b>	<b>100</b>	<b>241</b>	<b>100</b>

Figure 2.3.3 (a): Overall clinical presentation for FSGS, 2005-2007

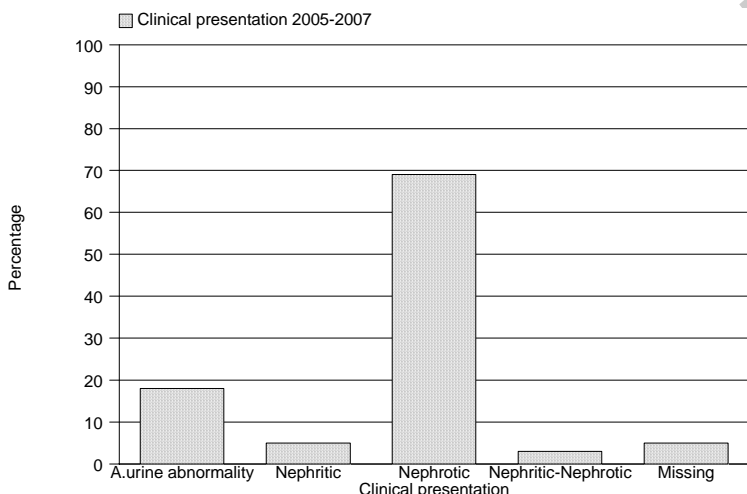


Table 2.3.3 (b): Presence of hypertension in FSGS, 2005-2007

Hypertension	Total	
	n	%
Present	19	8
Absent	222	92
Missing	0	0
<b>Total</b>	<b>241</b>	<b>100</b>

### 2.3.3.1: Clinical presentation by age

Nephrotic syndrome remains the commonest presentation across all age groups, accounting for 55-90% of presentations.

Table 2.3.3.1: Clinical presentation by age group for FSGS, 2005-2007

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	10	12	18	28	13	30	3	12	0	0	0	0	44	18
Nephritic syndrome	4	4	6	9	1	2	0	0	1	10	0	0	12	5
Nephrotic syndrome	74	80	35	55	27	61	18	72	9	90	4	67	167	69
Nephritic-Nephrotic syndrome	2	2	3	5	1	2	1	4	0	0	0	0	7	3
Missing	2	2	2	3	2	5	3	12	0	0	2	33	11	5
<b>Total</b>	<b>92</b>	<b>100</b>	<b>64</b>	<b>100</b>	<b>44</b>	<b>100</b>	<b>25</b>	<b>100</b>	<b>10</b>	<b>100</b>	<b>6</b>	<b>100</b>	<b>241</b>	<b>100</b>

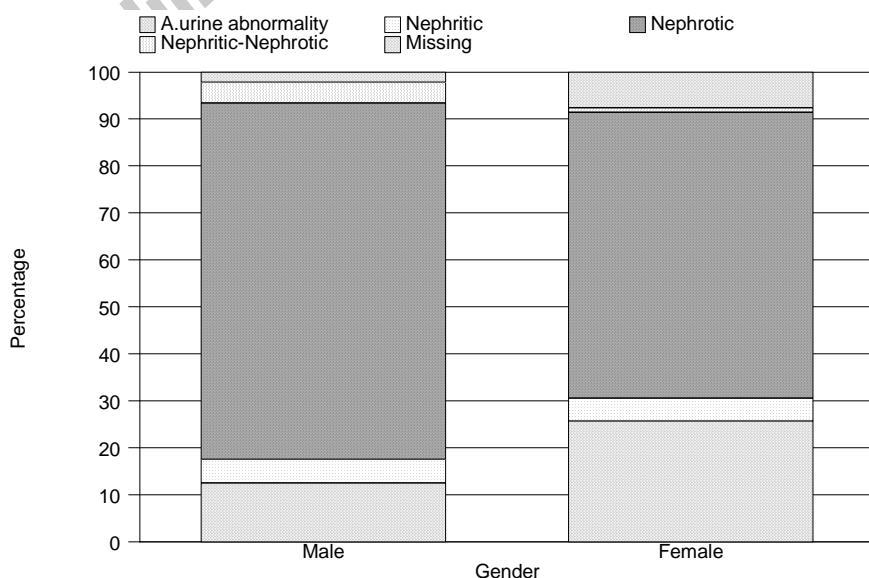
### 2.3.3.2: Clinical presentation by gender

From the 3 years of collected data, nephrotic syndrome appears more common in males while there are more females presenting as asymptomatic urine abnormality. The reason for this is unclear.

Table 2.3.3.2: Clinical presentation by gender for FSGS, 2005-2007

Clinical Presentation	2005		2006		2007		Total									
	Male	Female	Male	Female	Male	Female	Male	Female								
	n	%	n	%	n	%	n	%								
Asymptomatic urine abnormality	3	10	7	25	6	10	13	28	8	17	7	24	17	13	27	26
Nephritic syndrome	1	3	2	7	3	6	2	4	3	6	1	3	7	5	5	5
Nephrotic syndrome	26	84	16	57	46	79	29	62	31	66	19	63	103	76	64	60
Nephritic-Nephrotic syndrome	1	3	0	0	0	0	0	0	5	11	1	3	6	4	1	1
Missing	0	0	3	11	3	5	3	6	0	0	2	7	3	2	8	8
<b>Total</b>	<b>31</b>	<b>100</b>	<b>28</b>	<b>100</b>	<b>58</b>	<b>100</b>	<b>47</b>	<b>100</b>	<b>47</b>	<b>100</b>	<b>30</b>	<b>100</b>	<b>136</b>	<b>100</b>	<b>105</b>	<b>100</b>

Figure 2.3.3.2: Clinical presentation by gender for focal segmental glomerulosclerosis, 2005-2007



**2.3.4: Renal function at presentation**

Majority of cases (57%) had eGFR > 60 ml.min.1.73m<sup>2</sup> at presentation (table 2.3.4 (a)). There were 28% of cases in the eGFR range of 30-59 ml/min/1.73m<sup>2</sup>; 12% were 15-29ml/min/1.73m<sup>2</sup> and 3% were <15ml/min/1.73m<sup>2</sup> (Table & Figure 2.3.4.1).

Table 2.3.4(a): Impaired renal function in FSGS by year, 2005-2007

Renal function	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
eGFR ≥ 60	27	46	64	61	47	61	138	57
eGFR < 60	32	54	41	39	30	39	103	43
<b>Total</b>	<b>59</b>	<b>100</b>	<b>105</b>	<b>100</b>	<b>77</b>	<b>100</b>	<b>241</b>	<b>100</b>

**2.3.4.1 Renal function at presentation by age**

In general, there was a higher risk of renal impairment with increasing age (Table 2.3.4.1 & Figure 2.3.4.1 (a&b)).

Table 2.3.4.1: Renal function at presentation by age group for FSGS, 2005-2007

eGFR (ml/min/1.73m <sup>2</sup> )	15- <25		25- <35		35- <45		45- <55		55- <65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
≥90	35	38	16	25	6	14	0	0	0	0	0	0	57	24
60-89	31	34	25	39	11	25	9	36	3	30	2	33	81	33
30-59	20	22	14	22	17	39	10	40	4	40	2	33	67	28
15-29	4	4	9	14	9	20	4	16	2	20	1	17	29	12
<15	2	2	0	0	1	2	2	8	1	10	1	17	7	3
<b>Total</b>	<b>92</b>	<b>100</b>	<b>64</b>	<b>100</b>	<b>44</b>	<b>100</b>	<b>25</b>	<b>100</b>	<b>10</b>	<b>100</b>	<b>6</b>	<b>100</b>	<b>241</b>	<b>100</b>

Figure 2.3.4.1(a): Renal function at presentation by age group for FSGS, 2005-2007

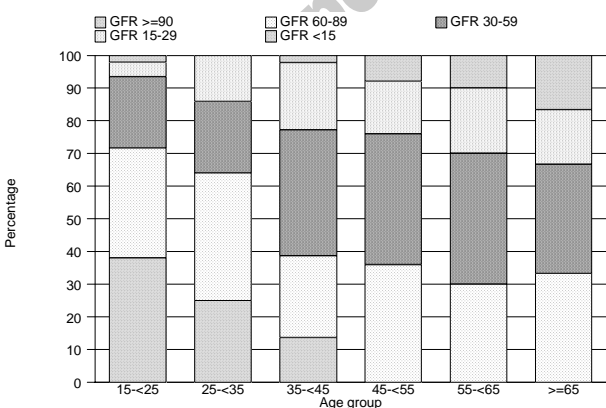
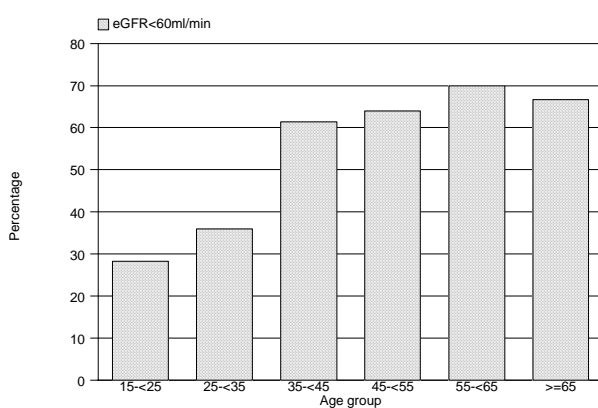


Figure 2.3.4.1(b): Impaired renal function in FSGS by age group, 2005-2007



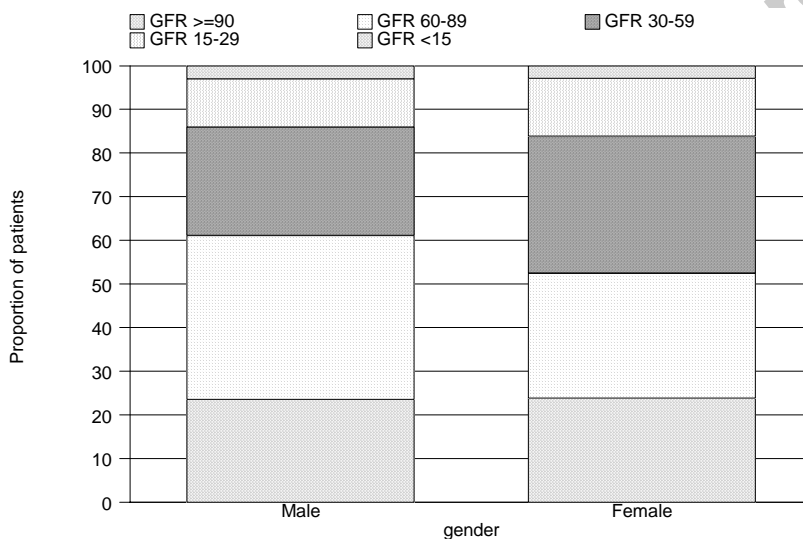
### 2.3.4.2 Renal function at presentation by gender

There were no significant gender differences with respect to renal function at presentation (Table & Figure 2.3.4.2).

Table 2.3.4.2: Renal function at presentation according to gender for FSGS, 2005-2007

eGFR (ml/min/1.73m <sup>2</sup> )	2005				2006				2007				Total			
	Male		Female		Male		Female		Male		Female		Male		Female	
	n	%	n.	%	No.	n	n	%	n	%	n	%	n.	%	n	%
≥90	9	29	4	14	16	28	11	23	7	14	10	34	32	24	25	24
60-89	7	23	7	25	23	40	14	30	21	45	9	30	51	37	30	29
30-59	10	32	11	39	12	20	13	28	12	26	9	30	34	25	33	31
15-29	3	10	5	18	6	10	8	17	6	13	1	3	15	11	14	13
<15	2	6	1	4	1	2	1	2	1	2	1	3	4	3	3	3
<b>Total</b>	<b>31</b>	<b>100</b>	<b>28</b>	<b>100</b>	<b>58</b>	<b>100</b>	<b>47</b>	<b>100</b>	<b>47</b>	<b>100</b>	<b>30</b>	<b>100</b>	<b>136</b>	<b>100</b>	<b>105</b>	<b>100</b>

Figure 2.3.4.2: Renal function at presentation according to gender for FSGS, 2005-2007



## 2.4: Idiopathic Membranous Nephropathy

### 2.4.1 Introduction

Membranous nephropathy is characterised by subepithelial immune deposits with spikes and thickening of the basement membrane. In Malaysia, this form of glomerulonephritis comprised only 8% of the total primary glomerulonephritis diagnosed, which is an unusually small number.

### 2.4.2: Patient population and characteristics

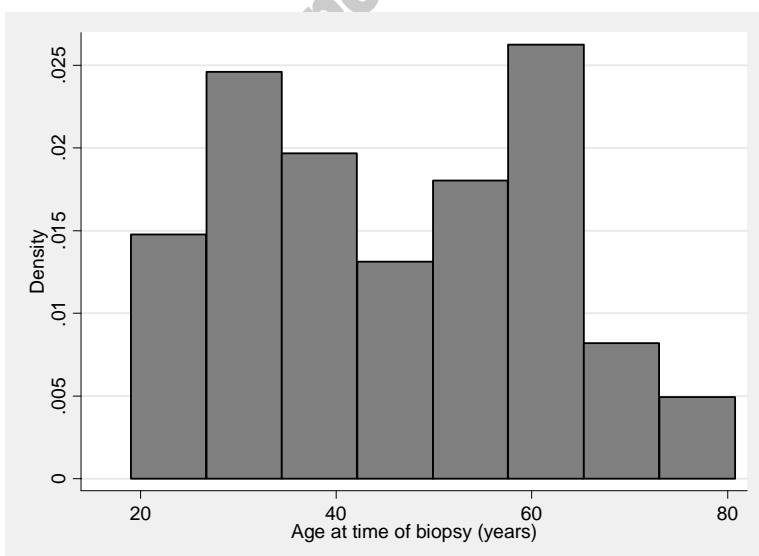
Over the three year period from 2005-2007, 79 cases of Idiopathic membranous nephropathy were reported. The mean age at biopsy was 46 + 15.5 years, with a range between 19 and 80.8 years. Similar to that described in literature<sup>(1,2)</sup>, there is a bi-modal peak in incidence, the first peak seen at 25-<35 years and the second in the 45-<65 years age groups ( Figure 2.4.2).

Overall, there was slightly more male than female.(Table 2.4.2). The overall racial distribution was 39% in Malays, 43% in Chinese, 4% in Indians and 10% in others. Data were missing in 4% of cases.

Table 2.4.2: Demographic characteristics for idiopathic membranous nephropathy, 2005-2007

Demographic characteristics		N=79	(%)
Age		46 ± 15.5	
Gender	Male	40	51
	Female	36	46
	Missing	3	3
Race	Malay	31	39
	Chinese	34	43
	Indian	3	4
	Others	8	10
	Missing	3	4

Figure 2.4.2: Age at time of biopsy (years) for idiopathic membranous nephropathy, 2005-2007



### 2.4.3: Clinical presentation

A little over half of the patients (57%) presented with overt nephrotic syndrome. Asymptomatic urinary abnormalities, nephritic syndrome and nephritic-nephrotic syndrome were found in 19%, 3% and 3% respectively (Table and Figure 2.4.3 (a)). Hypertension was present in 13% (Table 2.4.3(b)). The mean level of proteinuria was  $4.8 \pm 2.7$ g/d with a range from 1.7-19.8 g/d.

Table 2.4.3(a): Overall clinical presentation for idiopathic membranous nephropathy, 2005-2007

Clinical Presentations	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	1	5	7	22	7	27	15	19
Nephritic syndrome	1	5	1	3	0	0	2	3
Nephrotic syndrome	18	85	21	66	18	69	57	71
Nephritic-Nephrotic syndrome	1	5	1	3	0	0	2	3
Missing	0	0	2	6	1	4	3	4
<b>Total</b>	<b>21</b>	<b>100</b>	<b>32</b>	<b>100</b>	<b>26</b>	<b>100</b>	<b>79</b>	<b>100</b>

Figure 2.4.3(a): Overall clinical presentation for idiopathic membranous nephropathy, 2005-2007

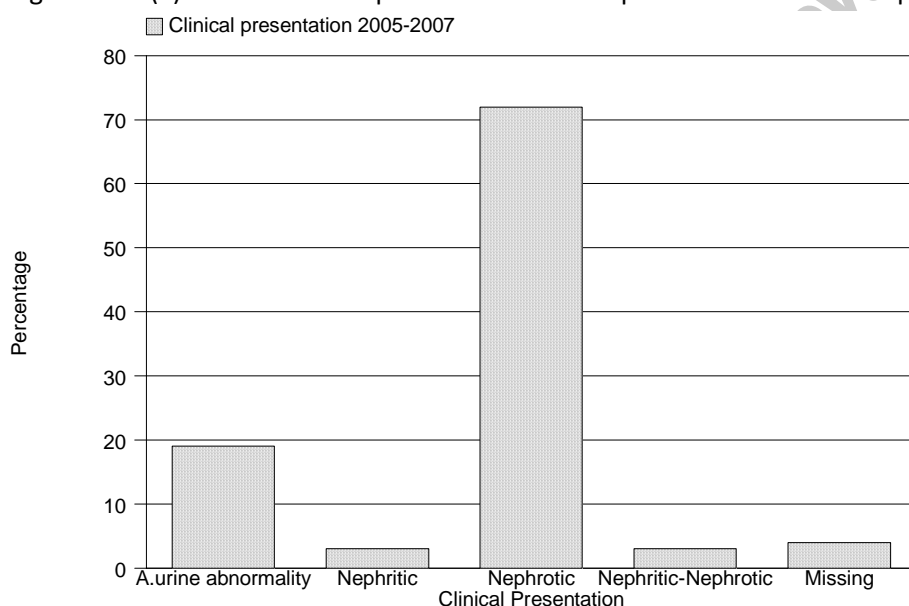


Table 2.4.3 (b): Presence of hypertension in idiopathic membranous nephropathy, 2005-2007

Hypertension	Total	
	n	%
Present	10	13
Absent	69	87
<b>Total</b>	<b>79</b>	<b>100</b>

**2.4.3.1: Clinical Presentation by age**

Nephrotic syndrome appeared to be the commonest clinical presentation in the younger age group. In the older patients, asymptomatic urine abnormality occurred at a higher frequency. (Table 2.4.3.1)

Table 2.4.3.1: Clinical presentation by age group for idiopathic membranous nephropathy, 2005-2007

Clinical Presentation	15- <25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	n	n	%
Asymptomatic urine abnormality	1	14	3	17	1	8	4	25	6	40	0	0	15	19
Nephritic syndrome	0	0	0	0	0	0	1	6	1	7	0	0	2	3
Nephrotic syndrome	5	72	14	77	11	84	10	63	7	47	10	100	57	71
Nephritic-Nephrotic syndrome	1	14	0	0	0	0	1	6	0	0	0	0	2	3
Missing	0	0	1	6	1	8	0	0	1	6	0	0	3	4
<b>Total</b>	<b>7</b>	<b>100</b>	<b>18</b>	<b>100</b>	<b>13</b>	<b>100</b>	<b>16</b>	<b>100</b>	<b>15</b>	<b>100</b>	<b>10</b>	<b>100</b>	<b>79</b>	<b>100</b>

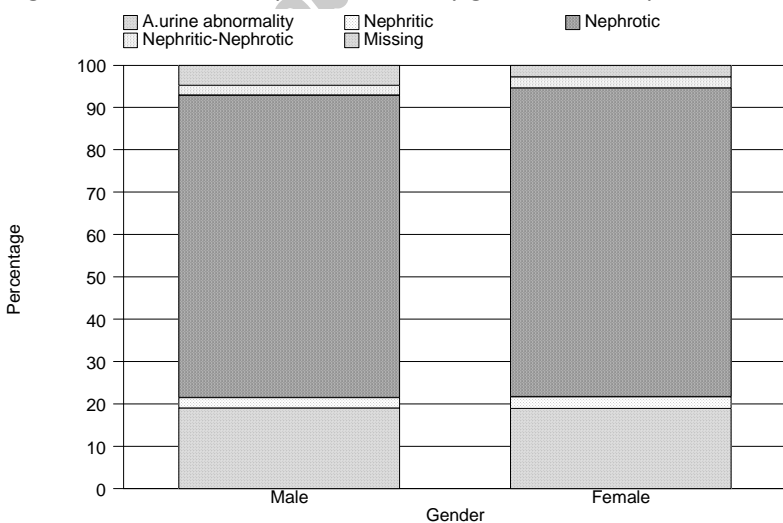
**2.4.3.2: Clinical presentation by gender**

Nephrotic syndrome was the commonest presentation in both genders. (Table& Figure 2.4.3.2)

Table 2.4.3.2: Clinical presentation by gender for idiopathic membranous nephropathy, 2005-2007

Clinical Presentations	Male		Female	
	n	%	n	%
Asymptomatic urine abnormality	8	20	7	19
Nephritic syndrome	1	2	1	3
Nephrotic syndrome	30	71	27	72
Nephritic-Nephrotic syndrome	1	2	1	3
Missing	2	5	1	3
<b>Total</b>	<b>42</b>	<b>100</b>	<b>37</b>	<b>100</b>

Figure 2.4.3.2: Clinical presentation by gender for idiopathic membranous nephropathy, 2005-2007



### 2.4.4: Renal function at presentation

Majority of cases (62%) had eGFR > 60 ml.min/1.73m<sup>2</sup> at presentation. There were 25% of cases in the eGFR range of 30-59 ml/min/1.73m<sup>2</sup>; 10% were 15-29ml/min/1.73m<sup>2</sup> and 3% were <15ml/min/1.73m<sup>2</sup> (Table & Figure 2.4.4(a)).

There is an increased incidence of renal impairment with increasing age (Table & Figure 2.4.4(a)) and in the male gender .Up to 45% of males vs. 30% females had a eGFR < 60 ml.min.1.73m<sup>2</sup> at presentation. (Table 2.4.4(b)).

Table 2.4.4 (a): Renal function at presentation by age group for idiopathic membranous nephropathy, 2005-2007

eGFR (ml/min/1.73m <sup>2</sup> )	15- <25		25- <35		35- <45		45- <55		55- <65		≥65		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
≥90	4	57	6	33	1	8	2	12	3	20	0	0	16	20
60-89	3	43	12	67	6	45	7	44	4	27	1	10	33	42
30-59	0	0	0	0	4	31	7	44	4	27	5	50	20	25
15-29	0	0	0	0	1	8	0	0	3	20	4	40	8	10
<15	0	0	0	0	1	8	0	0	1	6	0	0	2	3
<b>Total</b>	<b>7</b>	<b>100</b>	<b>18</b>	<b>100</b>	<b>13</b>	<b>100</b>	<b>16</b>	<b>100</b>	<b>15</b>	<b>100</b>	<b>10</b>	<b>100</b>	<b>79</b>	<b>100</b>

Figure 2.4.4 (a): Renal function at presentation by age group for idiopathic membranous nephropathy, 2005-2007

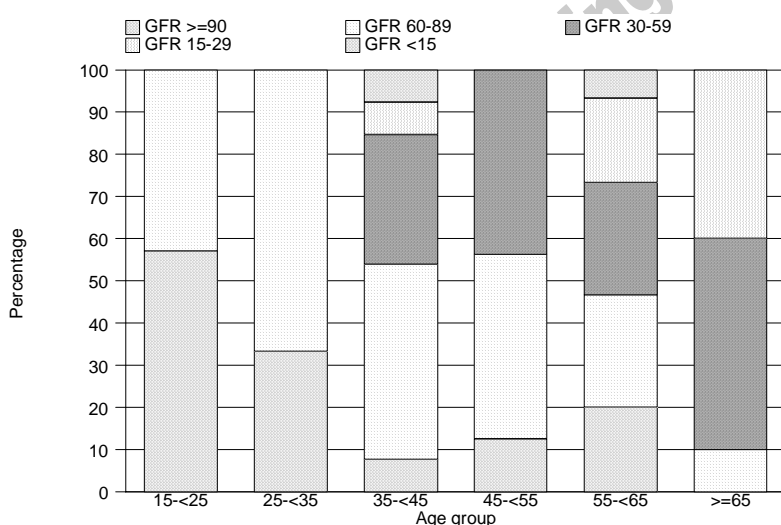


Table 2.4.4(b): Renal function at presentation according to gender for idiopathic membranous nephropathy, 2005-2007

eGFR (ml/min/1.73m <sup>2</sup> )	Male		Female	
	n	%	n	%
≥90	3	7	13	35
60-89	20	48	13	35
30-59	12	29	8	22
15-29	6	14	2	5
<15	1	2	1	3
<b>Total</b>	<b>42</b>	<b>100</b>	<b>37</b>	<b>100</b>

## 2.5: IgA 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 type of glomerulonephritis.

### 2.5.2 Patient population and characteristics

One hundred and twenty seven cases of IgA nephropathy were reported to the registry over the 3 year period of data collection. The mean age at biopsy was  $33.7 \pm 12.4$  years but there was a wide age range from 15 to 85.3 years. The majority of cases biopsied clustered around the 15 to 45-year age groups, peaking at the 25-<35 age group (Table & Figure 2.5.2(b)). Unlike the male preponderance of IgAN reported in literature, our data suggests an opposite trend. This may be due to the limited time period of data collection. The overall ethnic distribution was 48% in Malays, 27% in Chinese, 9% in Indians and 16% in others. (Table 2.5.2)

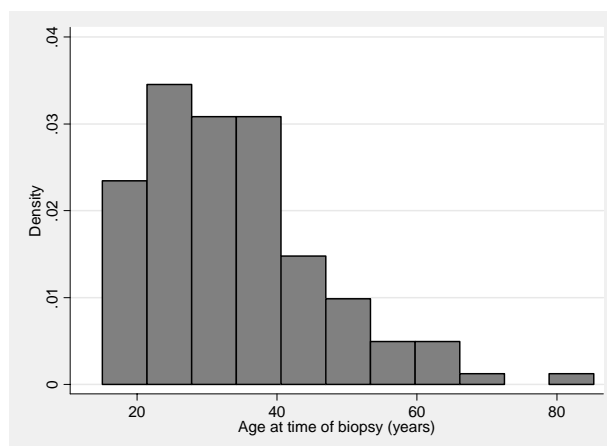
Table 2.5.2 (a): Demographic characteristics of patients with IgA nephropathy, 2005-2007

Demographic characteristics		N=127 (%)	
Age		33± 12.4	
Gender	Male	56	44
	Female	71	56
Race	Malay	61	48
	Chinese	34	27
	Indian	12	9
	Others	20	16

Table 2.5.2 (b): Age group at time of biopsy (years) for IgA nephropathy, 2005-2007

Age group (years)	2005		2006		2007		Total	
	n	%	n	%	No.	%	n	%
15-<25	4	13	16	31	14	31	34	27
25-<35	11	37	14	27	16	36	41	32
35-<45	10	33	11	21	7	16	28	21
45-<55	2	7	8	15	6	13	16	13
55-<65	2	7	2	4	2	4	6	5
≥65	1	3	1	2	0	0	2	2
<b>Total</b>	<b>30</b>	<b>100</b>	<b>52</b>	<b>100</b>	<b>45</b>	<b>100</b>	<b>127</b>	<b>100</b>

Figure 2.5.2 (b): Age at time of biopsy (years) for IgA nephropathy, 2005-2007



### 2.5.3: Clinical presentation

There is a wide range of clinical presentations in IgAN. Overall, 50% presented with some form of asymptomatic urinary abnormality. Up to 25% of those who were biopsied had nephrotic syndrome (Table & Figure 2.5.3 (a)). This figure is higher than the 5% quoted in literature<sup>(1)</sup> and may reflect relatively conservative local practices with regards to investigation of asymptomatic urinary abnormalities. Up to 25% of patients were hypertensive (Table 2.5.3 (b)). The mean level of proteinuria at biopsy was  $3.8 \pm 0.9$  g/d with a range from 2.8- 8.4 g/d.

Table 2.5.3 (a): Overall clinical presentation for IgA nephropathy, 2005-2007

Clinical presentation	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
Asymptomatic urine abnormality	18	60	21	40	25	56	64	50
Nephritic syndrome	1	3	3	6	4	9	8	6
Nephrotic syndrome	8	27	16	31	8	17	32	25
Nephritic-Nephrotic syndrome	0	0	3	6	4	9	7	6
Missing	3	10	9	17	4	9	16	13
<b>Total</b>	<b>30</b>	<b>100</b>	<b>52</b>	<b>100</b>	<b>45</b>	<b>100</b>	<b>127</b>	<b>100</b>

Figure 2.5.3 (a): Overall clinical presentation for IgA nephropathy, 2005-2007

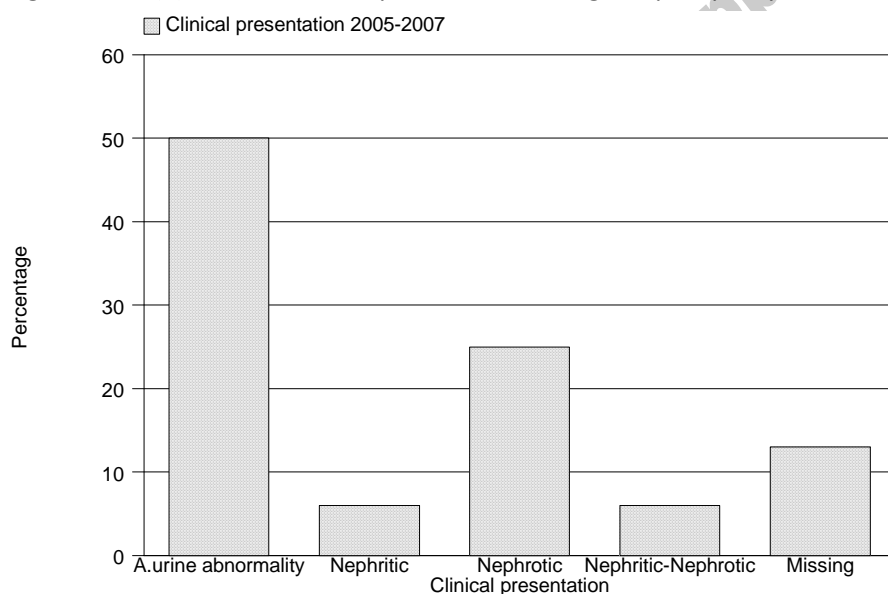


Table 2.5.3 (b): Presence of hypertension in IgA nephropathy, 2005-2007

Hypertension	Total	
	n	%
Present	31	24
Absent	96	76
<b>Total</b>	<b>127</b>	<b>100</b>

**2.5.3.1: Clinical presentation by age**

Comparisons across age groups are limited by the small numbers of patients in older age groups particularly those aged 55 years and above.

Table 2.5.3.1: Clinical presentation by age group for IgA nephropathy, 2005-2007

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	11	32	24	59	17	61	8	50	4	66	0	0	64	50
Nephritic syndrome	5	15	2	5	1	4	0	0	0	0	0	0	8	6
Nephrotic syndrome	12	35	8	19	8	28	4	24	0	0	0	0	32	25
Nephritic-Nephrotic syndrome	2	6	2	5	0	0	2	13	1	17	0	0	7	6
Missing	4	12	5	12	2	7	2	13	1	17	2	100	16	13
<b>Total</b>	<b>34</b>	<b>100</b>	<b>41</b>	<b>100</b>	<b>28</b>	<b>100</b>	<b>16</b>	<b>100</b>	<b>6</b>	<b>100</b>	<b>2</b>	<b>100</b>	<b>127</b>	<b>100</b>

**2.5.3.2: Clinical presentation by gender**

There were no differences in clinical presentation according to gender.

Table 2.5.3.2: Clinical presentation by gender for IgA nephropathy, 2005-2007

Clinical presentation	Male		Female	
	No.	%	No.	%
Asymptomatic urine abnormality	25	45	39	55
Nephritic syndrome	4	7	4	6
Nephrotic syndrome	15	27	17	23
Nephritic-Nephrotic syndrome	3	5	4	6
Missing	9	16	7	10
<b>Total</b>	<b>56</b>	<b>100</b>	<b>71</b>	<b>100</b>

### 2.5.4: Renal function at presentation

Half of the patients (48%) had eGFR < 60ml/min/1.72m<sup>2</sup> at presentation as expected, there is a tendency for older patients to have a greater degree of renal impairment when compared to younger age groups (Table 2.5.4 (a)). The distribution of level of renal function is shown in Table & Figure 2.5.4 (b). Male tend to have worse renal function compared to female, with 57% of male and only 42% of female had eGFR less than 60 ml/min/1.73 m<sup>2</sup>(Table 2.5.4(c)).

Figure 2.5.4 (a): Impaired renal function by age group, 2005-2007

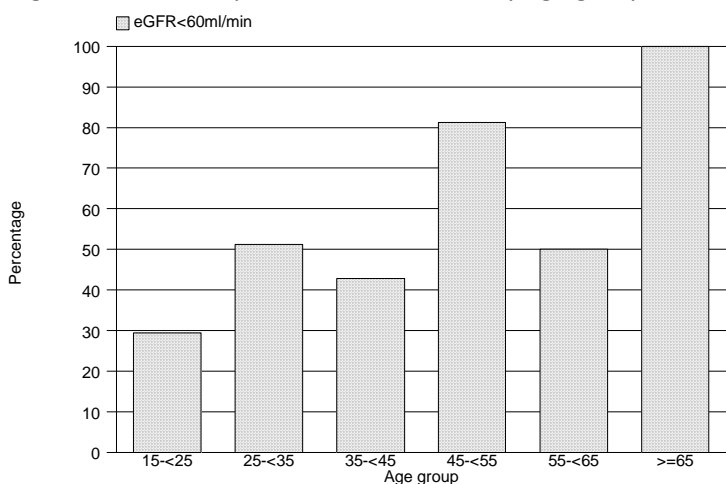


Table 2.5.4 (b): Renal function at presentation by age group for IgA nephropathy, 2005-2007

eGFR (ml/min/1.73m <sup>2</sup> )	15- <25		25- <35		35- <45		45- <55		55- <65		≥ 65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
≥90	9	26	5	12	3	11	0	0	1	17	0	0	18	14
60-89	15	44	15	37	13	46	3	19	2	33	0	0	48	38
30-59	6	18	10	24	7	25	9	56	2	33	0	0	34	27
15-29	2	6	6	15	4	14	1	6	0	0	1	50	14	11
<15	2	6	5	12	1	4	3	19	1	17	1	50	13	10
<b>Total</b>	<b>34</b>	<b>100</b>	<b>41</b>	<b>100</b>	<b>28</b>	<b>100</b>	<b>16</b>	<b>100</b>	<b>6</b>	<b>100</b>	<b>2</b>	<b>100</b>	<b>127</b>	<b>100</b>

Figure 2.5.4 (b): Renal function at presentation by age group for IgA nephropathy, 2005-2007

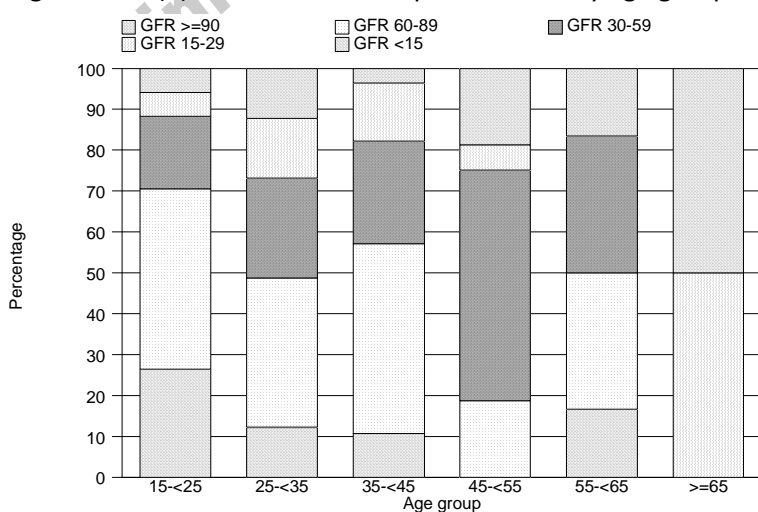


Table 2.5.4 (c): Renal function at presentation according to gender for IgA nephropathy, 2005-2007

eGFR (ml/min/1.73m <sup>2</sup> )	Male		Female	
	n	%	n	%
≥90	10	18	8	11
60-89	15	27	33	47
30-59	15	27	19	27
15-29	9	15	5	7
<15	7	13	6	8
<b>Total</b>	<b>56</b>	<b>100</b>	<b>71</b>	<b>100</b>

**References:**

1. Cattran DC. Idiopathic membranous glomerulonephritis. *Kidney Int* 2001, 59:1983-94.
2. Couser WG, Alpers CE. Membranous nephropathy. In: *Immunologic renal diseases*. Edited by Neilson EG, Couser WG. Lippincott Williams and Wilkins: 2001 ch 43: 1029- 36.
3. Couser WG, Shankland SJ. Membranous nephropathy. In: *Comprehensive Clinical Nephrology*. Edited by Feehally J, Johnson RJ. Mosby Elsevier Limited: 2003 ch 22: 295-307.
4. Zuchelli IP, Cagnoli L, Pasquali C. Clinical and morphologic evolution of idiopathic membranous nephropathy. *Am J Kidney Dis* 1986, 25:282-8.
5. Hogan SL, Muller KE, Jennette JC, FalkRJ. A review of therapeutic studies of idiopathic membranous glomerulopathy. *Am J Kidney Dis* 1995, 25:862-8.
6. Feehally J. IgA Nephropathy and Henoch-Schonlein Nephritis. In: *Comprehensive Clinical Nephrology*. Edited by Feehally J, Johnson RJ. Mosby Elsevier Limited: 2003 ch 24: 319-330.
7. Barratt J and Feehally J. IgA Nephropathy. *J Am Soc Nephrol* 2005,16:2088-97.

## **CHAPTER 3**

### **Secondary Glomerulonephritis**

Rosnawati Yahya  
Liew Yew Fong

Prelim Report Awaiting Approval from KKM

**3.1: LUPUS NEPHRITIS**

**3.1.1 Introduction**

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

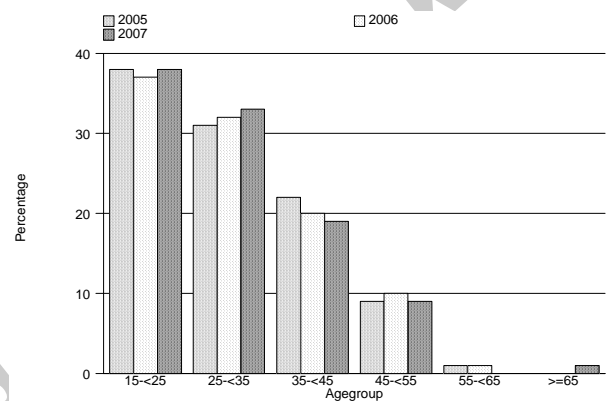
**3.1.2: Patient population and characteristics**

In the period of 1<sup>st</sup> Jan 2005 and 31<sup>st</sup> Dec 2007, there was a total of 736 biopsy-proven lupus nephritis in 711 patients were reported.

**3.1.2.1: Age at time of biopsy**

The mean age of patients with lupus nephritis at the time of biopsy was 30.2 ± 10.3 years (range 15-70.4). The most predominant age group was between 15 to 25 years old, which accounted about 1/3 of cases. The onset of lupus nephritis in the later part of life (> 45 years old) was uncommon and this constituted less than 10% of all patients. Lupus nephritis at an age older than 55 was extremely uncommon accounting for only 1%. Distribution by age can be seen in figure 3.1.2.1.

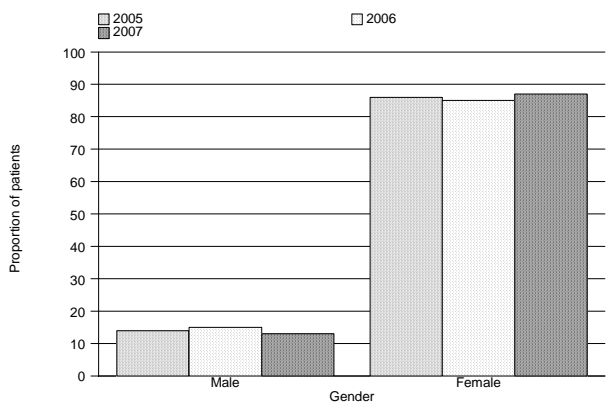
Figure 3.1.2.1: Age group at time of biopsy (years), 2005-2007



**3.1.2.2: Gender distribution**

Lupus nephritis predominantly affects female with female to male ratio of 6.2 to 1.

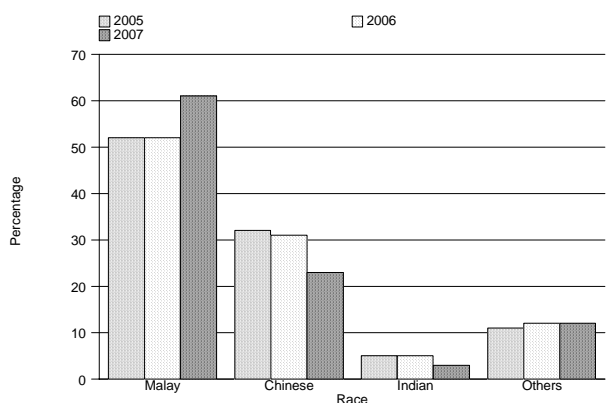
Figure 3.1.2.2: Gender distribution, 2005-2007



**3.1.2.3: Racial prevalence**

Fifty-six percent of patients with lupus nephritis were Malays, 28% were Chinese, 5% were Indian and 11% were of other races (mainly the indigenous population of East Malaysia). Over the 3 years of data collection, there seems to be an increasing trend of occurrence of lupus nephritis amongst Malay with an opposite trend in the Chinese.

Figure 3.1.2.3: Racial distribution, 2005-2007



### 3.1.3: Clinical presentation

In adult patients with lupus nephritis, 39% presented with urine abnormalities, 11% with nephritic syndrome, 29% with nephrotic syndrome and 6% presented with a combination of nephritic and nephrotic syndrome. Data was missing in 15% of cases. It appears that patients presenting with nephritic-nephrotic syndrome has increased over the years. At the time of presentation, up to 40% had impaired renal function (defined by e-GFR by modified MDRD of less than 60 ml/min/1.73 m<sup>2</sup>) and 17% were hypertensive. (Figure 3.1.3(a) & (b))

Table 3.1.3: Clinical presentation by year, 2005-2007

Clinical Presentation	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
Urine abnormality	99	41	114	41	77	35	290	39
Nephritic syndrome	26	11	27	10	25	11	78	11
Nephrotic syndrome	66	28	77	28	67	30	210	29
Nephrotic-nephritic syndrome	9	4	15	5	24	11	48	6
Missing	39	16	43	16	28	13	110	15
<b>Total</b>	<b>239</b>	<b>100</b>	<b>276</b>	<b>100</b>	<b>221</b>	<b>100</b>	<b>736</b>	<b>100</b>

Figure 3.1.3(a): Hypertension by year, 2005-2007

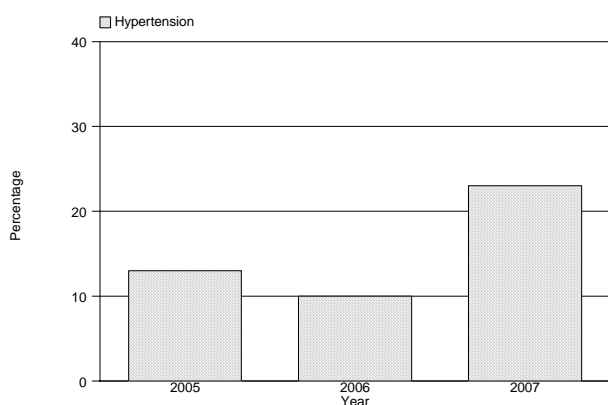
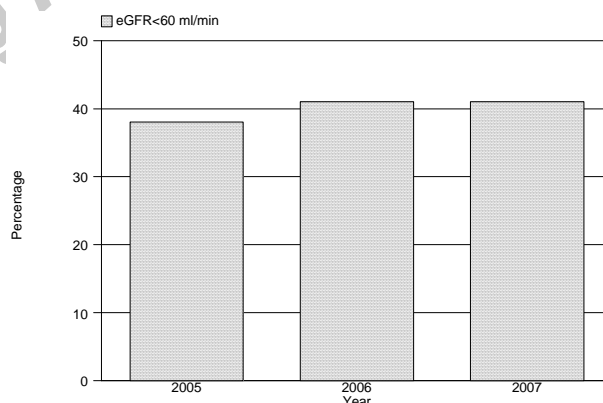


Figure 3.1.3(b): Impaired renal function by year, 2005-2007



**3.1.3.1: Clinical Presentation by age**

Urine abnormalities were the commonest presentation in all age groups, followed by nephrotic syndrome (Table & Figure 3.1.3.1(a)). In adult with lupus nephritis, the prevalence of hypertension was between 10-20% across all age groups except in those above 65 years old (Figure 3.1.3.1(b)). Forty of adult patients with lupus nephritis had e-GFR of less than 60 ml/min/1.73 m<sup>2</sup> at presentation and the prevalence was higher in the older age group, above 35 years old. (Figure 3.1.3.1(c))

Table 3.1.3.1(a): Clinical presentation by age group, 2005-2007

Age group (years)	15- <25		25-<35		35-<45		45-<55		55-<65		>=65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Urine abnormalities	100	36	93	40	64	42	30	43	2	50	1	33	290	39
Nephritic syndrome	29	12	31	13	15	10	2	3	1	25	0	0	78	11
Nephrotic syndrome	78	28	70	30	44	29	16	23	1	25	1	33	210	29
Nephrotic-nephritic syndrome	17	6	19	8	6	4	6	9	0	0	0	0	48	6
Missing	50	18	22	9	22	15	15	22	0	0	1	33	110	15
<b>TOTAL</b>	<b>274</b>	<b>100</b>	<b>235</b>	<b>100</b>	<b>151</b>	<b>100</b>	<b>69</b>	<b>100</b>	<b>4</b>	<b>100</b>	<b>3</b>	<b>100</b>	<b>736</b>	<b>100</b>

Figure 3.1.3.1(a): Clinical presentation by age group, 2005-2007

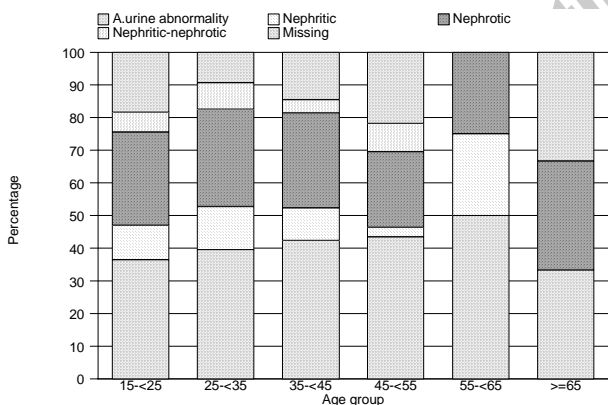


Figure 3.1.3.1(b): Hypertension by age group, 2005-2007

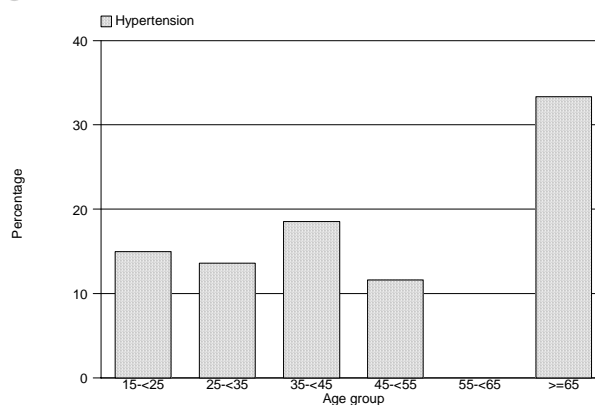
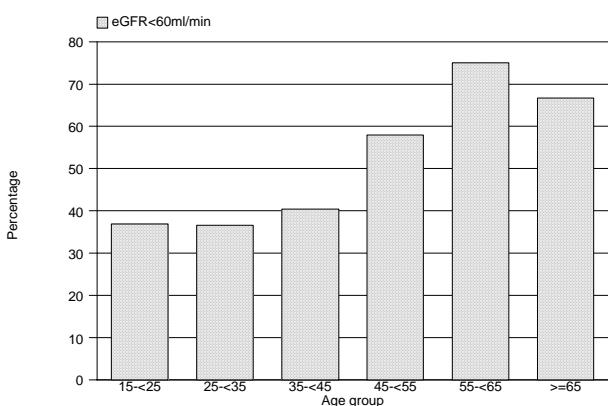


Figure 3.1.3.1(c): Impaired renal function by age group, 2005-2007



### 3.1.3.2: Clinical presentation by gender

There were no differences in the clinical presentation, prevalence of hypertension and impaired renal function between the two genders. (Figure 3.1.3.2 (a), (b), and (c))

Figure 3.1.3.2(a): Clinical presentation by gender, 2005-2007

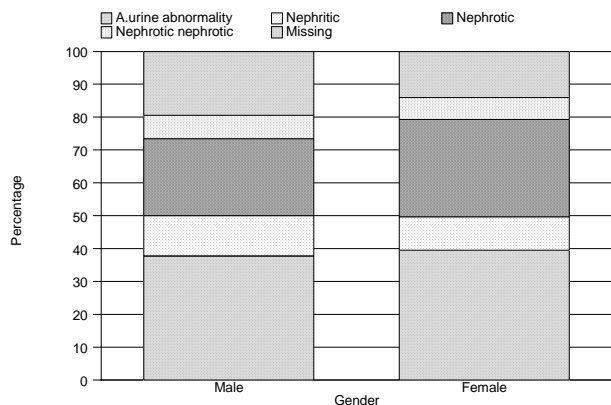


Figure 3.1.3.2(b): Hypertension by gender 2005-2007

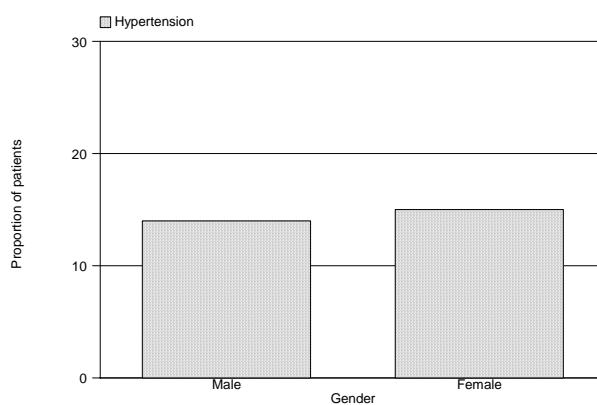
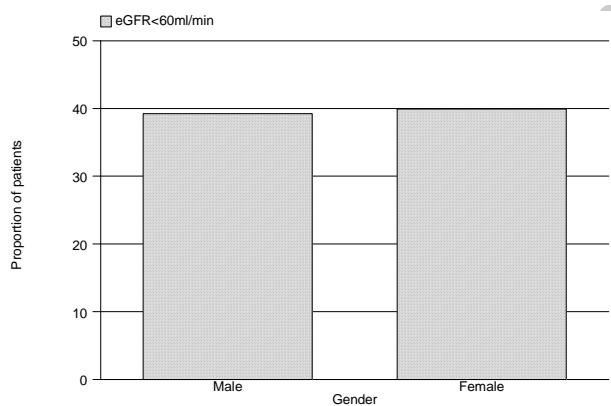


Figure 3.1.3.2(c): Impaired renal function by gender, 2005-2007



**3.1.3.3: Clinical Presentations by histopathology**

There were 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, with 52% had symptomatic renal disease at presentation. In comparison, those with class II, only 34% had symptomatic renal disease (Table & Figure 3.1.3.3(a)). The prevalence of hypertension was higher in class IV or class IV+V (Figure 3.1.3.3(b)). The prevalence of impaired kidney function correlated with histopathological findings. The proportion of patients with e-GFR <60 ml/min/m<sup>2</sup> were 46%, 34%, 29% and 16% in class IV or V+IV, class III or V+III, class V and class II respectively (Figure 3.1.3.3 (c)).

Table 3.1.3.3(a): Clinical presentations by histopathology, 2005-2007

Clinical Presentations	I		II		III or III+V		IV or IV+V		V or V+II		VI		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Urine abnormality	2	67	41	64	62	44	135	32	40	47	2	100	282	39
Nephritic syndrome	0	0	8	13	16	11	48	13	4	5	0	0	76	11
Nephrotic syndrome	1	33	10	16	38	27	131	31	26	31	0	0	206	28
Nephrotic–nephritic syndrome	0	0	4	5	4	4	35	8	3	3	0	0	46	7
Missing	0	0	1	2	20	14	68	16	12	14	0	0	101	15
<b>Total</b>	<b>3</b>	<b>100</b>	<b>64</b>	<b>100</b>	<b>140</b>	<b>100</b>	<b>417</b>	<b>100</b>	<b>85</b>	<b>100</b>	<b>2</b>	<b>100</b>	<b>711</b>	<b>100</b>

\* 25 cases are missing on lupus subclass

Figure 3.1.3.3(a): Clinical presentations by histopathology in lupus nephritis, 2005-2007

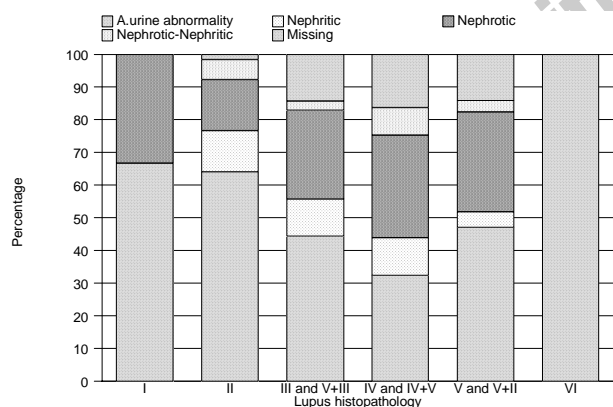


Figure 3.1.3.3(b): Prevalence of hypertension by histopathology, 2005-2007

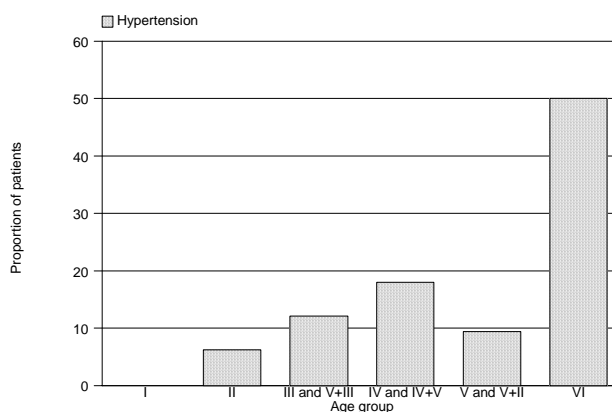
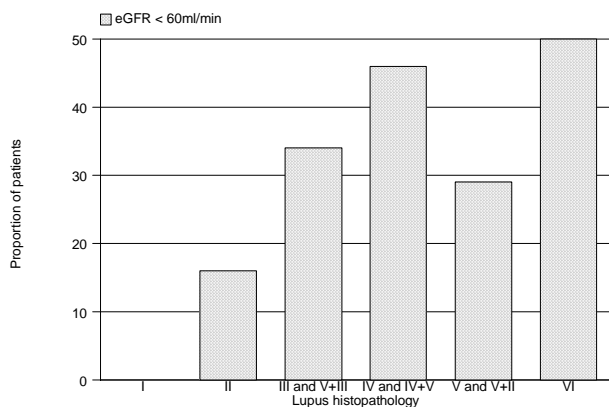


Figure 3.1.3.3(c): Prevalence of impaired renal function by histopathology, 2005-2007



### 3.1.4: Renal function at presentation

Forty percent of all patients have impaired renal function (defined as e-GFR < 60ml/min/1.73 m<sup>2</sup>) at the time of presentation. Seven percent had e-GFR of less than 15 ml/min.

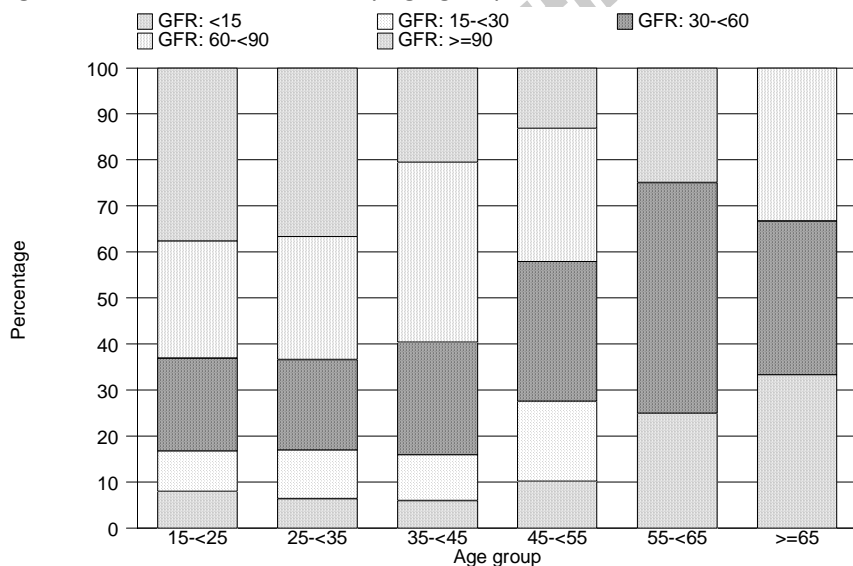
#### 3.1.4.1: Renal function at presentation by age group

The frequency of impaired renal function increases after the age of 35. Between 36-39% of patients had e-GFR of less than 60 ml/min/1.73 m<sup>2</sup> below the age of 35 and the proportion rises to 43% in the age group of 35 to 45 and 53% in age group of 45-to 55. (Table & Figure 3.1.4.1)

Table 3.1.4.1: Renal function by age group, 2005-2007

e-GFR (ml/min/1.73 m <sup>2</sup> )	15- <25		25-<35		35-<45		45-<55		55-<65		>=65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<15	22	8	15	6	9	6	7	11	1	25	1	33.3	55	7
15 to < 30	24	9	25	11	15	10	12	17	0	0	0	0	76	10
30 to < 60	55	19	46	20	37	25	21	30	2	50	1	33.3	162	23
60 to < 90	70	26	63	26	59	38	20	29	0	0	1	33.3	213	29
>=90	103	38	86	37	31	21	9	13	1	25	0	0	230	31
<b>Total</b>	<b>274</b>	<b>100</b>	<b>235</b>	<b>100</b>	<b>151</b>	<b>100</b>	<b>69</b>	<b>100</b>	<b>4</b>	<b>100</b>	<b>3</b>	<b>100</b>	<b>736</b>	<b>100</b>

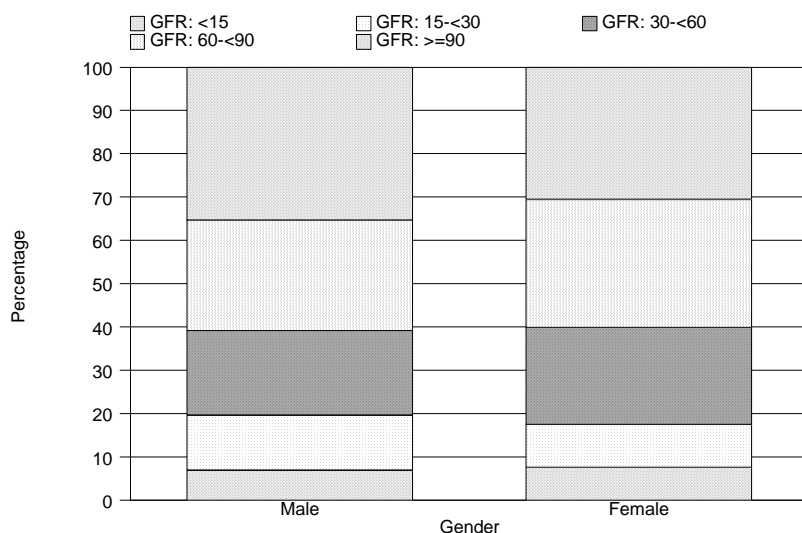
Figure 3.1.4.1: Renal function by age group, 2005-2007



**3.1.4.2: Renal function at presentation by gender**

There were no differences in the renal function at presentation between the two genders. (Figure 3.1.4.2)

Figure 3.1.4.2: Renal function by gender, 2005-2007



**3.1.4.3: Renal function at presentation by histopathology**

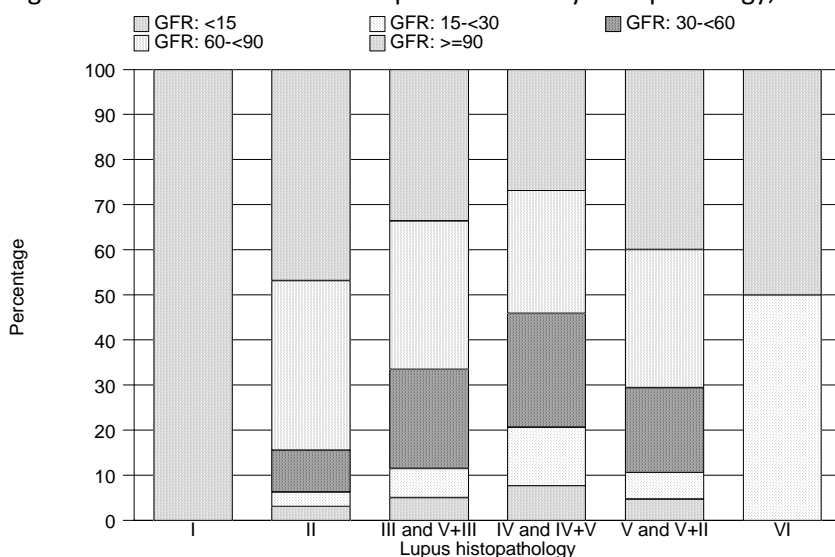
In the proliferative lupus nephritis (class III, IV, V+III and V+IV), class IV or V+IV have worse renal function than class III or class V+III (Table and Figure 3.1.4.3). However, we could not ascertain whether the renal failure at the time of presentation were acute or chronic.

Table 3.1.4.3: Renal function at presentation by histopathology, 2005-2007

e-GFR (ml/min/1.73 m <sup>2</sup> )	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	2	3	7	5	32	8	4	5	0	0	45	6
15 to <30	0	0	2	3	9	6	54	13	5	6	1	50	71	10
30 to <60	0	0	6	9	31	22	105	25	16	18	0	0	158	22
60 to <90	0	0	24	38	46	33	114	27	26	31	0	0	210	30
>=90	3	100	30	47	47	34	112	27	34	40	1	50	227	32
<b>Total</b>	<b>3</b>	<b>100</b>	<b>64</b>	<b>100</b>	<b>140</b>	<b>100</b>	<b>417</b>	<b>100</b>	<b>85</b>	<b>100</b>	<b>2</b>	<b>100</b>	<b>711</b>	<b>100</b>

\* 25 cases are missing on lupus subclass

Figure 3.1.4.3: Renal function at presentation by histopathology, 2005-2007



### 3.1.5: Histopathological diagnosis

There were a total of 736 adult biopsies with a diagnosis of lupus nephritis. Data on the lupus subclass were incomplete in 25 cases. The distribution of histopathological class based on WHO or ISN/RPS classification is summarized in table 3.1.5. Class IV and IV+V were 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 1 and VI lupus nephritis reported to the registry.

Table 3.1.5: Histopathological diagnosis, 2005-2007

WHO or ISN/ RPS classifica- tion	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
Class I	1	0	1	0	1	0	3	0
Class II	27	12	15	6	22	11	64	9
Class III or V+III	37	16	58	21	45	22	140	20
Class IV or IV+V	134	58	166	62	117	56	417	59
Class V or V+II	32	14	30	11	23	11	85	12
Class VI	1	0	0	0	1	0	2	0
<b>Total</b>	<b>232</b>	<b>100</b>	<b>270</b>	<b>100</b>	<b>209</b>	<b>100</b>	<b>711</b>	<b>100</b>

\* 25 cases are missing on lupus subclass

**3.1.5.1: Histopathological diagnosis by age**

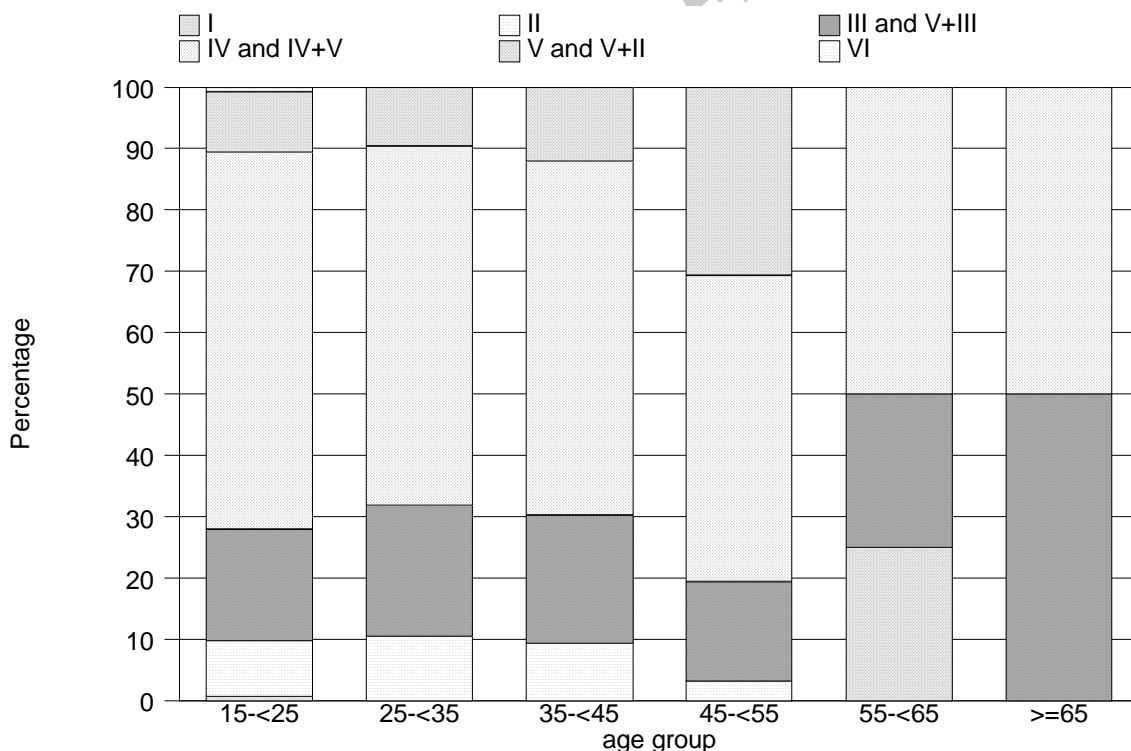
In adults, Class IV or IV+V were the most predominant lesion in all age groups. However, the frequency of class IV and IV+V were less with increasing age (Table 3.1.5.1).

Table 3.1.5.1: Histopathological diagnosis by age group, 2005-2007

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	2	1	0	0	0	0	0	0	1	25	0	0	3	0
Class II	24	9	24	10	14	9	2	3	0	0	0	0	64	9
Class III or V+III	48	18	49	21	31	21	10	16	1	25	1	50	140	20
Class IV or IV+V	163	61	134	59	86	58	31	50	2	50	1	50	417	59
Class V or V+II	26	10	22	10	18	12	19	31	0	0	0	0	85	12
Class VI	2	1	0	0	0	0	0	0	0	0	0	0	2	0
<b>Total</b>	<b>265</b>	<b>100</b>	<b>229</b>	<b>100</b>	<b>149</b>	<b>100</b>	<b>62</b>	<b>100</b>	<b>4</b>	<b>100</b>	<b>2</b>	<b>100</b>	<b>711</b>	<b>100</b>

\* 25 cases are missing on lupus subclass

Figure 3.1.5.1: Histopathological diagnosis by age group, 2005-2007



### 3.1.5.2: 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 3.1.5.2).

Table 3.1.5.2: Histopathological diagnosis by gender, 2005-2007

Histopathology	Male		Female		Total	
	n	%	n	%	n	%
Class I	1	1	2	0	3	0
Class II	6	6	58	10	64	9
Class III or V+III	23	23	117	19	140	20
Class IV or IV+V	51	52	366	60	417	59
Class V or V+II	18	18	67	11	85	12
Class VI	0	0	2	0	2	0
<b>Total</b>	<b>99</b>	<b>100</b>	<b>612</b>	<b>100</b>	<b>711</b>	<b>100</b>

\* 25 cases are missing on lupus subclass

### 3.1.5.3: Histopathological diagnosis by clinical presentation

Urine abnormalities were the most common clinical presentation, followed by nephrotic syndrome. 75% with nephritic-nephrotic, 64% with nephrotic and 63% with nephritic syndrome had class IV or class IV+V histopathological diagnosis. However, 47% with urine abnormalities alone also had class IV and class IV or IV.

Table 3.1.5.3: Histopathological diagnosis by clinical presentation, 2005-2007

Histopathology	Urine abnormality		nephritic		nephrotic		Nephritic-nephrotic		Missing		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
I	2	1	0	0	1	0	0	0	0	0	3	0
II	41	15	8	11	10	5	4	9	1	1	64	9
III or III + V	62	22	16	21	38	18	4	9	20	20	140	20
IV or IV+V	135	47	48	63	131	64	35	75	68	67	417	59
V or V+II	40	14	4	5	26	13	3	7	12	12	85	12
Class VI	2	1	0	0	0	0	0	0	0	0	2	0
<b>Total</b>	<b>282</b>	<b>100</b>	<b>76</b>	<b>100</b>	<b>206</b>	<b>100</b>	<b>46</b>	<b>100</b>	<b>101</b>	<b>100</b>	<b>711</b>	<b>100</b>

\* 25 cases are missing on lupus subclass

**3.1.6: Extra-renal involvement**

**3.1.6.1: 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

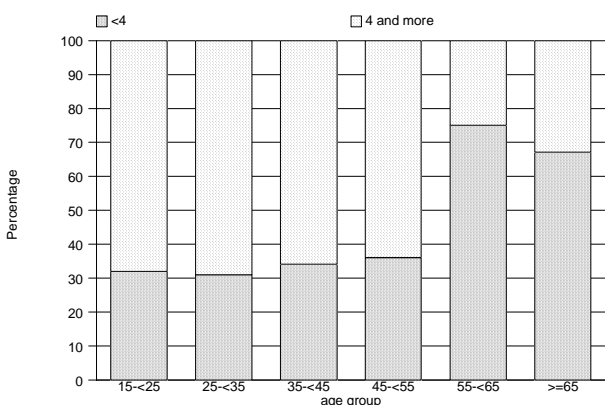
Table 3.1.6.1: ARA criteria in lupus nephritis, 2005-2007

No of ARA criteria	2005		2006		2007		Total	
	n	%	n	%	n	%	n	%
< 4	83	35	94	34	65	29	242	33
≥ 4	156	65	182	66	156	71	494	67
<b>Total</b>	<b>239</b>	<b>100</b>	<b>276</b>	<b>100</b>	<b>221</b>	<b>100</b>	<b>736</b>	<b>100</b>

**3.1.6.2: ARA criteria in lupus nephritis by age**

In patients less than 55 years of age, more than 2/3 satisfied the ARA criteria for the diagnosis of SLE. There were only 7 patients 55 years and above.

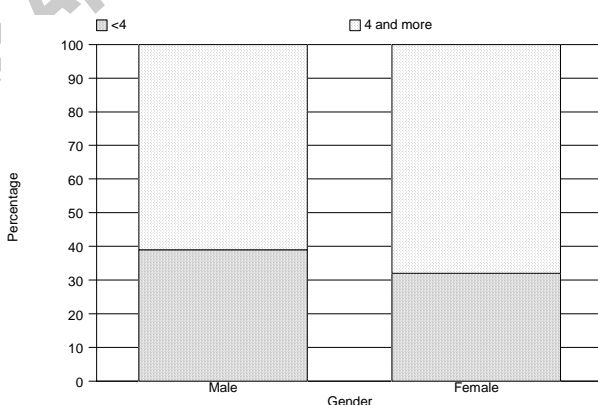
Figure 3.1.6.2: ARA criteria in lupus nephritis by age group, 2005-2007



**3.1.6.3: ARA criteria in lupus nephritis 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 (66% versus 60%).

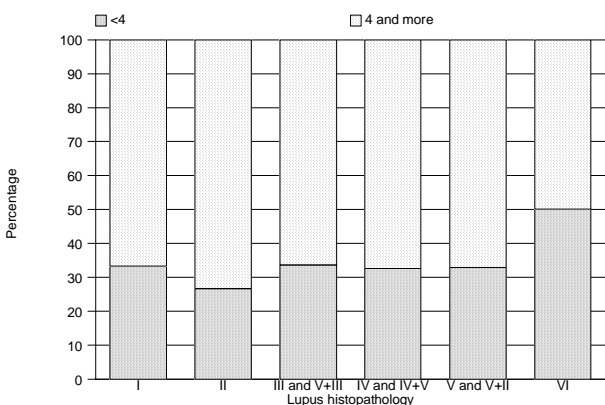
Figure 3.1.6.3 ARA criteria in lupus nephritis by gender, 2005-2007



**3.1.6.4: ARA criteria in lupus nephritis by histopathological findings**

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

Figure 3.1.6.4: ARA criteria in lupus nephritis by histopathology, 2005-2007



### 3.1.6.5: Extra-renal involvement

In patients with lupus nephritis, 54% had mucocutaneous involvement, 36% had arthritis, 10% had serositis, 12% had cerebral involvements and 43% had haematological involvement (Table 3.1.6.5(a)). Mucocutaneous involvement, serositis and especially arthritis were more common in females than males. Neurological and haematological involvements were slightly more common in males (Table & figure 3.1.6.5(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 3.1.6.5(a): Extra-renal involvement by gender, 2005-2007

Extra-renal involvement	Male (n=102)		Female (n=634)		Total (n=736)	
	n	%	n	%	n	%
Mucocutaneous	51	50	349	55	400	54
Arthritis	22	22	245	39	267	36
Serositis	8	8	66	10	74	10
Cerebral	16	16	70	11	86	12
Hematological	48	47	269	42	317	43
<b>Total</b>	<b>145</b>		<b>999</b>		<b>1144</b>	

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

Figure 3.1.6.5(a): Extra-renal involvement by gender, 2005-2007

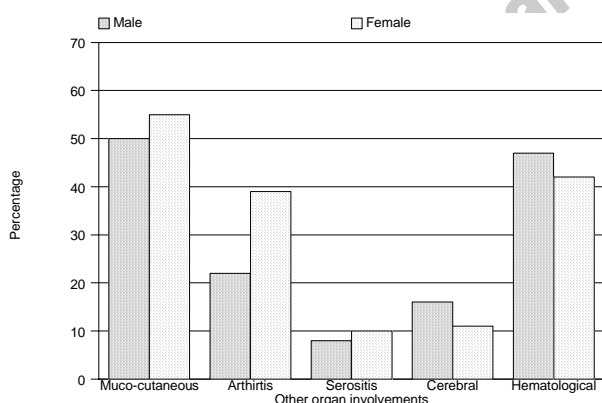


Figure 3.1.6.5(b): Mucocutaneous involvement by gender, 2005-2007

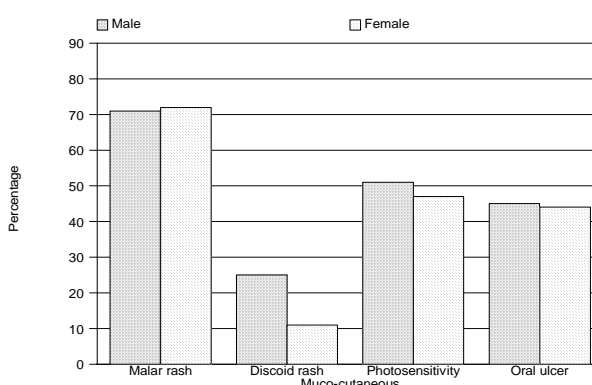


Table 3.1.6.5(b): Mucocutaneous involvement by gender, 2005-2007

Mucocutaneous involvements	Male (n=51)		Female (n=349)		Total (n=400)	
	n	%	n	%	n	%
Malar rash	36	71	253	72	289	72
Discoid rash	13	25	39	11	52	13
Photosensitivity	26	51	165	47	191	48
Oral ulcer	23	45	152	44	175	44
<b>Total</b>	<b>98</b>		<b>609</b>		<b>707</b>	

## **CHAPTER 4**

### **Paediatric Renal Biopsies**

Lee Ming Lee

Lim Yam Ngo

Lynster Liaw

Susan Pee

Wan Jazilah Wan Ismail

Yap Yok Chin

Prelim Report Awaiting Approval from KKM

#### 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 were collected from 1999 in Department of Paediatrics Hospital Kuala Lumpur. With the establishment of the Malaysian Renal Biopsy Registry (MRRB) in 2005, other Ministry of Health (MOH) Hospitals started submitting data on renal biopsies performed. This chapter includes data from 1999 to 2007 for Hospital Kuala Lumpur and from 2005 to 2007 for other MOH 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 640 renal biopsies in 579 children.

**4.2.2: Number of native renal biopsies from various hospitals**  
Hospital Kuala Lumpur reported an average of 35 native biopsies per year. The other MOH Hospitals collected data for 287 renal biopsies. (Table 4.2.2).

Table 4.2.2: Number of renal biopsies

Year	Hospital Kuala Lumpur	Other MOH Hospitals
1999	37	-
2000	29	-
2001	28	-
2002	29	-
2003	53	-
2004	36	1*
2005	40	83
2006	37	91
2007	30	112
<b>Total</b>	<b>319</b>	<b>287</b>

\* 1 submission from other MOH Hospital prior to MRRB

#### 4.3: Outcome of renal biopsies

Altogether 606(94.7%) renal biopsies were assessed to be adequate for diagnosis upon review by nephrologists and histopathologists. A total of 34(5.3%) biopsies were not conclusive. Thailand, United Kingdom and Japan reported success rates of between 93.4% and 98.7%.<sup>(1,2,3)</sup> Thus the success rate in the present report is comparable with figures reported by other centers.

#### 4.4: Patient characteristics

Table 4.4 shows that renal biopsies were performed on 275 (47.5%) boys and 304 (52.5%) girls. The higher number in girls was probably attributed to biopsies among children with systemic lupus erythematosus. The mean age at biopsy was  $9.3 \pm 3.9$  years. The racial distribution of the patients was Malay 64%, Chinese 19%, Indian 7.3% and other ethnic groups 9.7%.

Table 4.4: Gender and racial distribution

		No	%
Gender	Male	275	47.5
	Female	304	52.5
	<b>Total</b>	<b>579</b>	<b>100</b>
Race	Malay	371	64.0
	Chinese	110	19.0
	Indian	42	7.3
	Others	56	9.7
	<b>Total</b>	<b>579</b>	<b>100</b>

## 4.5: Clinical presentation

### 4.5.1: Clinical presentation at biopsy

Nephrotic syndrome was the most frequent clinical presentation accounting for 55.9%. The second commonest indication for performing renal biopsy was nephritic syndrome, which contributed to 14.0% of cases (Table 4.5.1).

Singapore, Hong Kong and Thailand reported nephrotic syndrome as their commonest clinical presentation at biopsy in 67%, 69% and 42.3% respectively. <sup>(1,4,5)</sup>

Table 4.5.1: Clinical presentation at biopsy

Clinical presentation	Number	%
Asymptomatic urine abnormalities	67	11.1
Nephritic syndrome	85	14.0
Nephrotic syndrome	339	55.9
Nephritic nephrotic syndrome	46	7.6
Unknown	69	11.4
<b>Total</b>	<b>606</b>	<b>100</b>

### 4.5.2: Renal function at biopsy

Twenty nine percent of biopsies were performed in the setting of impaired renal function. (Table 4.5.2)

Table 4.5.2: Renal function at biopsy

Renal function at biopsy	Number	%
Impaired	177	29.2
Normal	386	63.7
Unknown	43	7.1
<b>Total</b>	<b>606</b>	<b>100</b>

## 4.6: Diagnosis of paediatric renal biopsies

Of 606 with final diagnosis following renal biopsy, focal segmental glomerulosclerosis (FSGS) contributed the largest group at 27.2%. It is hence not surprising that FSGS is the commonest cause of childhood end stage renal disease secondary to glomerular disease in Malaysia. The other common glomerulonephritis (GN) was lupus nephritis (26.1%). Minimal change disease (MCD) was diagnosed in 17.8% of cases and post-infectious glomerulonephritis (GN) in 10.0%. IgA nephropathy accounted for 4.4% and Henoch Schonlein Purpura 2.6% (Table 4.6). In comparison, IgA nephropathy was the most common glomerulonephritis in Italy.<sup>(6)</sup> This is most probably due to differences in biopsy practices.

Table 4.6: Diagnosis of paediatric renal biopsies

Diagnosis	Number	%
FSGS	165	27.2
Lupus nephritis	158	26.1
MCD	108	17.8
Post-infectious GN	61	10.0
IgA nephropathy	27	4.4
Henoch Schonlein Purpura	16	2.6
Mesangial proliferative GN non-IgA	13	2.1
Advanced glomerulosclerosis	7	1.2
HUS/TTP	6	1.0
Membranoproliferative GN	6	1.0
Acute tubular necrosis	6	1.0
Vasculitis	3	0.5
Membranous nephropathy	3	0.5
Chronic interstitial nephritis	2	0.3
Acute interstitial nephritis	2	0.3
Alport's syndrome	2	0.3
Hereditary(others)	1	0.3
Malignancy	1	0.2
Crescentic GN	1	0.2
Idiopathic crescentic ANCA	1	0.2
Others	3	0.5
Unknown	14	2.3
<b>Total</b>	<b>606</b>	<b>100</b>

#### 4.7: Renal histopathology diagnosis of children presenting with nephrotic syndrome

Nephrotic syndrome was the clinical diagnosis in 339 biopsies. The indications for renal biopsy were steroid resistant nephrotic, atypical nephrotic syndrome, or for assessment of cyclosporine nephrotoxicity in steroid responsive nephrotic syndrome. As shown in table 4.7, FSGS was found in 44.5% and MCD in 28.3%.

In Hong Kong, the most common histology finding for nephrotic syndrome was minimal change (59%) followed by FSGS which accounted for 9% of cases. The indications for biopsy in their center included nephrotic syndrome with frequent relapses, steroid dependence and atypical features.<sup>(5)</sup> Minimal change disease was the most common underlying renal pathology in Korea<sup>(6)</sup>. The Korean indications for biopsy in nephrotic syndrome were unusual clinical manifestations or steroid resistance. The different histological findings may be due to different practice pattern.

#### 4.8: Renal histopathology diagnosis of children presenting with nephritic syndrome.

Renal biopsy was performed in 85 children with nephritic syndrome. The majority demonstrated post-infectious GN (44.7%), while the others had lupus nephritis (31.8%), Henoch Schonlein Purpura (5.9%) and IgA nephropathy (5.9%) (Table 4.8). In contrast, IgA nephropathy was the most frequent diagnosis of renal biopsies in children with nephritic syndrome in Italy<sup>7</sup>

Table 4.7: Renal histopathology diagnosis of children presenting with nephrotic syndrome

Diagnosis	Number	%
FSGS	151	44.5
MCD	96	28.3
Lupus nephritis	55	16.2
IgA nephropathy	9	2.6
Mesangial proliferative GN non-IgA	8	2.4
Post-infectious GN	6	1.8
Others*	12	3.5
Unknown	2	0.7
<b>Total</b>	<b>339</b>	<b>100.0</b>

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

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

Diagnosis	Number	%
Post-infectious GN	38	44.7
Lupus nephritis	27	31.8
Henoch Schonlein Purpura	5	5.9
IgA nephropathy	5	5.9
FSGS	3	3.5
Others*	5	5.9
Unknown	2	2.3
<b>Total</b>	<b>85</b>	<b>100.0</b>

\* (membranoproliferative GN, mesangial proliferative GN-non IgA, Alport's syndrome, acute tubular necrosis)

#### 4.9: Causes of acute renal failure

The causes of acute renal failure were post-infectious GN (29.8%), lupus nephritis (29.8%), FSGS (8.7%), and HUS/TTP (5.8%). In the registry, 5.8% of renal failure was due to advanced glomerulosclerosis (Table 4.9)

In Italy the three commonest causes of acute renal failure were crescentic glomerulonephritis, acute interstitial nephritis and hemolytic uremic syndrome, each accounting for 12%.<sup>(7)</sup>

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

Diagnosis	Number	%
Post-infectious GN	31	29.8
Lupus nephritis	31	29.8
FSGS	9	8.7
Advanced glomerulosclerosis	6	5.8
HUS/TTP	6	5.8
Acute tubular necrosis	4	3.8
MCD	3	2.9
Acute interstitial nephritis	2	1.9
IgA nephropathy	2	1.9
Others*	6	5.8
Unknown	4	3.8
<b>Total</b>	<b>104</b>	<b>100.0</b>

\*(membranoproliferative GN, mesangial proliferative GN non-IgA, crescentic, Henoch schlein 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

There was no difference in term of age at presentation, gender and urine albumin excretion rate in children with FSGS or MCD. However, there was a significant difference in the racial composition between the two groups. The percentage of Indian children with FSGS was much higher compared to MCD. Children with FSGS had lower creatinine clearance at biopsy. (Table 4.10.1)

Table 4.10.1: Characteristic of paediatric focal segmental glomerulosclerosis and minimal change disease

Clinical characteristics		FSGS	MCD	p Value
Number		165	108	
Mean age (year)		8.0 (SD=4.0)	8.5 (SD=4.3)	0.39
Median age (year)		8.3	9.0	
Race		N (%)	N (%)	0.04
	Malay	110 (66.7%)	69 (63.9%)	
	Indian	23 (13.9%)	6 (5.6%)	
	Chinese	19 (11.5%)	23 (21.3%)	
	Others	13 (7.9%)	10 (9.2%)	
	Total	165 (100%)	108 (100%)	
Gender		99/66 (1.5:1)	67/41 (1.6:1)	0.74
N		165	108	0.03
Creatinine Clearance (CrCl) ml/min/1.73m <sup>2</sup>	CrCL <30	14 (8.5%)	5 (4.6%)	
	CrCl 30-60	22 (13.3%)	5 (4.6%)	
	CrCl 60-90	25 (15.2%)	14 (13.0%)	
	CrCL > 90	104 (63.0%)	84 (77.8%)	
24HUP g (N, mean)		N=35, 3.6	N=30, 2.5	0.17
Urine albumin mg /m <sup>2</sup> /H (N, mean)		N=46, 182.8	N=26, 97.8	0.10
Albumin g/L (N, mean)		N=155, 24.08	N=100,26.55	0.08

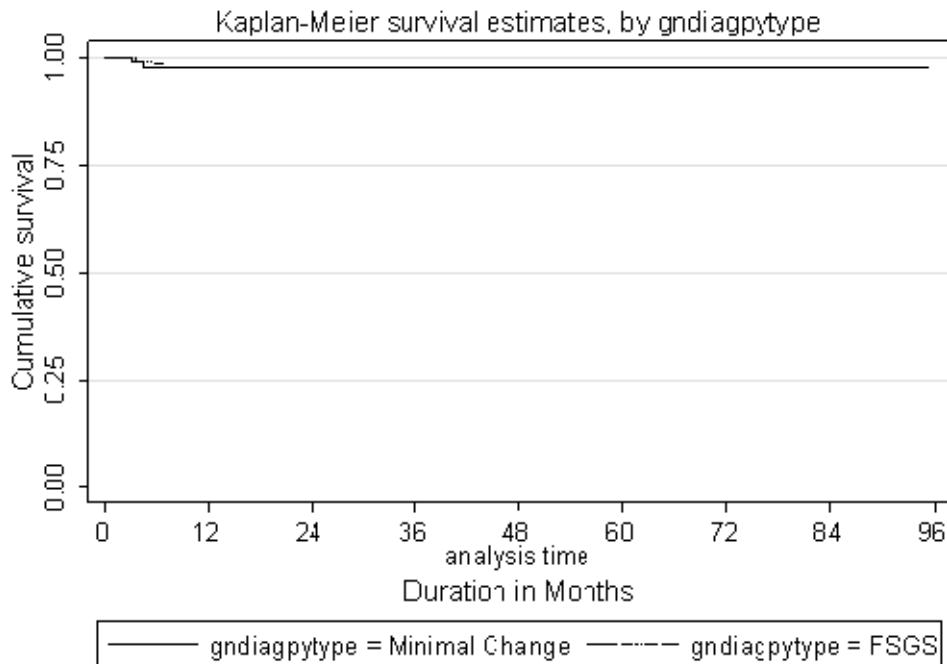
**4.10.2: Patient survival in focal segmental glomerulosclerosis and minimal change disease**

Table 4.10.2 and Figure 4.10.2 shows that patient survival was similar for both FSGS and MCD; 98% at 3years and 5years from the time of renal biopsy.

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

Clinical characteristics Interval (months)	Minimal change disease			FSGS		
	No	% survival	SE	No	% survival	SE
0	102	100	-	145	100	-
12	58	98	0	110	98	0
24	34	98	0	73	98	0
36	25	98	0	45	98	0
48	20	98	0	34	98	0
60	14	98	0	26	98	0
72	14	98	0	18	98	0
84	7	98	0	14	98	0
96	5	98	0	6	98	0

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



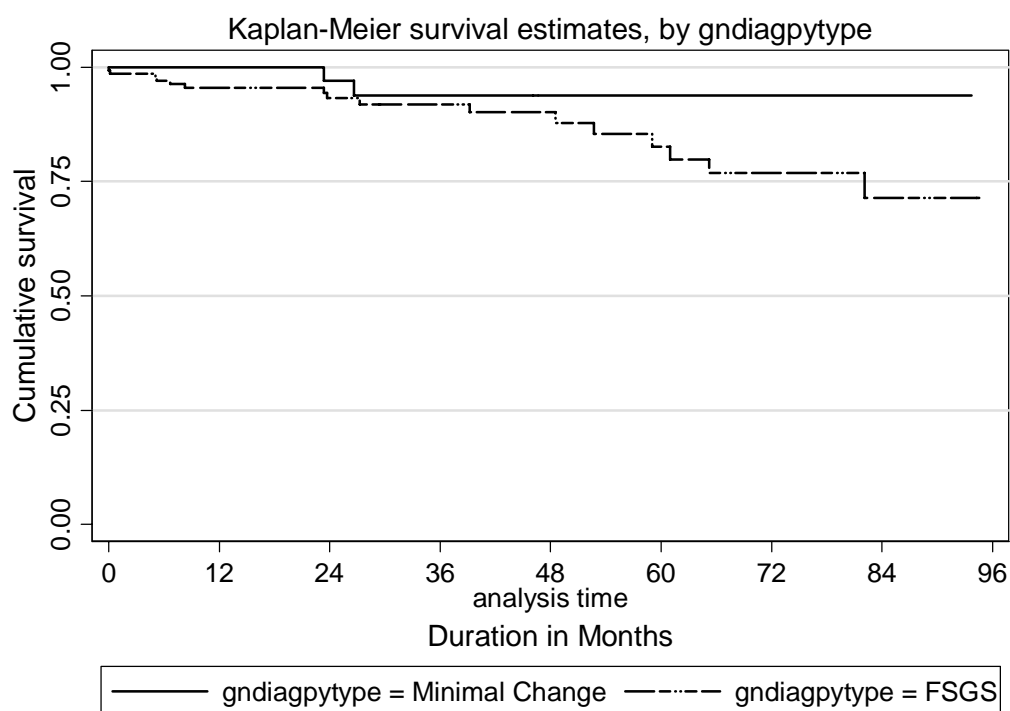
**4.10.3: Renal survival of patient with focal segmental glomerulosclerosis and minimal change disease**

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% and 82% at 3 years and 5 years respectively. Renal survival for MCD at 3 years and 5 years remained at 94%.

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

Clinical characteristics Interval (days)	Minimal change disease			FSGS		
	No	% survival	SE	No	% survival	SE
0	92	100	-	142	100	0
12	52	100	-	111	96	0
24	33	97	0	80	93	0
36	25	94	0	52	92	0
48	20	94	0	40	90	0
60	14	94	0	29	82	0
72	14	94	0	19	76	0
84	7	94	0	14	71	0
96	5	94	0	6	71	0

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



**4.11: Paediatric lupus nephritis**

There were 158 renal biopsies performed for 146 children with lupus.

**4.11.1: Patient characteristics of paediatric lupus nephritis**

The female: male ratio was 5.9:1 reflecting the preponderance of lupus in females. The racial distribution for paediatric lupus nephritis was Malay (63.7%), Chinese (26.7%), Indian (3.4%) and others (6.2%).

**4.11.2: Extra renal manifestation of paediatric SLE**

The most common extra renal manifestations among 130 children were cutaneous involvement (malar rash in 66.9%, photosensitivity in 39.2%, oral ulcers in 27.7% and discoid rash in 3.9%). This was followed by haematological involvement in 57.7%, joint involvement in 26.9%, serositis in 15.4% and cerebral involvement in 14.6%.

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.<sup>(8)</sup>

**4.11.3: 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 96 (65.7%) patients. Less frequent findings were class-III or V+III (17.1%), II (7.5%), V or V+II (6.9%) and VI (1.4%) lupus nephritis (Table 4.11.3). Hong Kong reported 54% in class IV.<sup>8</sup> Thailand reported 48.8% in class IV and 30.5% in class II.<sup>(9)</sup>

Table 4.11.3: Classification of paediatric lupus nephritis

WHO/ISN/RPS Class	Number	%
Class I	0	0
Class II	11	7.5
Class III or V+III	25	17.1
Class IV or V+IV	96	65.7
Class V or V+II	10	6.9
Class VI	2	1.4
Unknown	2	1.4
<b>Total</b>	<b>146</b>	<b>100</b>

**4.12: Renal outcome**

Of the 579 patients biopsied, 44 children were reported to the Malaysian Dialysis and Transplant registry with end stage renal disease.<sup>10</sup> FSGS was the most common known cause of end stage renal disease accounting for 36.4%. This was followed by lupus nephritis (11.4%), systemic vasculitis (11.4%), post-infectious GN (9.1%) and advanced glomerulosclerosis (6.8%). Two patients with minimal change and one patient with acute tubular necrosis progressed to end stage renal disease. (Table 4.12).

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

Causes	Number	%
FSGS	16	36.4
Lupus nephritis	5	11.4
Systemic vasculitis	5	11.4
Post-infectious GN	3	6.8
Advance glomerulosclerosis	3	6.8
HUS/TTP	2	4.5
Membranoproliferative GN	2	4.5
Minimal change	2	4.5
IgA nephropathy	2	4.5
Mesangial proliferative GN non-IgA	1	2.3
Acute tubular necrosis	1	2.3
Chronic interstitial nephritis	1	2.3
Unknown	1	2.3
<b>Total</b>	<b>44</b>	<b>100</b>

### 4.13: Biopsy failure and complication

#### 4.13.1: Risk factors for biopsy failure

Thirty-four out of the 640 (5.3%) renal biopsies were deemed to be inadequate for diagnosis.

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 failed renal biopsies. (Table 4.13.1).

Table 4.13.1: Risk factors for biopsy failure

Factors	N	No of failure	Risk ratio	95% CI	p Value	
Age (years)	≤2	23	0	-	-	
	3-≤5	98	1	0.79	(0.26, 2.41)	0.68
	6-≤10	186	0	1.40	(0.66, 2.94)	0.38
	10-14 (ref*)	333	7	1.00	-	-
Methods	No real-time guided ultrasound	300	2	1.22	(0.45, 3.34)	0.70
	Real-time guided ultrasound (ref*)	86	6	1.00	-	-
Previous biopsy	Previous failed biopsy	8	4	3.18	(0.31, 32.4)	0.33
	Successful biopsy (ref*)	93	4	1.00	-	-

#### 4.13.2: Complications

As shown in table 4.13.2, complications were reported in 5.4% of biopsies. The most common complication was gross haematuria, which occurred in 4.5% biopsies. Blood transfusion was needed in 1 patient. Six patients had perirenal haematoma. There were no cases of infection or arteriovenous fistula reported. 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%.<sup>(2)</sup> 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.<sup>(3)</sup>

Table 4.13.2: Frequency of complication

	Number	%
Total Number of biopsies	640	
Total Number of complication	38	5.4
<b>Type of complication</b>		
Gross haematuria	32	4.5
Perirenal collection/ haematoma	6	1.0
Infection	0	0
Arteriovenous malformation	0	0
Hypotension	0	0
Others	3	0.5
Unknown	1	0.2

**4.13.3: Risk factors for complication**

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

Table 4.13.3: Risk factors for complication

	Factors	N	No of complication	Hazard ratio	95% CI	p value
Age (years)	≤2	23	1	0.85	(0.10,6.90)	0.88
	>2-≤5	98	9	1.80	(0.77,4.22)	0.18
	>5-≤10	186	9	0.86	(0.38,1.96)	0.72
	>10 (ref*)	333	19	1.00		
Requirement for dialysis	Renal failure needed dialysis	59	10	2.41	(1.10,5.28)	0.03
	Renal failure not needed dialysis (ref*)	519	28	1.00		
	Unknown <sup>a</sup>	62	0			
Creatinine clearance	<15 ml/min/1.73m <sup>2</sup>	51	6	2.12	(0.78,5.76)	0.14
	15-<30 ml/min/1.73m <sup>2</sup>	42	2	0.79	(0.17,3.60)	0.76
	30-<60 ml/min/1.73m <sup>2</sup>	102	4	0.60	(0.20,1.83)	0.37
	60-<90 ml/min/1.73m <sup>2</sup>	110	7	1.22	(0.49,3.04)	0.68
	≥90 ml/min/1.73m <sup>2</sup> (ref*)	335	19	1.00		
Hemoglobin (Hgb) level	Hb ≤8g/dL	20	1	1.04	(0.13,8.49)	0.97
	Hb >8-≤10g/dL	122	8	0.98	(0.43,2.24)	0.97
	Hb ≥11g/dL (ref*)	482	29	1.00		
	Unknown <sup>b</sup>	16	0	-	-	-
Biopsy method (Realtime vs not)	Not realtime US guided	86	10	0.62	(0.28,1.36)	0.24
	Realtime US guided (ref*)	300	23	1.00		
	Unknown <sup>c</sup>	254	5	-	-	-
Biopsy method (Plug vs non-plug)	Plug biopsy **	5	0			
	Not plug biopsy (ref*)	361	32			
	Unknown <sup>d</sup>	274	6	-	-	-
<b>SLE</b>	SLE	163	8	0.70	(0.31,1.59)	0.40
	Non SLE (ref*)	477	30	1.00		
Needle size	14G	5	0	-	-	-
	16G (ref*)	383	36	1.00		
	18G	49	1	0.18	(0.02,1.37)	0.10
	Unknown <sup>e</sup>	203	1	-	-	-
Number of passes	Number of pass ≤2	250	16	0.47	(0.23,0.95)	0.04
	Number of pass 3-≤4 (ref)	144	18	1.00		
	Number of pass ≥ 5	17	3	1.92	(0.48,7.63)	0.36
	Unknown <sup>f</sup>	229	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

## References

1. Sumboonnanonda A, S Rajai K, Vongjirad A, Suntornpoch V, Parichatikanond P. Percutaneous renal biopsy in Children. *J Med assoc Thai* 2002; 85(Suppl 2): S755-61
2. M.D. Sinha, M.A. Lewis, M.G. Bradbury, N.J.A. Webb. Percutaneous real-time ultrasound-guided renal biopsy by automated biopsy gun in children : Safety and complications. *J Nephrol* 2006; 19: 41-44
3. Hidekazu Kamitsuji, Kazuo Yoshioka, Hiroshi Ito. Percutaneous renal biopsy in children: survey of pediatric nephrologists in Japan. *Pediatr Nephrol* 1999; 13: 693-696
4. YapHK, Murugasu B, Saw AH, Chiang GS, Tay JS, Wong HB, Tan CL, Lim CH. Pattern of Glomerulonephritis in Singapore children - A renal biopsy Perspective. *Ann Acad Med Singapore* 1989;18(1): 35-9
5. SN Wong, NKC Tse for Paediatric. Renal Diseases Surveillance Team Lessons from a limited Paediatric Renal Registry 1998-2000. *HK J Paeditr* 2004; 9(1): 24-29
6. Kwang Wook Ko, Il Soo Ha, Dong Kyu Jin. Childhood renal diseases in Korea. *Pediatr Nephrol* 1987; 1: 664-69
7. R Coppo, B Gianoglio, M G Porcellini, S Maringhini. Frequency of renal diseases and clinical indications for renal biopsy in children. (Report of the Italian National Registry of Renal Biopsies in Children). *Nephrol Dial Transplant* 1998; 13: 293-97
8. Sik-Nin Wong . Kei-Chiu Tse, Tsz-Leung Lee. Lupus nephritis in Chinese children – a territory-wide cohort study in Hong Kong. *Pediatr Nephrol* (2006) 21: 1104–1112
9. Pattaragarn A, Sumboonnanonda A, Parichatikanond P, Supavekin S, Suntornpoch V, Vongjirad A. Systemic lupus erythematosus in Thai children: clinicopathologic findings and outcome in 82 patients. *J Med Assoc Thai*. 2005 Nov; 88 Suppl 8: S232-41
10. YN Lim, TO Lim. 14th Report of The Malaysian Dialysis and Transplant Registry 2006

Prelim Report Awaiting Approval from KMA

## **CHAPTER 5**

### **Renal Allograft Biopsy**

Wong Hin Seng

Prelim Report Awaiting Approval from KKM

### 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.

### 5.2: Number of renal allograft biopsy

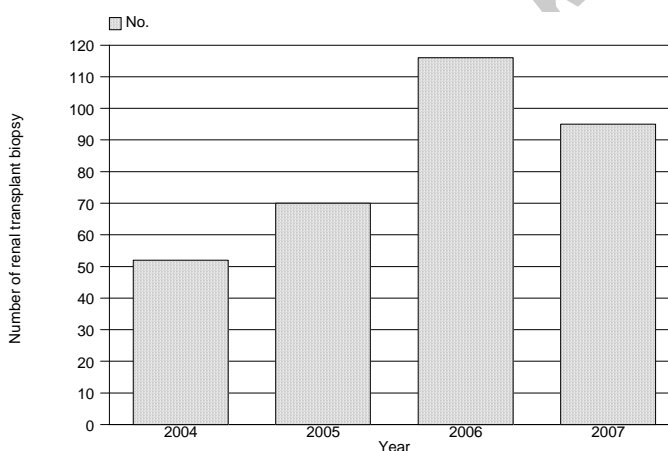
#### 5.2.1: Number of renal allograft biopsy by year

There is increasing trend in the number of renal allograft biopsy performed and the numbers has nearly doubled over the last 4 years despite a decreased in the number of new transplant recipients (189 new transplant recipients in 2004 compared to 86 in 2007) and only a marginal increased in the number of functioning renal graft (1590 functioning grafts in 2004 compared to 1726 in 2007) during the same period (Table & Figure 5.2.1.). This marked increased in the number of renal allograft biopsies performed in recent years is probably a result of the changing trend in the management of renal transplant recipients.

Table 5.2.1: Number of renal allograft biopsy, 2004-2007

Year	2004	2005	2006	2007	Total
No of renal allograft biopsy	52	70	116	95	333

Figure 5.2.1: Number of renal allograft biopsy, 2004-2007



#### 5.2.2: Number of renal allograft biopsy by year and site

In 2007, of the 21 participating centres, renal allograft biopsies were performed in only 9 centres with 92% of the biopsies performed in 4 centres in the Klang valley (Table 5.2.2). Three of these centres are renal transplant centres which are actively involved in the care of renal transplant recipients during the peri-operative and early post renal transplant period. The large number of renal allograft biopsies performed in these 4 centres is also partly contributed by the large number of renal transplant recipients that is being followed up in these centres.

Table 5.2.2: Number of renal allograft biopsy by year and SDP, 2004-2007

SDP	2004		2005		2006		2007		Total	
	n	%	n	%	n	%	n	%	n	%
1	47	90	28	40	50	43	43	45	168	50
2	0	0	0	0	0	0	0	0	0	0
3	0	0	12	17	11	9	2	2	25	8
4	0	0	0	0	1	1	0	0	1	0
5	0	0	1	1	2	2	2	2	5	2
6	0	0	5	7	10	8	13	14	28	8
7	0	0	0	0	1	1	1	1	2	1
8	0	0	0	0	0	0	0	0	0	0
9	0	0	0	0	2	2	1	1	3	1
10	0	0	0	0	2	2	0	0	2	1
11	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0
15	0	0	4	6	3	3	0	0	7	2
16	0	0	2	3	2	2	2	2	6	2
17	4	8	1	2	13	11	9	10	27	8
18	1	2	17	24	18	15	22	23	58	17
19	0	0	0	0	1	1	0	0	1	0
20	0	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0	0
<b>Total</b>	<b>52</b>	<b>100</b>	<b>70</b>	<b>100</b>	<b>116</b>	<b>100</b>	<b>95</b>	<b>100</b>	<b>333</b>	<b>100</b>

### 5.2.3: Number of renal allograft biopsy by year and age group.

Majority of the renal allograft biopsies were performed in the age group of 15 to <55years and this pattern remained relative unchanged over the last 4 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 45 yrs old) has increased from 11% in 2004 to 30% in 2007 (Table 5.2.3).

Table 5.2.3 Renal allograft biopsy by year and age group, rate (per million population), 2004-2007

Age group	2004			2005			2006			2007			Total		
	n	%	Rate	n	%	Rate	n	%	Rate	n	%	Rate	n	%	Rate
<15	3	6	0.1	0	0	0	5	4	0.2	6	6	0.2	14	4	0.1
15-<25	14	27	0.5	15	21	0.6	26	22	1	16	17	0.6	71	21	0.7
25-<35	15	29	0.6	11	16	0.4	24	21	0.9	12	13	0.4	62	19	0.6
35-<45	14	27	0.5	23	33	0.9	25	22	0.9	32	34	1.2	94	28	0.9
45-<55	4	7	0.2	12	17	0.5	24	21	0.9	20	21	0.7	60	18	0.6
55-<65	2	4	0.1	6	9	0.2	8	7	0.3	9	9	0.3	25	8	0.2
≥65	0	0	0	3	4	0.1	4	3	0.2	0	0	0	7	2	0.1
<b>Total</b>	<b>52</b>	<b>100</b>	<b>2</b>	<b>70</b>	<b>100</b>	<b>2.7</b>	<b>116</b>	<b>100</b>	<b>4.4</b>	<b>95</b>	<b>100</b>	<b>3.4</b>	<b>333</b>	<b>100</b>	<b>3.2</b>

### 5.3: Clinical presentation at biopsy

The most common indications for renal allograft biopsy were impaired renal allograft function and acute renal allograft dysfunction. This remained unchanged over the last 4 years and in 2007 accounted for 94% of the total number of renal allograft biopsies performed (Table 5.3).

Table 5.3: Indications for renal allograft biopsy, 2004-2007

Indications for biopsy		2004		2005		2006		2007		Total	
		n	%	n	%	n	%	n	%	n	%
Urine abnormalities	Asymptomatic hematuria	0	0	0	0	2	2	0	0	2	1
	Asymptomatic hematuria&proteinuria	0	0	0	0	0	0	0	0	0	0
	Asymptomatic proteinuria	0	0	0	0	0	0	0	0	0	0
	Nephrotic syndrome	1	2	0	0	3	3	2	2	6	2
	Gross haematuria	0	0	0	0	0	0	1	1	1	0
Acute deterioration of graft function		34	64	39	56	54	45	47	48	174	51
Creeping creatinine		5	9	24	34	49	41	35	36	113	33
Non/Poor delayed graft function		8	15	6	9	10	8	9	10	33	10
Missing*		5	9	1	1	1	1	3	3	10	3
<b>Total</b>		<b>53</b>	<b>100</b>	<b>70</b>	<b>100</b>	<b>119</b>	<b>100</b>	<b>97</b>	<b>100</b>	<b>339</b>	<b>100</b>

Patients may have one or more clinical presentation

\* No information on clinical presentation

For 2004, 1 patient has 2 indications

For 2006, 3 patients have 2 indications

For 2007, 2 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 4 years (Table 5.4). The increased in the numbers of renal allograft biopsies performed in 2007 is contributed by the marked increased in the renal allograft biopsies performed in recipients after 1 year post transplant (Table and Figure 5.4). This reflects the increasingly importance of chronic allograft nephropathy among renal transplant recipients.

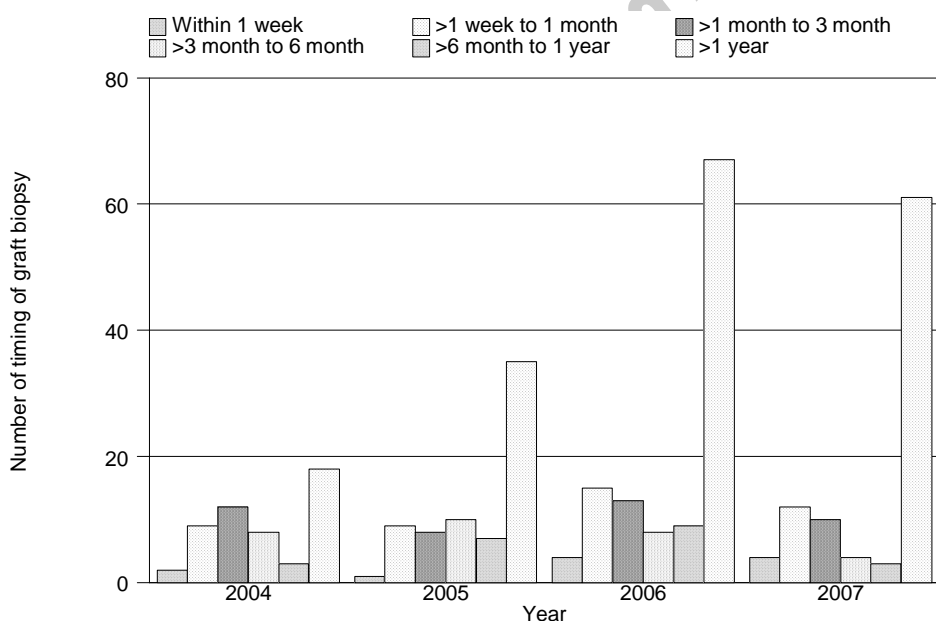
Table 5.4: Timing of renal allograft biopsy, 2004-2007

Timing of allograft biopsy *	Within 1 week		>1 wk to 1 mth		>1 mth to 3 mths		>3 mths to 6 mths		>6 mths to 1 year		>1 yr		Missing**		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
2004	2	4	9	16	12	23	8	15	3	6	18	35	0	0	52	100
2005	1	1	9	13	8	11	10	14	7	10	35	50	0	0	70	100
2006	4	3	15	13	13	11	8	7	9	8	67	58	0	0	116	100
2007	4	4	12	13	10	11	4	4	3	3	61	64	1	1	95	100
<b>Total</b>	<b>11</b>	<b>4</b>	<b>45</b>	<b>14</b>	<b>43</b>	<b>13</b>	<b>30</b>	<b>9</b>	<b>22</b>	<b>7</b>	<b>181</b>	<b>54</b>	<b>1</b>	<b>0</b>	<b>333</b>	<b>100</b>

\*Timing of renal allograft biopsy: from date of transplantation

\*\* No data information on date of graft treatment

Figure 5.4: Timing of renal allograft biopsy, 2004-2007



## 5.5: Biopsy Procedure

### 5.5.1: Biopsy method

Over the last 4 years, nearly all renal allograft biopsies were performed under ultrasonographic guidance with real-time guidance accounting for at least 57% in 2007 (Table 5.5.1). When incomplete data are censored, ultrasonographic guidance with real-time renal allograft biopsy accounts for 84% in 2007 (Figure 5.5.1).

Table 5.5.1: Biopsy method, 2004-2007

Method	2004		2005		2006		2007		Total	
	n	%	n	%	n	%	n	%	n	%
Blind (no ultrasound biopsy)	0	0	1	1	1	1	1	1	3	1
USS guided: real-time	45	86	26	37	62	54	54	57	187	56
USS guided: not real-time	2	4	32	46	33	28	9	9	76	23
Missing*	5	10	11	16	20	17	31	33	67	20
<b>Total</b>	<b>52</b>	<b>100</b>	<b>70</b>	<b>100</b>	<b>116</b>	<b>100</b>	<b>95</b>	<b>100</b>	<b>333</b>	<b>100</b>

\* Missing means no data on biopsy technique

Figure 5.5.1: Biopsy method (censored for missing data), 2004-2007

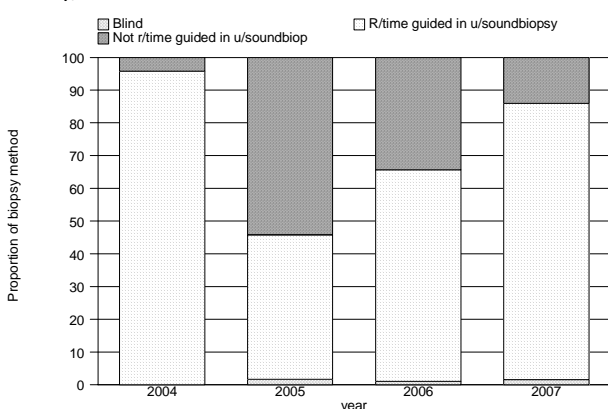
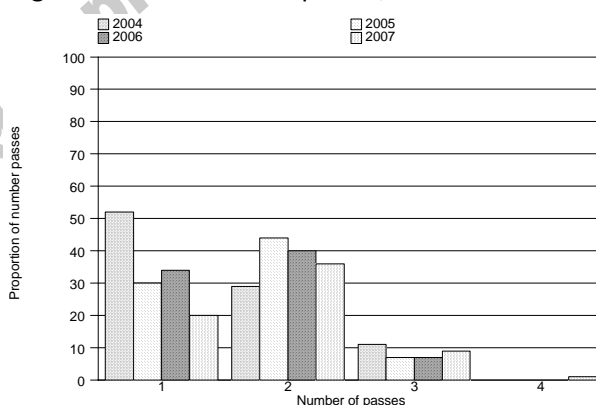


Figure 5.5.2: Number of passes, 2004-2007



### 5.5.2: Number of passes

The average passes for renal allograft biopsy remained unchanged over the last 4 years. In 2007, the average passes made during allograft biopsy was 1.87 (after censoring incomplete data) with only 1% requiring more than 3 passes (Table & Figure 5.5.2).

Table 5.5.2: Number of passes, 2004-2007

Number of passes	2004		2005		2006		2007		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
1	27	52	21	30	39	33	19	20	106	32
2	15	29	31	44	46	40	34	36	126	38
3	6	11	5	7	8	7	9	9	28	8
4	0	0	0	0	0	0	1	1	1	0
Missing*	4	8	13	19	23	20	32	34	72	22
<b>Total</b>	<b>52</b>	<b>100</b>	<b>70</b>	<b>100</b>	<b>116</b>	<b>100</b>	<b>95</b>	<b>100</b>	<b>333</b>	<b>100</b>

\* No data information on number of passes

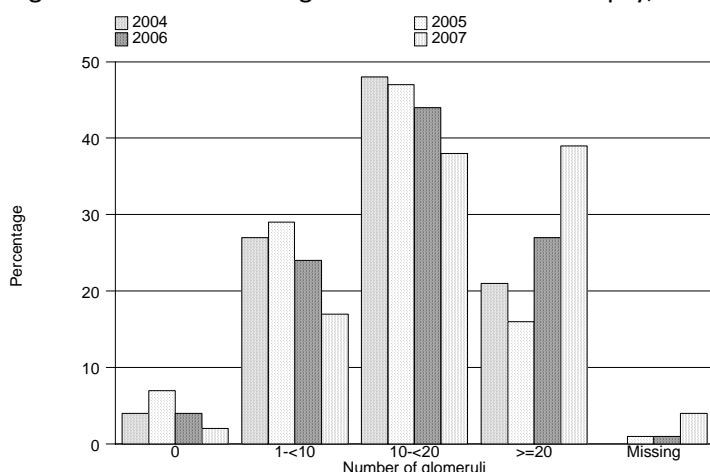
**5.5.3: Number of glomeruli obtained on biopsy**

With an average of less than 2 passes made, 71% of the renal allograft biopsies performed over the last 4 years yield at least 10 glomeruli (Table & Figure 5.5.3). Renal allograft biopsy without any glomerulus is uncommon and accounted for only 4%. Over the last 4 years, the number of renal allograft biopsies yielding less than 10 glomeruli has gradually decreased and in 2007 accounted for only 19%.

Table 5.5.3: Number of glomeruli obtained on biopsy, 2004-2007

No of glomeruli obtained	2004		2005		2006		2007		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
0	2	4	5	7	5	4	2	2	14	4
1-9	14	27	20	29	28	24	16	17	78	23
10-19	25	48	33	47	51	44	36	38	145	44
>20	11	21	11	16	31	27	37	39	90	27
Missing/Unknown*	0	0	1	1	1	1	4	4	6	2
<b>Total</b>	<b>52</b>	<b>100</b>	<b>70</b>	<b>100</b>	<b>116</b>	<b>100</b>	<b>95</b>	<b>100</b>	<b>333</b>	<b>100</b>

Figure 5.5.3: Number of glomeruli obtained on biopsy, 2004-2007

**5.5.4: Type of complications**

Complication rates from renal allograft biopsy were uncommon and major complications occurred in less than 2% of all allograft biopsies (Table 5.5.4).

Table 5.5.4: Type of complications, 2004-2007

Type of complications	2004		2005		2006		2007		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
No complication	35	67	51	74	92	79	54	57	232	70
Mild complication <sup>a</sup>	1	2	1	1	1	1	3	3	6	2
Severe complication <sup>b</sup>	0	0	1	1	0	0	1	1	2	1
Missing / Unknown <sup>c</sup>	16	31	17	24	23	20	37	39	93	27
<b>Total</b>	<b>52</b>	<b>100</b>	<b>70</b>	<b>100</b>	<b>116</b>	<b>100</b>	<b>95</b>	<b>100</b>	<b>333</b>	<b>100</b>

<sup>a</sup> Mild complication is defined as presence of gross haematuria, peri-renal collection, hematoma, or AVM that do not require intervention

<sup>b</sup> Severe complication is defined as presence of hypotension or complications requiring intervention.

<sup>c</sup> No data information for complications

### 5.6: Histological diagnosis

Acute rejection (acute and borderline) has remained the most common histological diagnosis of renal allograft biopsies over the last 4 years (Table 5.6), accounting for 31-34% of all allograft biopsies. During the same period, both the absolute number and percentage of renal allograft biopsies having histological diagnosis of chronic allograft nephropathy have increased (14% in 2004 compared to 19% in 2006), reflecting the change in biopsy indications among nephrologists.

Table 5.6: Histological diagnosis, 2004-2007

Histological Diagnosis	2004		2005		2006		2007		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Acute rejection	23	33	25	31	52	31	38	34	138	32
Borderline rejection	3	4	9	11	5	3	6	5	23	5
Calcineurine inhibitor toxicity	13	19	20	25	29	17	17	15	79	18
Chronic allograft nephropathy	10	14	12	15	37	22	21	19	80	19
Acute tubular necrosis	14	20	8	10	21	13	20	18	63	15
PTLD *	1	2	0	0	6	3	1	1	8	2
De novo GN	2	3	2	3	6	3	4	3	14	3
Recurrent GN	2	3	2	3	5	3	1	1	10	2
Diabetic nephropathy	0	0	0	0	5	3	1	1	6	1
Others	1	2	2	2	2	2	4	5	9	1
<b>Total</b>	<b>69</b>	<b>100</b>	<b>80</b>	<b>100</b>	<b>168</b>	<b>100</b>	<b>113</b>	<b>100</b>	<b>430</b>	<b>100</b>

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

## APPENDIX

**Prelim Report Awaiting Approval from KKM**

**APPENDIX I : ANALYSIS CRITERIA AND STATISTICAL METHODOLOGY**

Hoo Ling Ping

**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 2005-2007**

The analysis set in Chapter 1 includes all patients who underwent native and graft kidney biopsies from 2005-2007.

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, 2005-2007**

The analysis set in Chapter 1 includes patients who underwent native renal biopsy from 2005-2007.

**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 2005-2007.

**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 2005-2007.

**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 2004-2007.

**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.

### **Lab 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 modeling 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, discoid 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 II : 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.

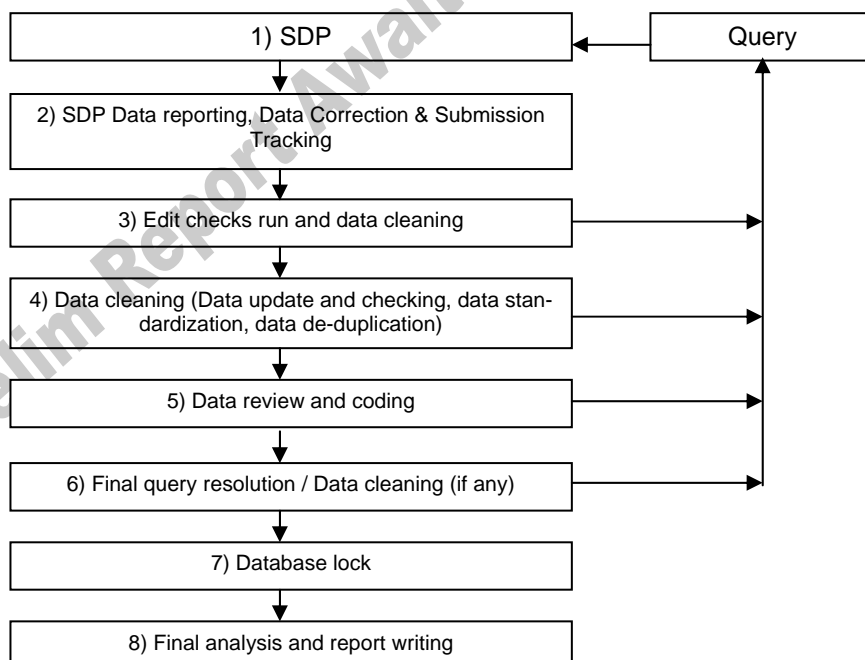
### Data sources

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. However, this report (2005-2007) is only confined to Ministry of Health hospitals with overall coverage rate of 93.3%.

### 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), First Report of the Malaysian Registry of Renal Biopsy 2005-2007. Kuala Lumpur 2008.

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](http://www.msn.org.my/nrr).

Prelim Report Awaiting Approval from KKM

### APPENDIX III : 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
FSGS	Focal Segmental Glomerulosclerosis
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**

Schwartz Formula =  $K \times \text{Height (cm)}$

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

Prelim Report Awaiting Approval from KKM