

## **CHAPTER 3**

### **SECONDARY GLOMERULONEPHRITIS**

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### 3.1: Introduction

This chapter covers the main secondary glomerulonephritis that were reported to the MRRB from the year 2005-2012.

Lupus nephritis consistently remained to be the commonest secondary glomerulonephritis in Malaysia, contributing to 80.9% of all secondary glomerulonephritis followed by diabetic nephropathy, which contributed 13.2%. (Table 3.1)

Other causes of secondary glomerulonephritis are relatively uncommon. Post-infectious GN was reported in 2.4 % of patients with secondary GN. There were only 24 cases of renal amyloidosis reported to the registry during the 8-year period of 2005-2012.

**Table 3.1: Causes of secondary glomerulonephritis in adult, 2005-2012**

Type of secondary GN	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
<b>Lupus nephritis</b>	<b>1756</b>	<b>82.2</b>	<b>446</b>	<b>78.5</b>	<b>450</b>	<b>78.4</b>	<b>2652</b>	<b>80.9</b>
<b>Diabetic nephropathy</b>	<b>279</b>	<b>13.1</b>	<b>73</b>	<b>12.9</b>	<b>81</b>	<b>14.1</b>	<b>433</b>	<b>13.2</b>
Post infectious GN	40	1.9	20	3.5	19	3.3	79	2.4
Amyloidosis	11	0.5	7	1.2	6	1.0	24	0.7
Other infection	14	0.7	1	0.2	3	0.5	18	0.5
Systemic vasculitis	6	0.3	3	0.5	5	0.9	14	0.4
Henoch Schoenlein Purpura	7	0.3	3	0.5	2	0.3	12	0.4
Multiple myeloma	12	0.6	0	0.0	0	0.0	12	0.4
HUS/TTP*	0	0.0	2	0.4	1	0.2	3	0.1
Polyarteritis nodosa	0	0.0	0	0.0	0	0.0	0	0.0
Malignancy	3	0.1	2	0.4	0	0.0	5	0.2
Light/heavy chain disease	4	0.2	0	0.0	1	0.2	5	0.2
Anti-GBM antibody disease	0	0.0	0	0.0	1	0.2	1	0.0
Immunotactoid glomerulopathy	0	0.0	1	0.2	0	0.0	1	0.0
Idiopathic Crescentic GN	0	0.0	0	0.0	0	0.0	0	0.0
Not available/Missing	5	0.2	10	1.8	5	0.9	20	0.6
<b>Total</b>	<b>2137</b>	<b>100.0</b>	<b>568</b>	<b>100.0</b>	<b>574</b>	<b>100.0</b>	<b>3279</b>	<b>100.0</b>

\* Hemolytic uraemic syndrome/Thrombotic thrombocytopenic purpura

### 3.2: Lupus Nephritis

#### 3.2.1: Introduction

This section focuses on lupus nephritis, which was the commonest form of secondary glomerulonephritis in adults (defined as >15 years of age) in Malaysia.

#### 3.2.2: Patient population and characteristics

There was a total of 2652 biopsy-proven lupus nephritis reported over the 8 years period (from 1<sup>st</sup> January 2005 to 31<sup>st</sup> December 2012).

### 3.2.2.1: Age at time of biopsy

The mean age of adult patients with lupus nephritis at the time of biopsy was  $30.28 \pm 10.67$  years (range: 15-78.87 years) (Table 3.2.2.1(a)). There has been no change in the age at which SLE patients underwent renal biopsy over the last 8-year observation period.

The most predominant age group was between 15 to 25 years old, which accounted for 38.5% of cases. The onset of lupus above the age of 45 was uncommon and only constituted about 11.5% of cases. (Table & Figure 3.2.2.1(b)).

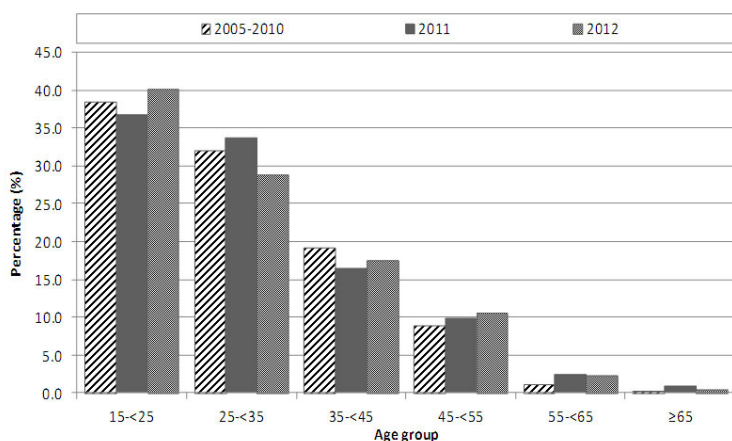
**Table 3.2.2.1 (a): Age group at time of biopsy (years), 2005-2012**

Year	2005 - 2010	2011	2012	Total
N	1756	446	450	2652
Mean	30.13	30.75	30.41	30.28
Standard Deviation	10.45	11.07	11.13	10.67
Median	27.90	27.93	27.60	27.85
Minimum	15.00	15.00	15.15	15.00
Maximum	78.87	72.13	72.43	78.87

**Table 3.2.2.1 (b): Age group at time of biopsy (years), 2005-2012**

Age group (years)	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
15-<25	675	38.4	164	36.8	181	40.2	1020	38.5
25-<35	563	32.1	150	33.6	130	28.9	843	31.8
35-<45	336	19.1	73	16.4	79	17.6	488	18.4
45-<55	156	8.9	44	9.9	48	10.7	248	9.4
55-<65	20	1.1	11	2.5	10	2.2	41	1.6
≥65	6	0.3	4	0.9	2	0.4	12	0.5
<b>Total</b>	<b>1756</b>	<b>100.0</b>	<b>446</b>	<b>100.0</b>	<b>450</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

**Figure 3.2.2.1: Age group at time of biopsy (years), 2005-2012**



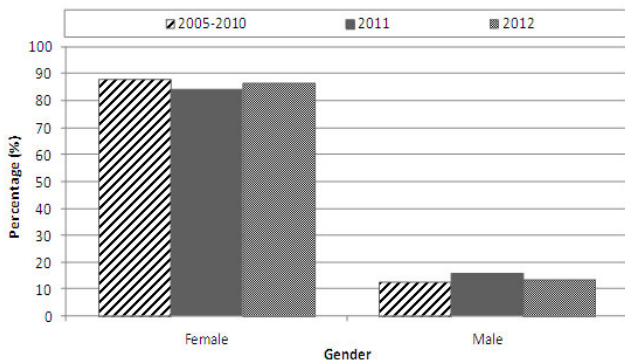
**3.2.2.2: Gender distribution**

As reported elsewhere, lupus nephritis predominantly affected females. In Malaysia, the female: male ratio of 6.6:1 was reported.

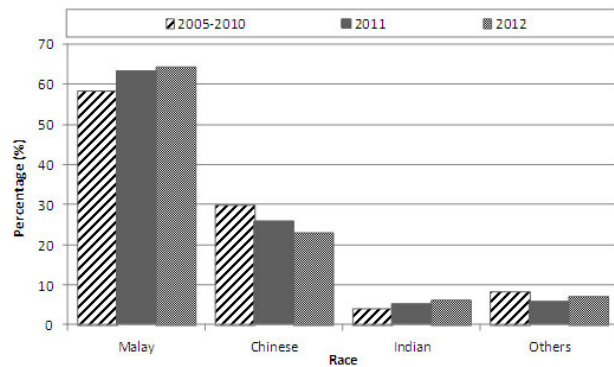
**Table 3.2.2.2: Gender distribution, 2005-2012**

Gender	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
Female	1486	87.7	362	84.2	387	86.6	2235	86.9
Male	209	12.3	68	15.8	60	13.4	337	13.1
<b>Total</b>	<b>1695</b>	<b>100.0</b>	<b>430</b>	<b>100.0</b>	<b>447</b>	<b>100.0</b>	<b>2572</b>	<b>100.0</b>

**Figure 3.2.2.2: Gender distribution, 2005-2012**



**Figure 3.2.2.3: Ethnic distribution, 2005-2012**



**3.2.2.3: Ethnic prevalence**

Sixty percent of patients with lupus nephritis were Malays, 27.8% Chinese, 4.5% Indians and 7.5% were of other races (predominantly the indigenous population of Malaysia) (Table & Figure 3.2.2.3). Hence, we concluded that there was no preponderance of the disease in certain ethnic groups in the Malaysian population.

**Table 3.2.2.3: Ethnic distribution, 2005-2012**

Ethnic	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
Malay	987	58.2	272	63.3	287	64.2	1546	60.1
Chinese	503	29.7	111	25.8	102	22.8	716	27.8
Indian	68	4.0	22	5.1	27	6.0	117	4.5
Others	137	8.1	25	5.8	31	6.9	193	7.5
<b>Total</b>	<b>1695</b>	<b>100.0</b>	<b>430</b>	<b>100.0</b>	<b>447</b>	<b>100.0</b>	<b>2572</b>	<b>100.0</b>

### 3.2.3: Clinical presentation

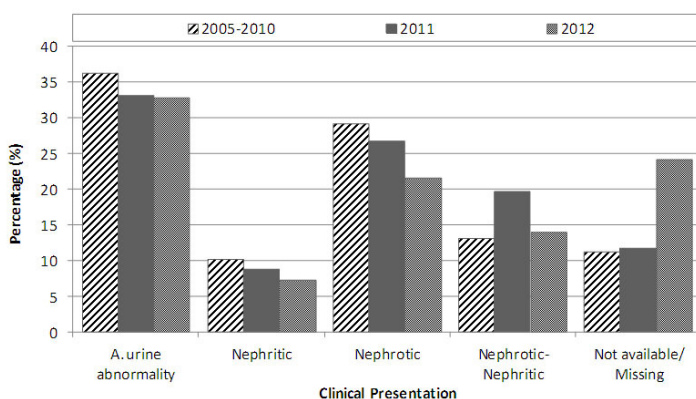
In adult patients with lupus nephritis, 35.2% presented with urine abnormalities, 9.4% with nephritic syndrome, 27.5% with nephrotic syndrome and 14.4% presented with a combination of nephritic and nephrotic features. Data was missing in about 13.5% of cases.

At the time of presentation, 74.7% had impaired renal function (defined by eGFR by modified MDRD of less than 60 ml/min/1.73m<sup>2</sup>). Thirty-three percent of the patients already had hypertension on presentation.

**Table 3.2.3: Clinical presentation by year, 2005-2012**

Clinical Presentation	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
Urine abnormality	638	36.3	148	33.2	148	32.9	934	35.2
Nephritic syndrome	178	10.1	39	8.7	33	7.3	250	9.4
Nephrotic syndrome	513	29.2	119	26.7	97	21.6	729	27.5
Nephrotic-nephritic syndrome	230	13.1	88	19.7	63	14.0	381	14.4
Not available/ Missing	197	11.2	52	11.7	109	24.2	358	13.5
<b>Total</b>	<b>1756</b>	<b>100.0</b>	<b>446</b>	<b>100.0</b>	<b>450</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

**Figure 3.2.3: Clinical presentation by year, 2005-2012**



**Table 3.2.3 (a): Hypertension by year, 2005-2012**

Hypertension	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
Present	523	29.8	191	42.8	161	35.8	875	33.0
Absent	1116	63.6	184	41.3	171	38.0	1471	55.5
Not available/Missing	117	6.7	71	15.9	118	26.2	306	11.5
<b>Total</b>	<b>1756</b>	<b>100.0</b>	<b>446</b>	<b>100.0</b>	<b>450</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

Figure 3.2.3 (a): Hypertension by year, 2005-2012

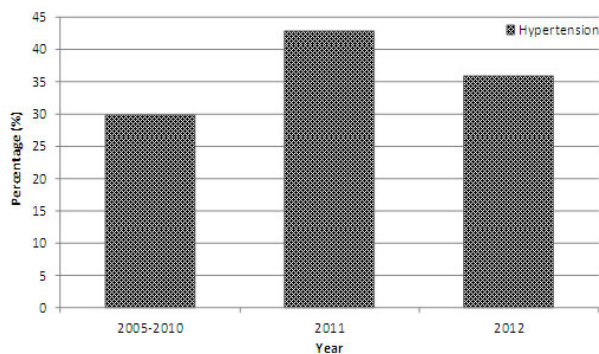


Figure 3.2.3 (b) Impaired renal function by year, 2005-2012

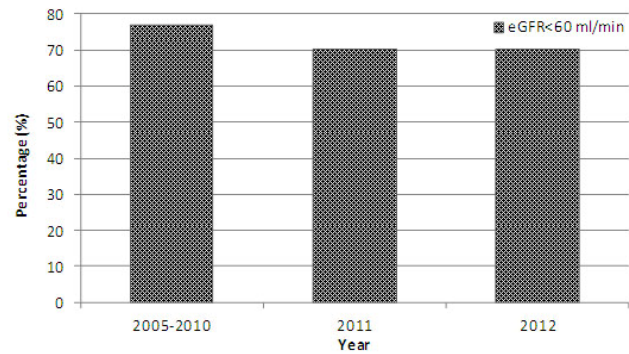


Table 3.2.3 (b) Renal function by year, 2005-2012

GFR (ml/min/1.72m <sup>2</sup> )	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
<15	105	19.9	19	13.8	16	14.0	140	18.0
15-29	118	22.4	27	19.6	29	25.4	174	22.3
30-59	182	34.5	51	37.0	35	30.7	268	34.4
60-89	63	12.0	27	19.6	18	15.8	108	13.9
≥90	39	7.4	9	6.5	7	6.1	55	7.1
Missing*	20	3.8	5	3.6	9	7.9	34	4.4
<b>Total</b>	<b>527</b>	<b>100.0</b>	<b>138</b>	<b>100.0</b>	<b>114</b>	<b>100.0</b>	<b>779</b>	<b>100.0</b>

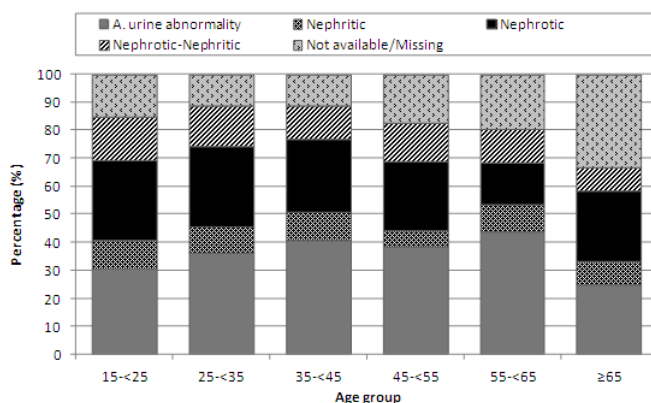
\*Total of 34 cases are missing on GFR, including 6 cases with GFR>200 (GFR range between 201 to 566) Figure 3.2.3

### 3.2.3.1: Clinical Presentation by age

Urine abnormalities was the commonest clinical presentation of lupus nephritis in all age groups. This was followed by nephrotic syndrome. However, there was a significant number of cases where data was not available, especially for those aged 55 years and above (Table & Figure 3.2.3.1(a))

The prevalence of hypertension was between 16-42% across all age groups. The prevalence of hypertension in those aged 65 years and above may be falsely low as there was a significant number of missing data in this group of patients. The prevalence of impaired kidney function (e-GFR of < 60ml/min/1.73 m<sup>2</sup>) was higher in the older age groups.

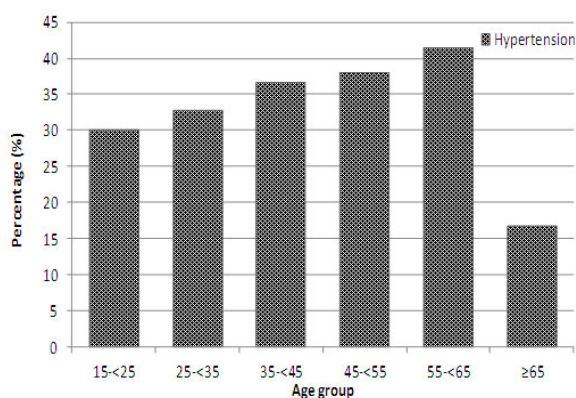
Figure 3.2.3.1(a): Clinical presentation by age group, 2005-2012



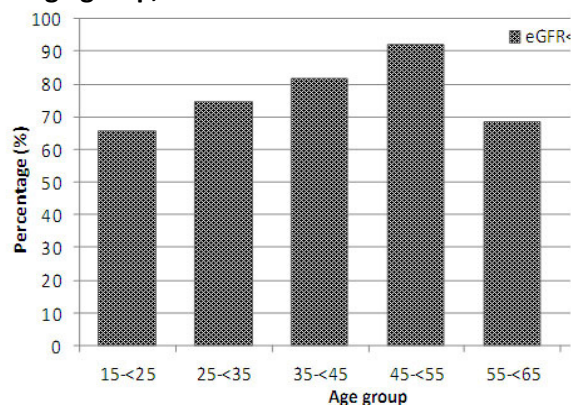
**Table 3.2.3.1(a): Clinical presentation by age group, 2005-2012**

Age group (Years)	15-<25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Urine abnormality	312	30.6	306	36.3	199	40.8	96	38.7	18	43.9	3	25.0	934	35.2
Nephritic syndrome	102	10.0	79	9.4	50	10.2	14	5.6	4	9.8	1	8.3	250	9.4
Nephrotic Syndrome	293	28.7	240	28.5	126	25.8	61	24.6	6	14.6	3	25.0	729	27.5
Nephrotic-Nephritic	160	15.7	122	14.5	59	12.1	34	13.7	5	12.2	1	8.3	381	14.4
Not available/ Missing	153	15.0	96	11.4	54	11.1	43	17.3	8	19.5	4	33.3	358	13.5
<b>TOTAL</b>	<b>1020</b>	<b>100.0</b>	<b>843</b>	<b>100.0</b>	<b>488</b>	<b>100.0</b>	<b>248</b>	<b>100.0</b>	<b>41</b>	<b>100.0</b>	<b>12</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

**Figure 3.2.3.1(b) Hypertension by age group 2005-2012**



**Figure 3.2.3.1(c): Impaired renal function by age group, 2005-2012**



**Table 3.2.3.1(b) Hypertension by age group 2005-2012**

Hypertension	15-<25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Present	307	30.1	276	32.7	179	36.7	94	37.9	17	41.5	2	16.7	875	33.0
Absent	611	59.9	475	56.3	240	49.2	120	48.4	18	43.9	7	58.3	1471	55.5
Not available/ Missing	102	10.0	92	10.9	69	14.1	34	13.7	6	14.6	3	25.0	306	11.5
<b>TOTAL</b>	<b>1020</b>	<b>100.0</b>	<b>843</b>	<b>100.0</b>	<b>488</b>	<b>100.0</b>	<b>248</b>	<b>100.0</b>	<b>41</b>	<b>100.0</b>	<b>12</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

**Table 3.2.3.1(c): Renal function by age group, 2005-2012**

GFR (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	%
<15	48	16.4	42	17.9	24	17.3	21	23.1	4	25.0	1	16.7	140	18.0
15-29	47	16.1	51	21.7	43	30.9	29	31.9	1	6.3	3	50.0	174	22.3
30-59	97	33.2	83	35.3	47	33.8	34	37.4	6	37.5	1	16.7	268	34.4
60-89	55	18.8	35	14.9	13	9.4	4	4.4	0	0.0	1	16.7	108	13.9
≥90	33	11.3	12	5.1	5	3.6	2	2.2	3	18.8	0	0.0	55	7.1
Missing*	12	4.1	12	5.1	7	5.0	1	1.1	2	12.5	0	0.0	34	4.4
<b>TOTAL</b>	<b>292</b>	<b>100.0</b>	<b>235</b>	<b>100.0</b>	<b>139</b>	<b>100.0</b>	<b>91</b>	<b>100.0</b>	<b>16</b>	<b>100.0</b>	<b>6</b>	<b>100.0</b>	<b>779</b>	<b>100.0</b>

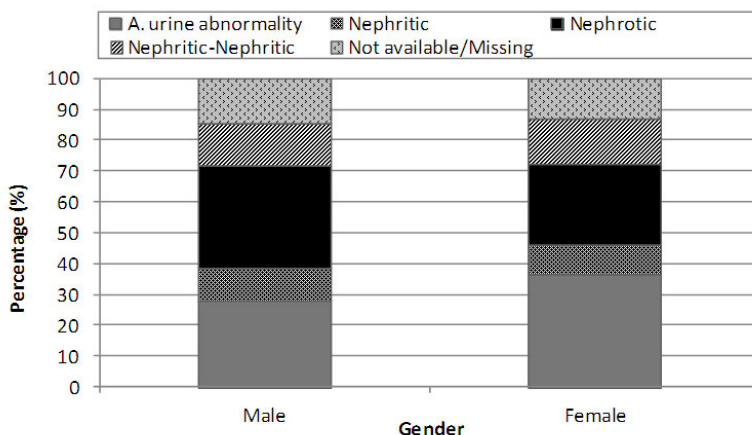
\*Total of 34 cases are missing on GFR, including 6 cases with GFR>200 (GFR range between 201 to 566)

### 3.2.3.2: Clinical presentation by gender

There were no differences in the clinical presentation, prevalence of hypertension and proportion of patients with impaired renal function between the two genders (Table & Figure 3.2.3.2 (a)).

**Table 3.2.3.2 (a): Clinical presentation by gender, 2005-2012**

Clinical Presentation	Male		Female		Total	
	n	%	n	%	n	%
Urine abnormality	96	27.9	838	36.3	934	35.2
Nephritic syndrome	36	10.5	214	9.3	250	9.4
Nephrotic syndrome	114	33.1	615	26.6	729	27.5
Nephritic-nephritic syndrome	46	13.4	335	14.5	381	14.4
Not available/Missing	52	15.1	306	13.3	358	13.5
<b>TOTAL</b>	<b>344</b>	<b>100.0</b>	<b>2308</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

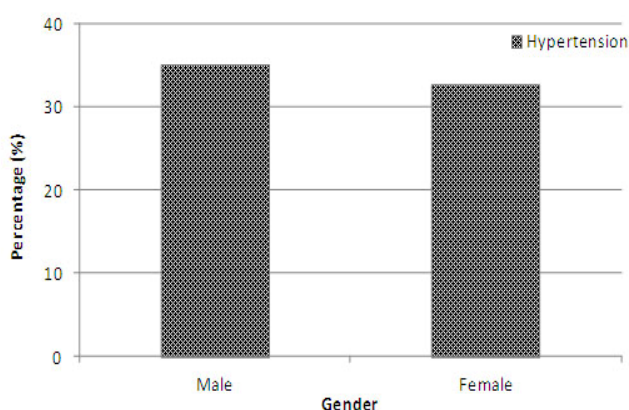
**Figure 3.2.3.2 (a): Clinical presentation by gender, 2005-2012**



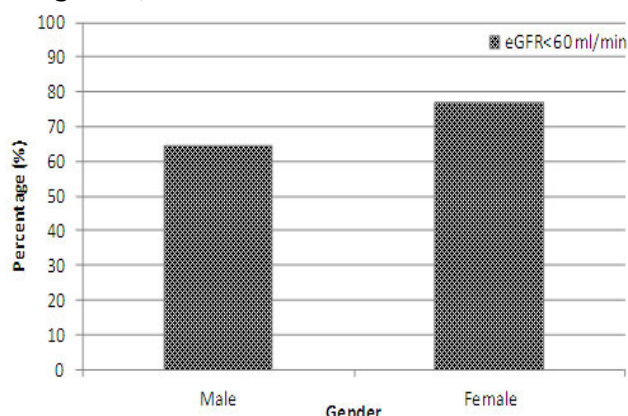
**Table 3.2.3.2(b): Hypertension by gender, 2005-2012**

Hypertension	Male		Female		Total	
	n	%	n	%	n	%
Present	121	35.2	754	32.7	875	33.0
Absent	185	53.8	1286	55.7	1471	55.5
Missing	38	11.0	268	11.6	306	11.5
<b>Total</b>	<b>344</b>	<b>100.0</b>	<b>2308</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

**Figure 3.2.3.2(b): Hypertension by gender, 2005-2012**



**Figure 3.2.3.2(c): Impaired renal function by gender, 2005-2012**



**Table 3.2.3.2(c): Renal function by gender, 2005-2012**

GFR (ml/min/1.72m <sup>2</sup> )	Male		Female		Total	
	n	%	n	%	n	%
<15	15	12.1	125	19.1	140	18.0
15-29	24	19.4	150	22.9	174	22.3
30-59	41	33.1	227	34.7	268	34.4
60-89	28	22.6	80	12.2	108	13.9
≥90	11	8.9	44	6.7	55	7.1
Missing*	5	4.0	29	4.4	34	4.4
<b>Total</b>	<b>124</b>	<b>100.0</b>	<b>655</b>	<b>100.0</b>	<b>779</b>	<b>100.0</b>

\*Total of 34 cases are missing on GFR, including 6 cases with GFR>200 (GFR range between 201 to 566)

### 3.2.3.3: Clinical Presentation by histopathology

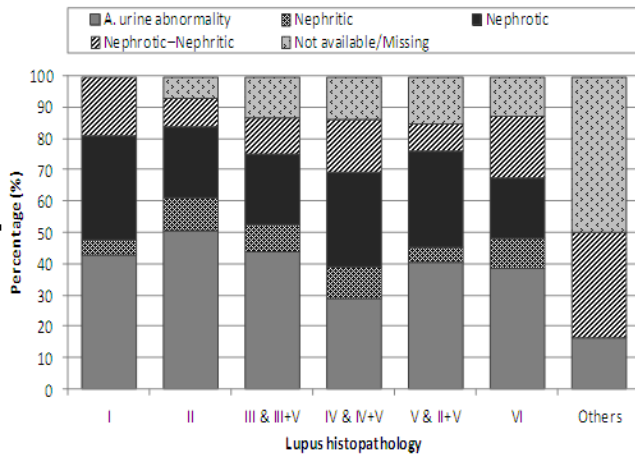
Seventy-nine percent of the biopsy proven lupus nephritis was proliferative in nature (i.e. class III&III+V or IV&IV+V). However, there was no clear correlation between histopathological findings and clinical presentation. The prevalence of hypertension was highest in class VI lupus nephritis, followed by class IV & IV+V lupus nephritis. The prevalence of impaired kidney function correlated with histopathological findings. The proportion of patients with e-GFR < 60 ml/min/1.72 m<sup>2</sup> were 90.4%, 76.5%, 69.4%, 64.8% and 35% in class VI, IV or IV+V, class III or III+V, class V and class II respectively (Table 3.2.3.3(c)).

**Table 3.2.3.3 (a): Clinical presentation by histopathology in lupus nephritis, 2005-2012**

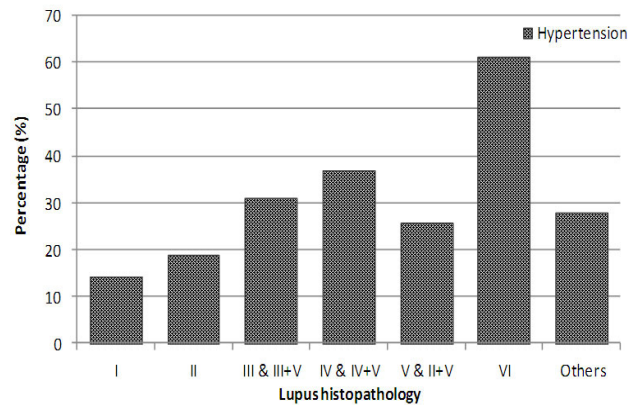
Clinical Presentations	I		II		III & III+V		IV & IV+V		V & II+V		VI		Others		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Urine abnormality	9	42.9	96	50.5	258	44.1	430	28.9	114	40.7	12	38.7	3	16.7	922	35.3
Nephritic syndrome	1	4.8	20	10.5	51	8.7	157	10.5	13	4.6	3	9.7	0	0.0	245	9.4
Nephrotic syndrome	7	33.3	43	22.6	131	22.4	445	29.9	86	30.7	6	19.4	0	0.0	718	27.5
Nephrotic-nephritic syndrome	4	19.0	18	9.5	67	11.5	251	16.8	24	8.6	6	19.4	6	33.3	376	14.4
Not available/Missing	0	0.0	13	6.8	78	13.3	207	13.9	43	15.4	4	12.9	9	50.0	354	13.5
<b>Total</b>	<b>21</b>	<b>100</b>	<b>190</b>	<b>100</b>	<b>585</b>	<b>100</b>	<b>1490</b>	<b>100</b>	<b>280</b>	<b>100</b>	<b>31</b>	<b>100</b>	<b>18</b>	<b>100</b>	<b>2615</b>	<b>100</b>

\* 37 cases are missing on lupus subclass

**Figure 3.2.3.3 (a): Clinical presentation by histopathology in lupus nephritis, 2005-2012**



**Figure 3.2.3.3 (b): Hypertension by histopathology in lupus nephritis, 2005-2012**



**Table 3.2.3.3(b): Hypertension by histopathology, 2005-2012**

Hypertension	I		II		III & III+V		IV & IV+V		V & II+V		VI		Others		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Present	3	14.3	36	18.9	182	31.1	549	36.8	72	25.7	19	61.3	5	27.8	866	33.1
Absent	17	81.0	133	70.0	333	56.9	772	51.8	175	62.5	7	22.6	13	72.2	1450	55.4
Not available/Missing	1	4.8	21	11.1	70	12.0	169	11.3	33	11.8	5	16.1	0	0.0	299	11.4
<b>Total</b>	<b>21</b>	<b>100</b>	<b>190</b>	<b>100</b>	<b>585</b>	<b>100</b>	<b>1490</b>	<b>100</b>	<b>280</b>	<b>100</b>	<b>31</b>	<b>100</b>	<b>18</b>	<b>100</b>	<b>2615</b>	<b>100</b>

**Table 3.2.3.3(c): Renal function by histopathology, 2005-2012**

GFR (ml/min/1.73m <sup>2</sup> )	I		II		III & III+V		IV & IV+V	
	n	%	n	%	n	%	n	%
<15	0	0.0	2	1.1	15	2.6	124	8.3
15-29	1	4.8	3	1.6	19	3.2	177	11.9
30-59	1	4.8	14	7.4	96	16.4	340	22.8
60-89	3	14.3	47	24.7	143	24.4	349	23.4
≥90	15	71.4	102	53.7	268	45.8	379	25.4
Missing**	1	4.8	22	11.6	44	7.5	121	8.1
<b>Total</b>	<b>21</b>	<b>100.0</b>	<b>190</b>	<b>100.0</b>	<b>585</b>	<b>100.0</b>	<b>1490</b>	<b>100.0</b>

GFR (ml/min/1.73m <sup>2</sup> )	V & II+V		VI		Others		Total	
	n	%	n	%	n	%	n	%
<15	5	1.8	10	32.3	11	61.1	167	6.4
15-29	15	5.4	5	16.1	2	11.1	222	8.5
30-59	29	10.4	5	16.1	1	5.6	486	18.6
60-89	67	23.9	2	6.5	0	0.0	611	23.4
≥90	143	51.1	5	16.1	1	5.6	913	34.9
Missing**	21	7.5	4	12.9	3	16.7	216	8.3
<b>Total</b>	<b>280</b>	<b>100.0</b>	<b>31</b>	<b>100.0</b>	<b>18</b>	<b>100.0</b>	<b>2615</b>	<b>100.0</b>

\*37 cases are missing on lupus subclass

\*\*Total of 216 cases are missing on GFR, including 53 cases with GFR>200 (GFR range between 201 to 2463)

### 3.2.4: Renal function at presentation.

Thirty-four percent of all patients had impaired renal function (defined as eGFR <60ml/min/1.73 m<sup>2</sup>) at the time of presentation and 6.6% had eGFR < than 15 ml/min. (Table & Figure 3.2.4.1)

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

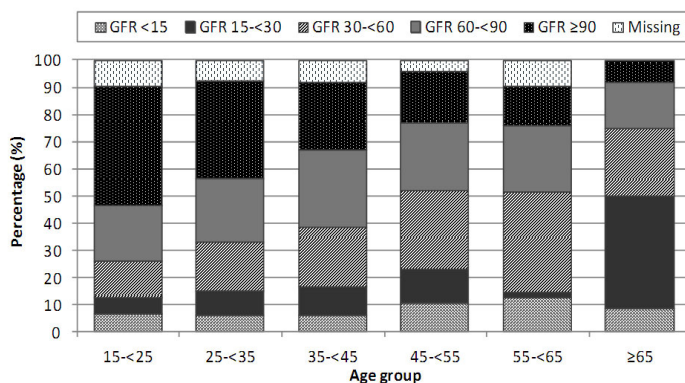
The frequency of impaired renal function increased after the age of 35. Between 26-33% had eGFR less than 60 ml/min below the age of 35 and it rose to 38.5% in the age group of 35 to 45 and 52% in age group of 45 to 55. For those above the age of 55, about 51-75% has eGFR of less than 60ml/min (Table & Figure 3.2.4.1)

**Table 3.2.4.1: Renal function by age group in lupus nephritis, 2005-2012**

GFR (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	%
<15	66	6.5	48	5.7	28	5.7	26	10.5	5	12.2	1	8.3	174	6.6
15 to < 30	61	6.0	76	9.0	52	10.7	31	12.5	1	2.4	5	41.7	226	8.5
30 to < 60	139	13.6	153	18.1	108	22.1	72	29.0	15	36.6	3	25.0	490	18.5
60 to < 90	208	20.4	198	23.5	137	28.1	62	25.0	10	24.4	2	16.7	617	23.3
≥ 90	446	43.7	301	35.7	124	25.4	46	18.5	6	14.6	1	8.3	924	34.8
Missing*	100	9.8	67	7.9	39	8.0	11	4.4	4	9.8	0	0.0	221	8.3
<b>Total</b>	<b>1020</b>	<b>100.0</b>	<b>843</b>	<b>100.0</b>	<b>488</b>	<b>100.0</b>	<b>248</b>	<b>100.0</b>	<b>41</b>	<b>100.0</b>	<b>12</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

\*Total of 221 cases are missing on GFR, including 54 cases with GFR>200 (GFR range between 201 to 2463)

**Figure 3.2.4.1: Renal function by age group in lupus nephritis, 2005-2012**



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

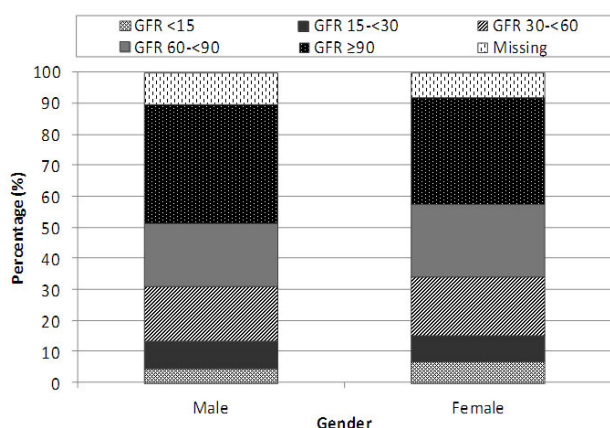
At presentation, male patients had better eGFR than female patients . There were 38% of male patients compared to 34.3 % female patients who had eGFR ≥ 90 ml/min/1.73m<sup>2</sup>. Thirty-four percent of female and 30.8 % of male patients had eGFR of < 60 ml/min/1.73m<sup>2</sup>. In addition , there were more female patients presenting with eGFR of <15 than male patients (Table & figure 3.2.4.2)

**Table 3.2.4.2: Renal function at presentation by gender, 2005-2012**

GFR (ml/min/1.73m <sup>2</sup> )	Male		Female		Total	
	n	%	n	%	n	%
<15	15	4.4	159	6.9	174	6.6
15 to < 30	31	9.0	195	8.4	226	8.5
30 to < 60	60	17.4	430	18.6	490	18.5
60 to < 90	71	20.6	546	23.7	617	23.3
≥ 90	132	38.4	792	34.3	924	34.8
Missing	35	10.2	186	8.1	221	8.3
<b>Total</b>	<b>344</b>	<b>100.0</b>	<b>2308</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

\*Total of 221 cases are missing on GFR, including 54 cases with GFR>200 (GFR range between 201 to 2463)

**Figure 3.2.4.2: Renal function at presentation by gender, 2005-2012**



### 3.2.4.3: Renal function at presentation by histopathology

There was an association between diffuse proliferative lupus nephritis with the degree of eGFR at presentation. Class VI or in combination with class V contributed to 74.3% of all cases presenting with eGFR <15, 79.7% ( eGFR 15-29) , 70% (eGFR 30-59).On the other hand , class IV or in combination with class V contributed only to 41.4 % of all cases presenting with with eGFR of ≥90. (Table & Figure 3.2.4.3)

**Table 3.2.4.3: Renal function at presentation by histopathology, 2005-2012**

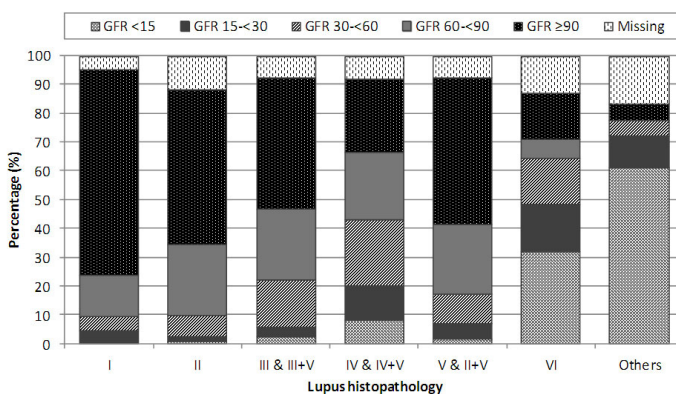
GFR (ml/min/1.73m <sup>2</sup> )	I		II		III & III+V		IV & IV+V	
	n	%	n	%	n	%	n	%
<15	0	0.0	2	1.1	15	2.6	124	8.3
15-29	1	4.8	3	1.6	19	3.2	177	11.9
30-59	1	4.8	14	7.4	96	16.4	340	22.8
60-89	3	14.3	47	24.7	143	24.4	349	23.4
≥90	15	71.4	102	53.7	268	45.8	379	25.4
Missing**	1	4.8	22	11.6	44	7.5	121	8.1
<b>Total</b>	<b>21</b>	<b>100.0</b>	<b>190</b>	<b>100.0</b>	<b>585</b>	<b>100.0</b>	<b>1490</b>	<b>100.0</b>

GFR (ml/min/1.73m <sup>2</sup> )	V & II+V		VI		Others		Total	
	n	%	n	%	n	%	n	%
<15	5	1.8	10	32.3	11	61.1	167	6.4
15-29	15	5.4	5	16.1	2	11.1	222	8.5
30-59	29	10.4	5	16.1	1	5.6	486	18.6
60-89	67	23.9	2	6.5	0	0.0	611	23.4
≥90	143	51.1	5	16.1	1	5.6	913	34.9
Missing**	21	7.5	4	12.9	3	16.7	216	8.3
<b>Total</b>	<b>280</b>	<b>100.0</b>	<b>31</b>	<b>100.0</b>	<b>18</b>	<b>100.0</b>	<b>2615</b>	<b>100.0</b>

\*37 cases are missing on lupus subclass

\*\*Total of 216 cases are missing on GFR, including 53 cases with GFR>200 (GFR range between 201 to 2463)

**Figure 3.2.4.3: Renal function at presentation by histopathology, 2005-2012**



### 3.2.5: Histopathological diagnosis

Class IV /class IV in combination with class V Lupus nephritis was the predominant histopathological diagnosis accounting for 61.3% of patients diagnosed with lupus nephritis. Class V and II +V contributed to 11.5% of all cases. About 8.7 % were due to milder forms of lupus nephritis namely Class I and Class II lupus nephritis. 1.3% patients unfortunately had the advanced sclerosing lupus nephritis at the time of biopsy. (Table 3.2.5)

**Table 3.2.5: Histopathological diagnosis in lupus nephritis by year, 2005-2012**

WHO or ISN/ RPS classification	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
Class I	12	0.7	4	1.0	5	1.3	21	0.9
Class II	139	8.4	28	6.9	23	6.2	190	7.8
Class III and III+V	367	22.2	114	28.1	104	28.0	585	24.1
Class IV and IV+V	1004	60.7	250	61.7	236	63.4	1490	61.3
Class V and II+V	179	10.8	37	9.1	64	17.2	280	11.5
Class VI	15	0.9	8	2.0	8	2.2	31	1.3
Others	17	1.0	0	0.0	1	0.3	18	0.7
<b>Total</b>	<b>1733</b>	<b>104.8</b>	<b>441</b>	<b>108.9</b>	<b>441</b>	<b>118.5</b>	<b>2615</b>	<b>107.6</b>

\*37 cases are missing on lupus subclass

#### 3.2.5.1: Histopathological diagnosis by age

Class IV / in combination with class V was the commonest histological diagnosis for all age groups. There was an increasing trend of Class V cases among the older age group. None of the patients older than 55 had advanced sclerosing lupus nephritis. (Table 3.2.5.1)

**Table 3.2.5.1: Histopathological diagnosis by age group in lupus nephritis, 2005-2012**

Histopathology	15-<25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Class I	10	1.0	5	0.6	3	0.6	2	0.8	0	0.0	1	8.3	21	0.8
Class II	81	8.0	59	7.1	32	6.7	15	6.2	3	7.7	0	0.0	190	7.3
Class III and III+V	214	21.2	195	23.4	113	23.5	49	20.2	11	28.2	3	25.0	585	22.4
Class IV and IV+V	599	59.4	477	57.3	264	55.0	125	51.4	18	46.2	7	58.3	1490	57.0
Class V and II+V	86	8.5	83	10.0	61	12.7	44	18.1	5	12.8	1	8.3	280	10.7
Class VI	10	1.0	10	1.2	6	1.3	4	1.6	1	2.6	0	0.0	31	1.2
Others	8	0.8	4	0.5	1	0.2	4	1.6	1	2.6	0	0.0	18	0.7
<b>Total</b>	<b>1008</b>	<b>100.0</b>	<b>833</b>	<b>100.0</b>	<b>480</b>	<b>100.0</b>	<b>243</b>	<b>100.0</b>	<b>39</b>	<b>100.0</b>	<b>12</b>	<b>100.0</b>	<b>2615</b>	<b>100.0</b>

\*37 cases are missing on lupus subclass

### 3.2.5.2: Histopathological diagnosis by gender

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

**Table 3.2.5.2: Histopathological diagnosis by gender in lupus nephritis, 2005-2012**

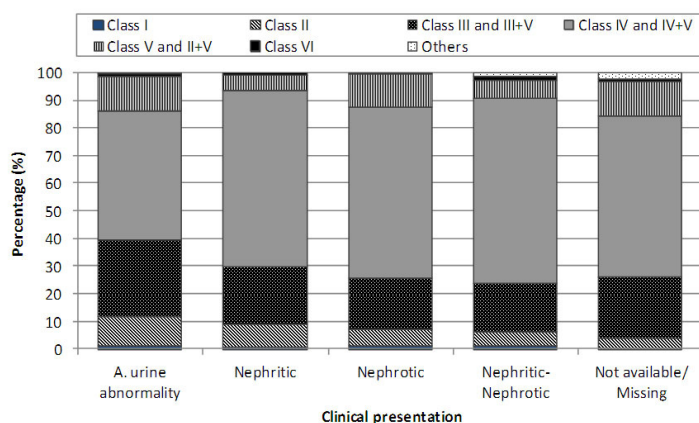
Histopathology	Male		Female		Total	
	n	%	n	%	n	%
Class I	3	0.9	18	0.8	21	0.8
Class II	25	7.3	165	7.3	190	7.3
Class III and III+V	86	25.1	499	22.0	585	22.4
Class IV and IV+V	178	51.9	1312	57.7	1490	57.0
Class V and II+V	45	13.1	235	10.3	280	10.7
Class VI	3	0.9	28	1.2	31	1.2
Others	3	0.9	15	0.7	18	0.7
<b>Total</b>	<b>343</b>	<b>100.0</b>	<b>2272</b>	<b>100.0</b>	<b>2615</b>	<b>100.0</b>

\*37 cases are missing on lupus subclass

### 3.2.5.3: Histopathological diagnosis by clinical presentation

Urine abnormalities was the most common clinical presentation for lupus nephritis. Class IV and IV +V occurred in highest frequency among all groups of clinical presentation: 46% with urine abnormalities, 65.4% with nephritic syndrome, 62.2% with nephrotic syndrome and 66.1% with nephritic-nephrotic syndrome. (Table & Figure 3.2.5.3)

**Figure 3.2.5.3: Histopathological diagnosis by clinical presentation, 2005-2012**



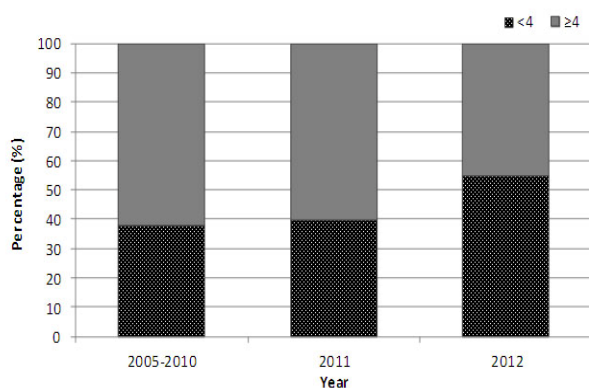


**Table 3.2.5.3: Histopathological diagnosis by clinical presentation, 2005-2012**

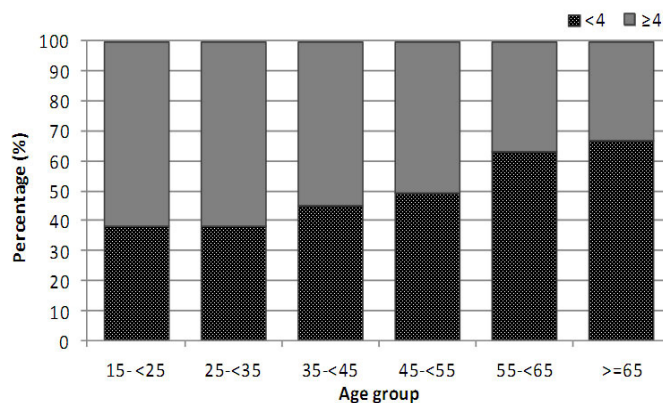
Histopathology	Urine abnormality		Nephritic		Nephrotic		Nephritic-Nephrotic		Not available/ Missing		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Class I	9	1.0	1	0.4	7	1.0	4	1.1	0	0.0	21	0.8
Class II	96	10.4	20	8.2	43	6.0	18	4.8	13	3.7	190	7.3
Class III and III+V	258	28.0	51	20.8	131	18.2	67	17.8	78	22.0	585	22.4
Class IV and IV+V	430	46.6	157	64.1	445	62.0	251	66.8	207	58.5	1490	57.0
Class V and II+V	114	12.4	13	5.3	86	12.0	24	6.4	43	12.1	280	10.7
Class VI	12	1.3	3	1.2	6	0.8	6	1.6	4	1.1	31	1.2
Others	3	0.3	0	0.0	0	0.0	6	1.6	9	2.5	18	0.7
<b>Total</b>	<b>922</b>	<b>100.0</b>	<b>245</b>	<b>100.0</b>	<b>718</b>	<b>100.0</b>	<b>376</b>	<b>100.0</b>	<b>354</b>	<b>100.0</b>	<b>2615</b>	<b>100.0</b>

\*37 cases are missing on lupus subclass

**Figure 3.2.6.1: ARA criteria in lupus nephritis, 2005-2012**



**Figure 3.2.6.2: ARA criteria by age group, 2005-2012**



### 3.2.6: Extra-renal involvement

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

About 2/5th of all cases of lupus nephritis did not fulfil the ARA criteria for SLE at presentations. Only 63.6% were diagnosed to have SLE at presentations with the ARA criteria. Thus, It is important that histopathological diagnosis is recognised as one of the important diagnostic criteria. (Table & Figure 3.2.6.1)

**Table 3.2.6.1: ARA criteria in lupus nephritis, 2005-2012**

Number of ARA criteria	2005-2010		2011		2012		Total	
	n	%	n	%	n	%	n	%
<4	666	37.9	177	39.7	245	54.4	1088	41.0
4 and more	1090	62.1	269	60.3	205	45.6	1564	59.0
<b>Total</b>	<b>1756</b>	<b>100.0</b>	<b>446</b>	<b>100.0</b>	<b>450</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

### 3.2.6.2: ARA criteria in lupus nephritis by age

In patients less than 35 years old , about 2/3rd satisfied the ARA criteria for the diagnosis of SLE. There was a higher proportion of patients fulfilling the ARA criteria when they are younger. (Table & Figure 3.2.6.2)

**Table 3.2.6.2: ARA criteria by age group, 2005-2012**

Number of ARA criteria	15-<25		25-<35		35-<45		45-<55		55-<65		≥65		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<4	390	38.2	321	38.1	221	45.3	122	49.2	26	63.4	8	66.7	1088	41.0
4 and more	630	61.8	522	61.9	267	54.7	126	50.8	15	36.6	4	33.3	1564	59.0
<b>Total</b>	<b>1020</b>	<b>100.0</b>	<b>843</b>	<b>100.0</b>	<b>488</b>	<b>100.0</b>	<b>248</b>	<b>100.0</b>	<b>41</b>	<b>100.0</b>	<b>12</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

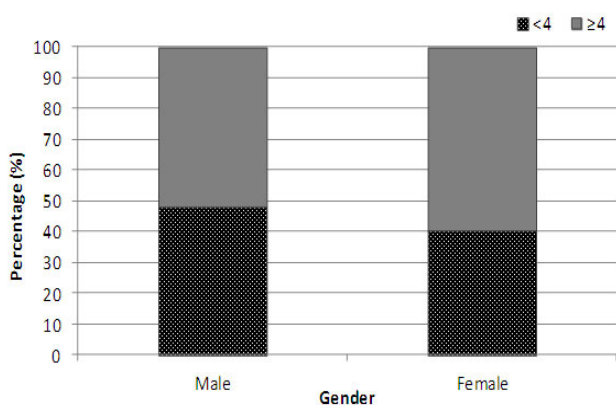
### 3.2.6.3: ARA criteria by gender

About 2/5th of both female and male patients did not fulfill the 4 or more ARA criteria for SLE. (Table 3.2.6.3)

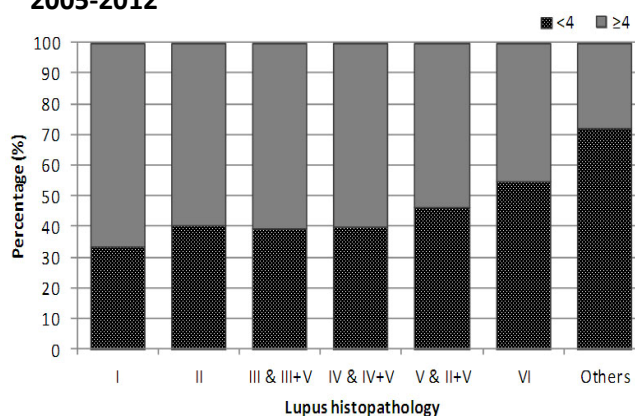
**Table 3.2.6.3: ARA criteria by gender, 2005-2012**

Number of ARA criteria	Male		Female		Total	
	n	%	n	%	n	%
<4	165	48.0	923	40.0	1088	41.0
4 and more	179	52.0	1385	60.0	1564	59.0
<b>Total</b>	<b>344</b>	<b>100.0</b>	<b>2308</b>	<b>100.0</b>	<b>2652</b>	<b>100.0</b>

**Figure 3.2.6.3: ARA criteria by gender, 2005-2012**



**Figure 3.2.6.4: ARA criteria by histopathology, 2005-2012**



### 3.2.6.4: ARA criteria by histopathological findings

Histopathological diagnosis did not influence the proportion of number of ARA criteria. Overall, 2/5 of all patients had less than 4 ARA criteria. (Table 3.2.6.4)

**Table 3.2.6.4: ARA criteria by histopathology, 2005-2012**

Number of ARA criteria	I		II		III & III+V		IV & IV+V	
	n	%	n	%	n	%	n	%
<4	7	33.3	77	40.5	230	39.3	592	39.7
4 and more	14	66.7	113	59.5	355	60.7	898	60.3
<b>Total</b>	<b>21</b>	<b>100.0</b>	<b>190</b>	<b>100.0</b>	<b>585</b>	<b>100.0</b>	<b>1490</b>	<b>100.0</b>

GFR (ml/min/1.73m2)	V & II+V		VI		Others		Total	
	n	%	n	%	n	%	n	%
<4	130	46.4	17	54.8	13	72.2	1066	40.8
4 and more	150	53.6	14	45.2	5	27.8	1549	59.2
<b>Total</b>	<b>280</b>	<b>100.0</b>	<b>31</b>	<b>100.0</b>	<b>18</b>	<b>100.0</b>	<b>2615</b>	<b>100.0</b>

\*37 missing on lupus subclass

### 3.2.6.5: Extra-renal involvement

Mucocutaneous involvement was the commonest extra-renal involvement followed by hematological involvement and arthritis. Severe manifestation like neurological involvement was present in 10.6% of all cases. Mucocutaneous involvement, serositis and arthritis was more common in females than males. Neurological and hematological manifestations were slightly more common in males. Malar rash was the commonest mucocutaneous manifestation. At least 40% of them had photosensitivity or oral ulcers. Discoid rash was only reported in 16.3%. ( Table & Figure 3.2.6.5 (a), Table & Figures 3.2.6.5 (b))

**Table 3.2.6.5(a): Extra-renal involvement by gender, 2005-2012**

Other organs involvement	Male (n=344)		Female (n=2308)		Total (n=2652)	
	n	%	n	%	n	%
Mucocutaneous	147	42.7	1155	50.0	1302	49.1
Arthritis	62	18.0	792	34.3	854	32.2
Serositis	26	7.6	187	8.1	213	8.0
Cerebral	41	11.9	219	9.5	260	9.8
Haematological	133	38.7	876	38.0	1009	38.0
<b>Total</b>	<b>409</b>		<b>3229</b>		<b>3638</b>	

Figure 3.2.6.5 (a): Extra-renal involvement by gender, 2005-2012

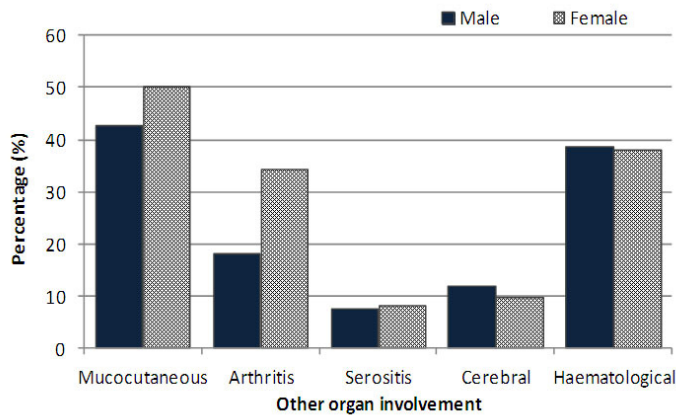
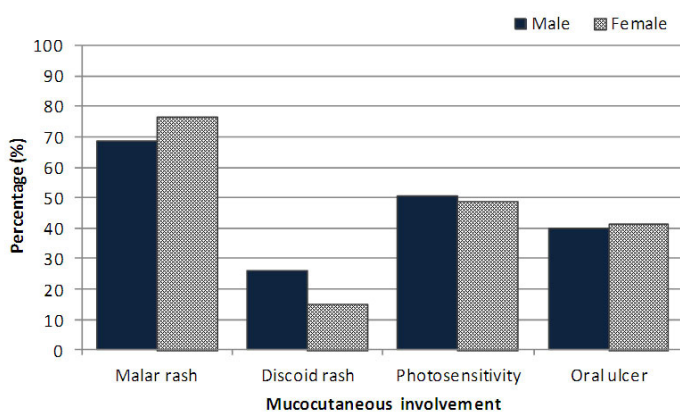


Table 3.2.6.5(b): Mucocutaneous involvement by gender in lupus nephritis, 2005-2012

Mucocutaneous involvements	Male (n=147)		Female (n=1155)		Total (n=1302)	
	n	%	n	%	n	%
Malar rash	101	68.7	883	76.5	984	75.6
Discoid rash	38	25.9	174	15.1	212	16.3
Photosensitivity	74	50.3	563	48.7	637	48.9
Oral ulcer	59	40.1	477	41.3	536	41.2
<b>Total</b>	<b>272</b>		<b>2097</b>		<b>2369</b>	

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

Figure 3.2.6.5(b): Mucocutaneous involvement by gender in lupus nephritis, 2005-2012



### 3.2.7: Survival in lupus nephritis

To evaluate patient and renal survival, data on the date of death was obtained by data mapping based on the patient's new identity card (NRIC) from the Jabatan Pendaftaran Negara ( National Registration Department) and Malaysian Dialysis and Transplant Registry Outcome Notification.

Data on the onset of End Stage Renal Failure was obtained from The Malaysian Dialysis and Transplant Registry

#### 3.2.7.1: Death in patients with lupus nephritis

**Table 3.2.7.1: Death in patients with biopsy proven lupus nephritis 2005-2012**

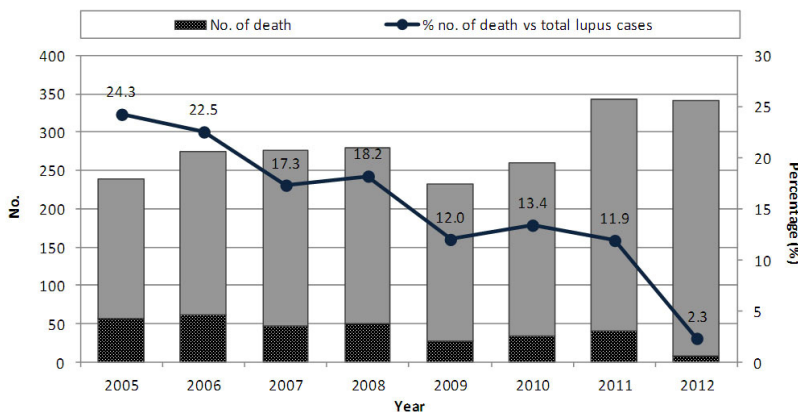
	Lupus nephritis		
	Number with Lupus nephritis	Number of Death	% Death
2005	239	58	24.3
2006	275	62	22.5
2007	277	48	17.3
2008	280	51	18.2
2009	233	28	12
2010	261	35	13.4
2011	344	41	11.9
2012	343	8	2.3
<b>Total</b>	<b>2252</b>	<b>331</b>	<b>14.7</b>

There appears to be a reduction in the number of patients dying and the death rate among patients diagnosed to have lupus nephritis during the last eight years of observation.

In 2008, almost 1 in 5 patients with lupus nephritis died. This may be due to late presentation, severe multi-organ involvement and concomitant infective complications that these patients usually presented with.

The continuous improvement observed may be attributed to increasing awareness among the public thus seeking modern medical treatment earlier which had resulted in timely intervention, the introduction of evidence based guidelines for the management of lupus nephritis, better vigilance in infective complications and more efficacious antimicrobial therapy to treat these complications.

**Figure 3.2.7.1: Death from lupus nephritis**



### 3.2.7.2: Patient survival in lupus nephritis

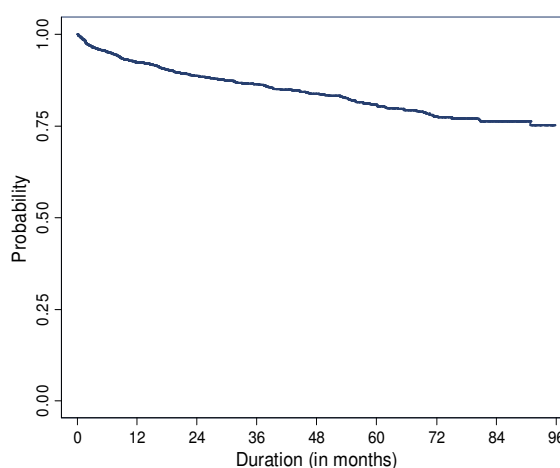
Overall patient survival was 92.8% at 1 year , 86.3 % at 3 years and 80.4% at 5 years from the time of renal biopsy (Table & Figure 3.2.7.1). This observed survival rate among lupus nephritis in Malaysia is far worse than what was being reported in other countries . For example, Dr Chan TM (1) reported patient survival rate of 98.6% and 98.2% at 5 and 10 years respectively in his cohort in Hong Kong.

**Table 3.2.7.2: Patients Survival estimates for death in lupus nephritis, 2005-2012**

Interval (months)	SLE patients survival		
	n	% survival	n
0	2244	100.0	-
12	1712	92.4	0.006
24	1334	88.7	0.007
36	1065	86.3	0.008
48	833	83.8	0.009
60	580	80.4	0.011
72	343	77.6	0.012

Event = death;  
censored status as at 31 Dec 2012 or last follow-up.

**Figure 3.2.7.2: Patients Survival estimates for death in lupus nephritis, 2005-2012**



*\*Missing of 8 cases (5 censored cases where the outcome date < date of 1<sup>st</sup> biopsy; and 3 censored cases of the same date).*

### 3.2.7.3: Renal survival in lupus nephritis

**Table 3.2.7.3: Death-censored Renal Survival estimates for lupus nephritis, 2005-2012**

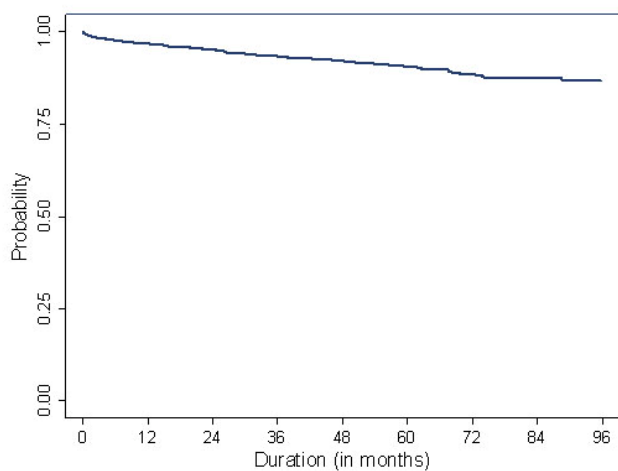
Interval (months)	Renal survival		
	n	% survival	SE
0	2241	100.0	-
12	1688	96.8	0.004
24	1316	95.2	0.005
36	1051	93.3	0.006
48	823	92.2	0.007
60	573	90.7	0.008
72	343	88.5	0.010

Event = ESRF;  
Status as at 31 Dec 2012 or died or last follow-up.

Table & Figure 3.2.7.2 shows that death censored renal survival was 96.8% at 1 year, 96.2% at 3 years and 90.7% at 5 years from the time of renal biopsy

This again is worse than what was seen in Hong Kong , where Dr Chan TM and his co-workers reported death censored renal survival of 99.5% at 5 years and 98% at 10 years.

**Figure 3.2.7.3: Death-censored Renal Survival estimates for lupus nephritis**



\*Missing of 11 cases (4 event and 3 censored cases where the outcome date < date of 1<sup>st</sup> biopsy; and 1 event and 3 censored cases of the same date).

*(based on first biopsy date to the first ESRF outcome for adult patients with history of lupus nephritis, or as at 31 December 2012)*

#### References

1. Desmond Y.H. Yap, Colin S.O. Tang, Maggie K.M. Ma, Man Fai Lam and Tak Mao Chan. Survival analysis and causes of mortality in patients with lupus nephritis. *Nephrol Dial Transplant* (2012) 27: 3248–3254