

## **CHAPTER 3**

### **Secondary Glomerulonephritis**

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### 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)

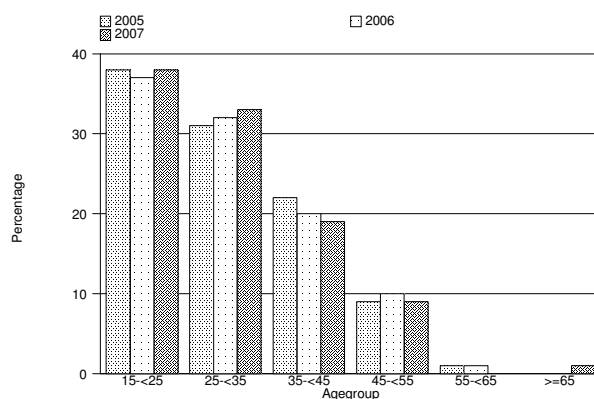
#### 3.1.2: Patient population and characteristics

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.

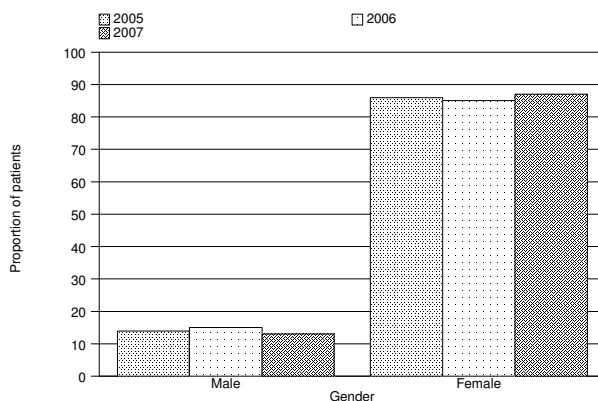
Figure 3.1.2.1: Age group at time of biopsy (years), 2005-2007



##### 3.1.2.2: Gender distribution

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

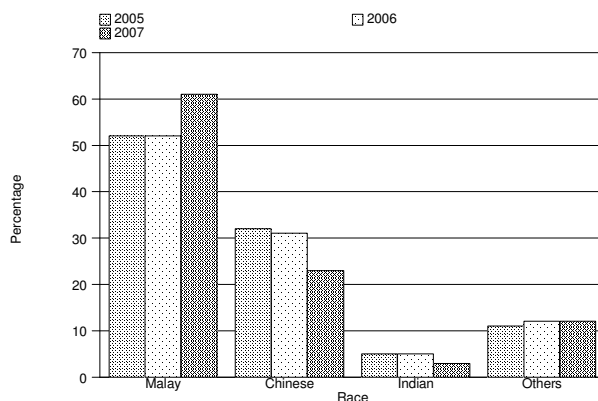
Figure 3.1.2.2: Gender distribution, 2005-2007



##### 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

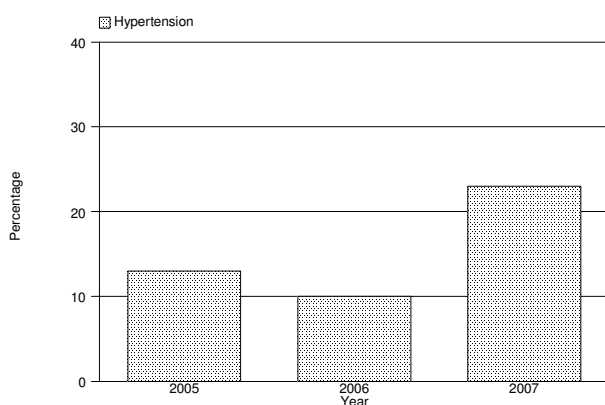
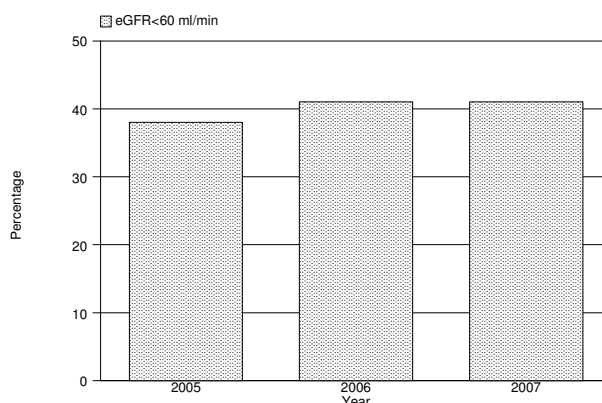


Figure 3.1.3(b): Impaired renal function by year, 2005-2007



**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

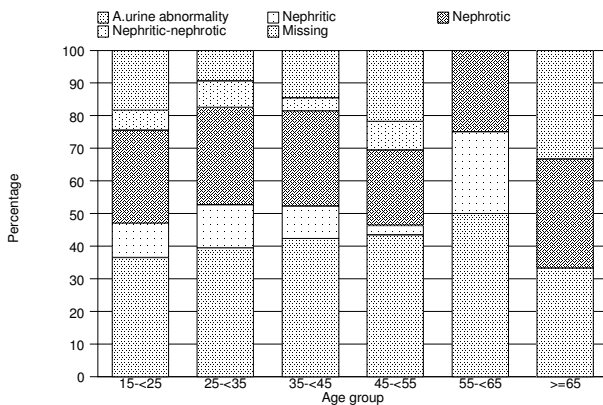


Figure 3.1.3.1(b): Hypertension by age group, 2005-2007

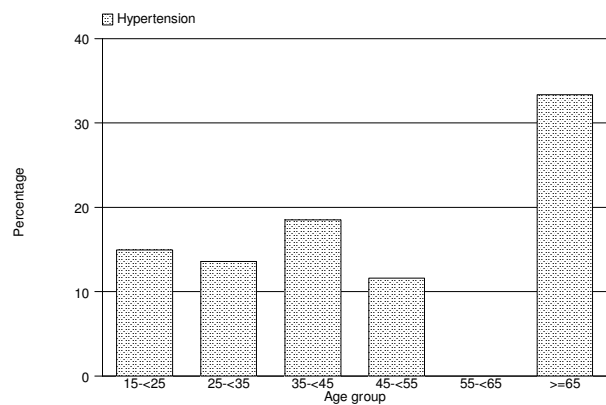
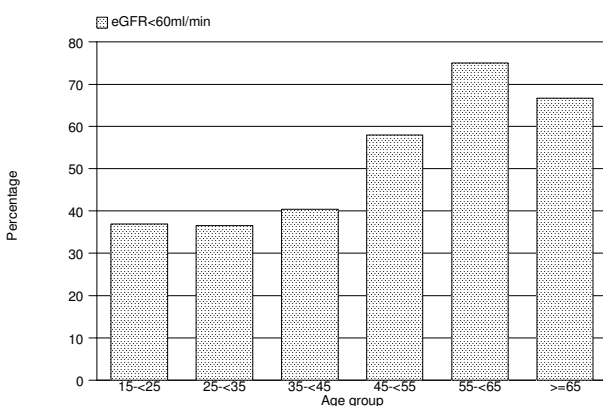


Figure 3.1.3.1(c): Impaired renal function by age group, 2005-2007



### 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

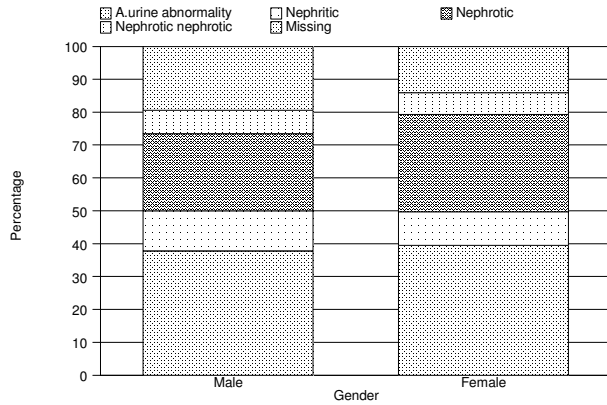


Figure 3.1.3.2(b): Hypertension by gender 2005-2007

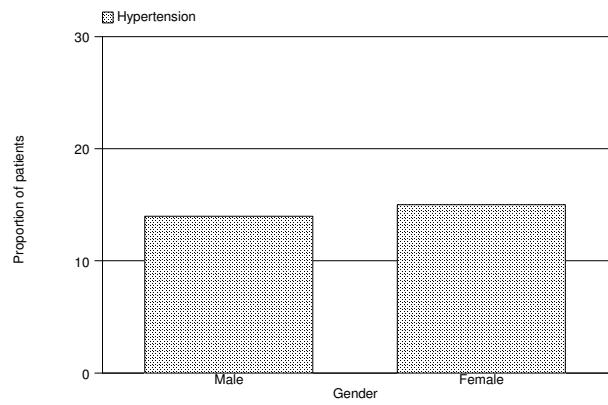
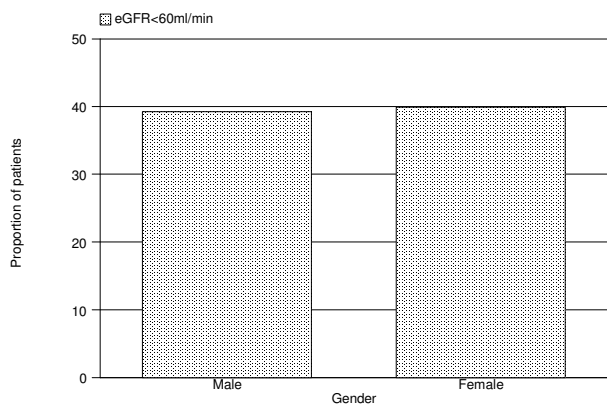


Figure 3.1.3.2(c): Impaired renal function by gender, 2005-2007



**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

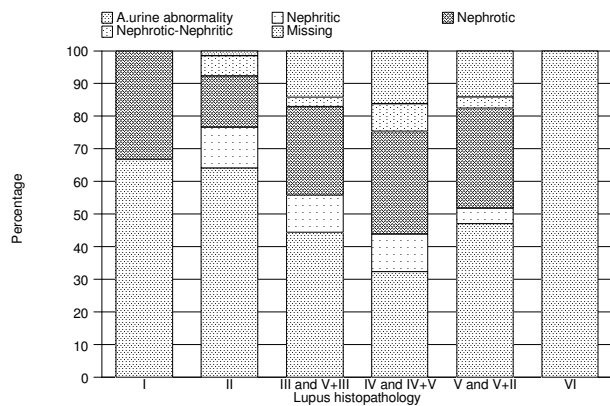


Figure 3.1.3.3(b): Prevalence of hypertension by histopathology, 2005-2007

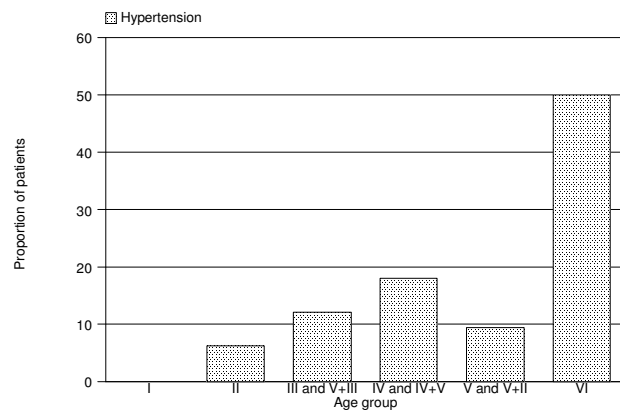
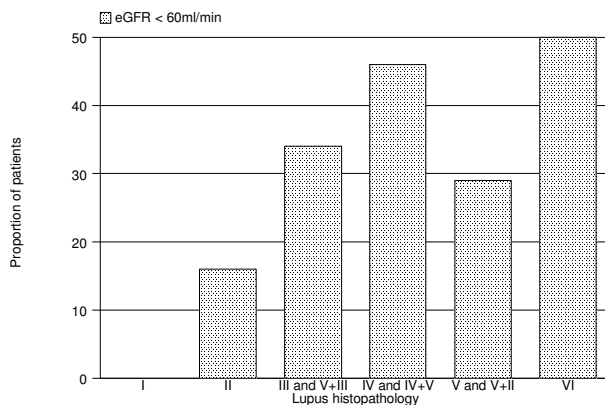


Figure 3.1.3.3(c): Prevalence of impaired renal function by histopathology, 2005-2007



### 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.

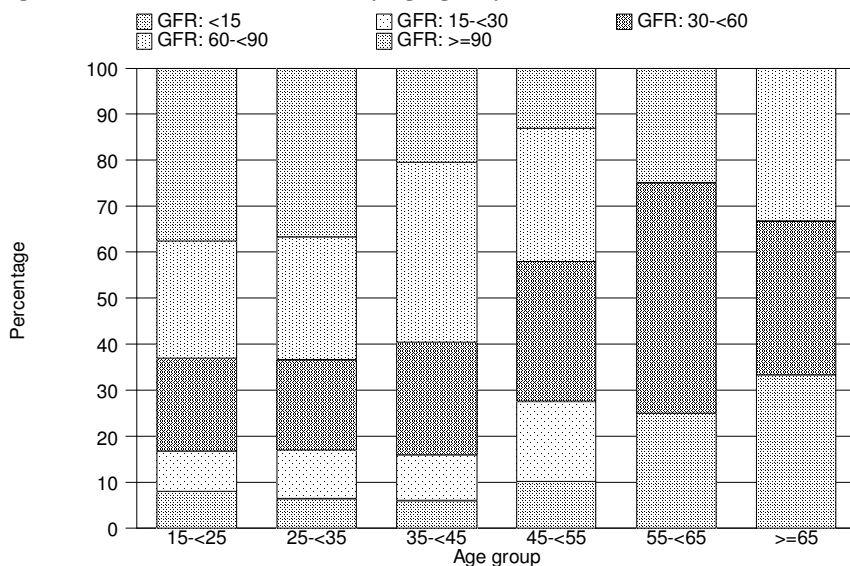
#### 3.1.4.1: Renal function at presentation by age group

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>

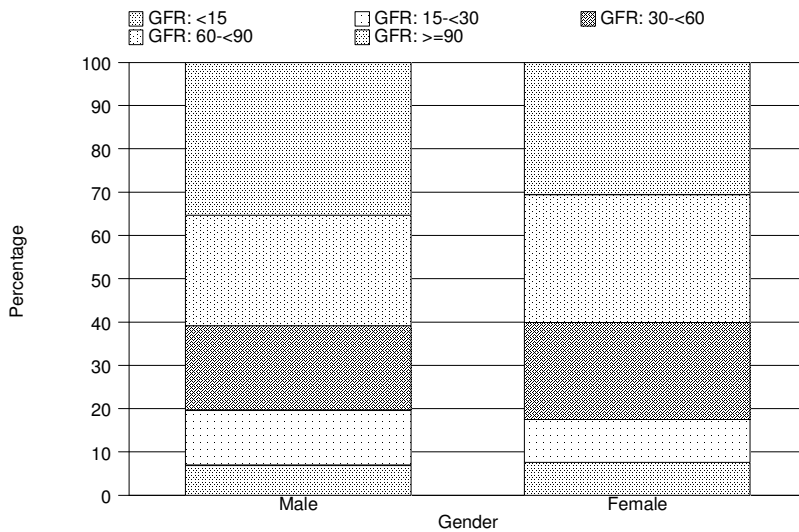
Figure 3.1.4.1: Renal function by age group, 2005-2007



**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.

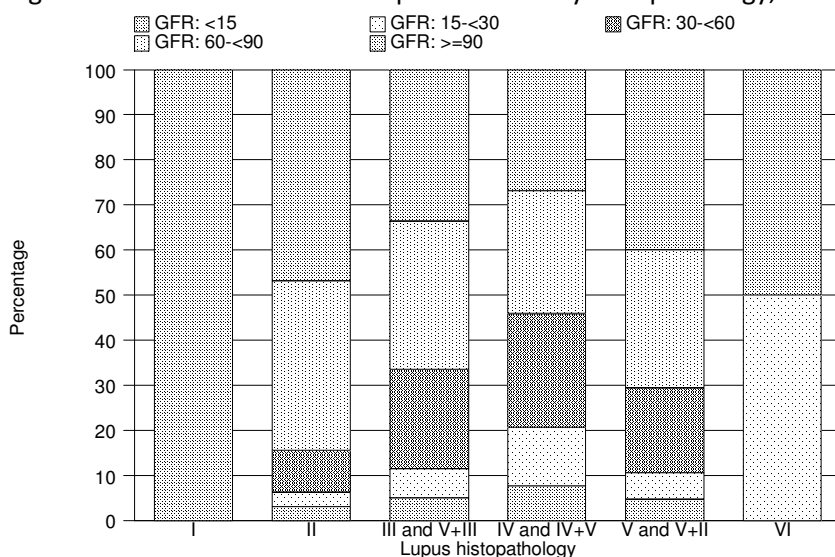
Table 3.1.4.3: Renal function at presentation by histopathology, 2005-2007

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**

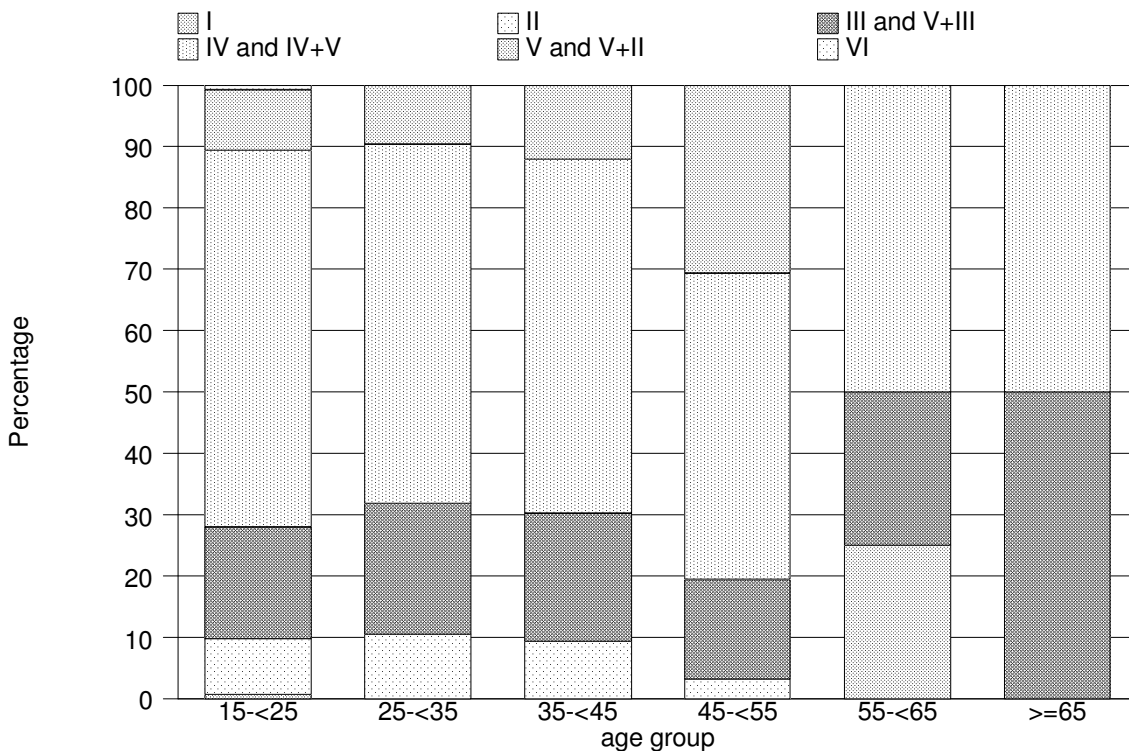
In adults, Class IV or IV+V were the most predominant lesion in all age groups. However, the frequency of class IV and IV+V were less with increasing age (Table 3.1.5.1).

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

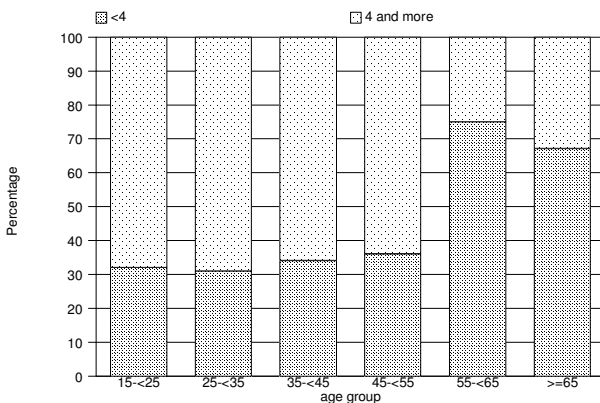
Table 3.1.6.1: ARA criteria in lupus nephritis, 2005-2007

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.

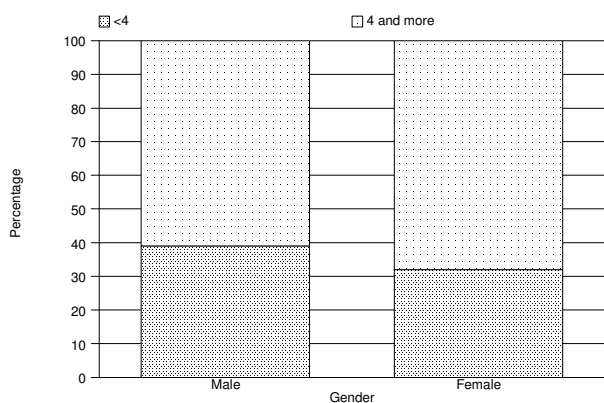
Figure 3.1.6.2: ARA criteria in lupus nephritis by age group, 2005-2007



**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%).

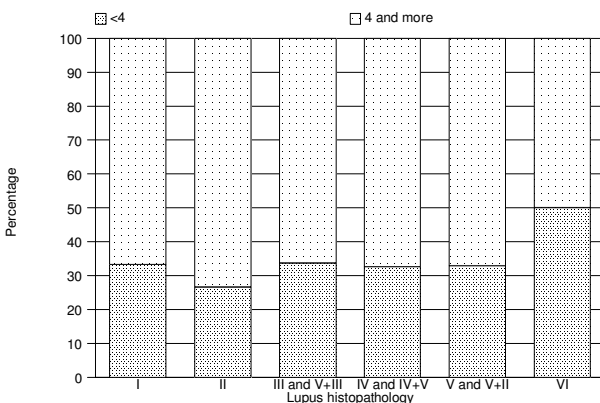
Figure 3.1.6.3 ARA criteria in lupus nephritis by gender, 2005-2007



**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

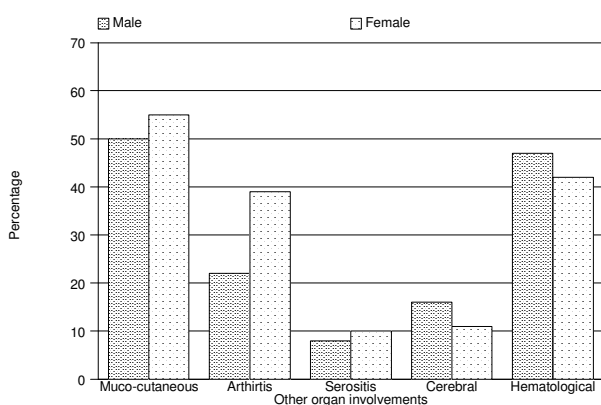


Figure 3.1.6.5(b): Mucocutaneous involvement by gender, 2005-2007

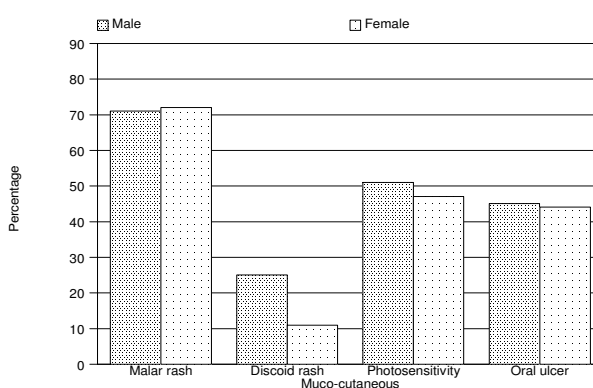


Table 3.1.6.5(b): Mucocutaneous involvement by gender, 2005-2007

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>	