

## **CHAPTER 3**

# **SECONDARY GLOMERULONEPHRITIS**

**Thong Kah Mean  
Benjamin Tan Wei Wang  
Anim Md Shah**

### 3.1 Introduction

- This chapter reports the main secondary glomerular diseases in adults (defined as individuals above 15 years old) between 2005 and 2022.
- Lupus nephritis (LN) was the most common cause of biopsy proven secondary glomerular disease (78.7%) (Table 3.1). This could be attributed to routine practice of urinary screening followed by renal biopsy in systemic lupus erythematosus (SLE) patients with proteinuria with or without active urine sediments and positive lupus serology markers.
- Diabetic nephropathy was the second most frequent biopsy proven secondary glomerular diseases in Malaysia (15%) despite being the most common cause of end stage kidney disease (ESKD) in Malaysia and globally. This discrepancy could be due to variations in renal biopsy practices amongst patients with diabetic kidney disease. Nevertheless, the data showed an increasing trend in cases being reported, from 10.1% in the initial years of registry to 25.2% in 2022.
- Post infectious GN was the third most common cause (2.7%). The incidence appeared to be decreasing from 3.1 -3.2% in the year of 2010-2019 to 1.4% in 2022. This may reflect improved living conditions in Malaysia.
- Other causes of secondary glomerular disease were generally uncommon, and probably under-diagnosed due to limited availability of electron microscopy and special staining.

Table 3.1: Causes of secondary glomerulonephritis in adult, 2005-2022

Type of secondary GN	2005-2009 (n=1657)		2010-2014 (n=2797)		2015-2019 (n=3164)		2020 (n=686)		2021 (n=488)		2022 (n=644)		Total (n=9436)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Lupus Nephritis	1414	85.3	2221	79.4	2496	78.9	490	71.4	349	71.5	454	70.5	7424	78.7
Diabetic nephropathy	167	10.1	373	13.3	443	14.0	157	22.9	113	23.2	162	25.2	1415	15.0
Post Infectious GN	32	1.9	93	3.3	98	3.1	13	1.9	7	1.4	9	1.4	252	2.7
Amyloidosis	9	0.5	20	0.7	23	0.7	8	1.2	7	1.4	2	0.3	69	0.7
Other infection	8	0.5	19	0.7	16	0.5	4	0.6	0	0.0	3	0.5	50	0.5
Systemic vasculitis	4	0.2	14	0.5	9	0.3	0	0.0	1	0.2	2	0.3	30	0.3
Henoch-Schonlein Purpura	7	0.4	7	0.3	3	0.1	0	0.0	2	0.4	0	0.0	19	0.2
Multiple myeloma	8	0.5	4	0.1	7	0.2	1	0.1	0	0.0	2	0.3	22	0.2
Light / Heavy chain deposit disease	2	0.1	2	0.1	6	0.2	1	0.1	0	0.0	2	0.3	13	0.1
HUS / TTP	0	0.0	3	0.1	5	0.2	2	0.3	0	0.0	0	0.0	10	0.1
Malignancy	3	0.2	4	0.1	2	0.1	0	0.0	0	0.0	0	0.0	9	0.1
Anti GBM disease	0	0.0	3	0.1	8	0.3	3	0.4	2	0.4	1	0.2	17	0.2
Immunotactoid / fibrillary GN	0	0.0	1	0.0	2	0.1	1	0.1	0	0.0	1	0.2	5	0.1
Not Available	3	0.2	33	1.2	46	1.5	6	0.9	7	1.4	6	0.9	101	1.1

### 3.2 Lupus nephritis (LN)

#### 3.2.1 Introduction

- Lupus Nephritis was the commonest form of biopsy-proven secondary GN (78.7%) in adults (Table 3.1).
- From 2015 till 2022, LN was reported to account for 40.4% of all adult native renal biopsies in Malaysia.

#### 3.2.2 Patient population and characteristics

##### 3.2.2.1 Age at time of biopsy

- The mean age of diagnosis of LN patients was 31.4 years old ± 11.32 years with a median of 29.11 years old (Table 3.2.2.1).
- LN predominantly affected young SLE patients with majority (>80%) being 45 years old or younger (Figure 3.2.2.1).
- The most common age groups were 15-25 years old (29-39%) and 25-35 years old (32-35%). The age group distribution remained similar over the last 18-year observational period.

Table 3.2.2.1: Age group at time of biopsy (years), 2005-2022

Age group (years)	2005 (n=240)	2006 (n=275)	2007 (n=286)	2008 (n=312)	2009 (n=290)	2010 (n=311)	2011 (n=434)	2012 (n=437)	2013 (n=451)	2014 (n=478)
Mean	30.48	30.89	29.83	30.53	29.26	30.44	30.78	30.51	30.57	31.14
Standard deviation	10.59	10.32	10.18	11.03	9.71	10.96	10.98	11.46	10.17	10.61
Median	29.00	29.64	27.50	28.37	27.75	27.90	27.96	27.53	28.49	29.69

Age group (years)	2015 (n=459)	2016 (n=409)	2017 (n=463)	2018 (n=543)	2019 (n=495)	2020 (n=487)	2021 (n=349)	2022 (n=451)	Total (n=7170)
Mean	31.58	32.56	31.68	31.65	32.81	31.16	33.00	33.53	31.39
Standard deviation	12.06	12.07	11.36	11.00	12.00	11.76	12.56	12.05	11.32
Median	29.45	30.11	29.70	29.53	31.25	27.83	30.94	30.95	29.11

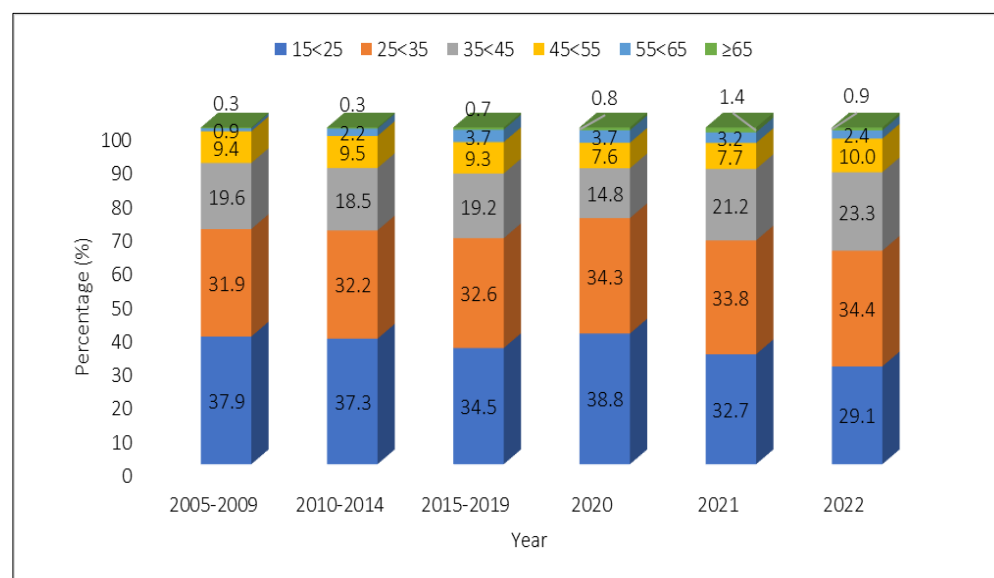


Figure 3.2.2.1: Age group at time of biopsy (years), 2005-2022

### 3.2.2.2 Gender distribution

- The majority of patients were females, accounting for nearly 90% of total patients with LN (Figure 3.2.2.2(a))
- The median age at time of renal biopsy were 27.6 and 29.1 years old in males and females respectively (Figure 3.2.2.2(b) and (c)).

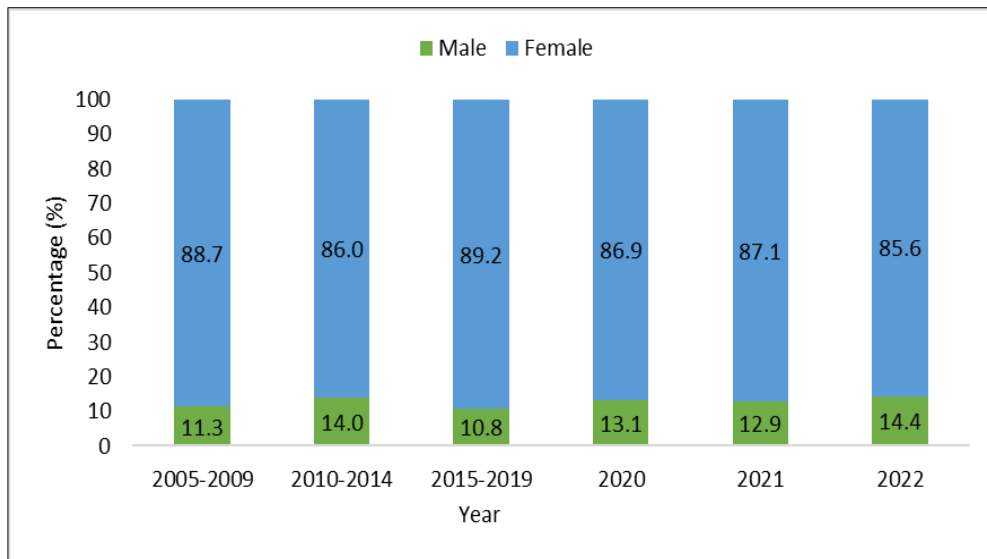


Figure 3.2.2.2(a): Gender distribution, 2005-2022

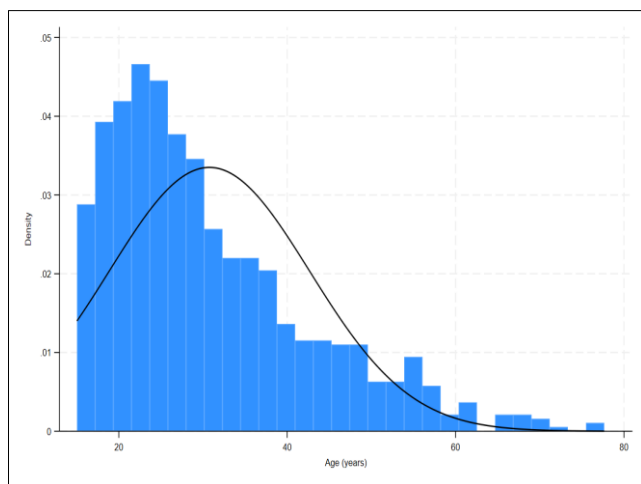


Figure 3.2.2.2(b): Age distribution (Male), 2005-2022

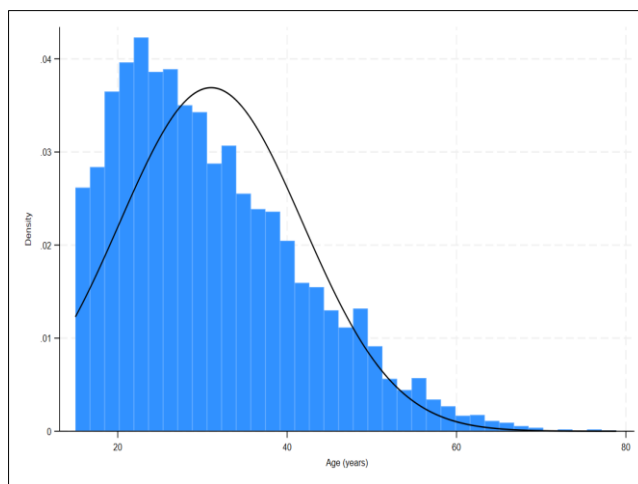


Figure 3.2.2.2(c): Age distribution (Female), 2005-2022

**3.2.2.3 Ethnic prevalence**

- Malays formed the biggest proportion (56.8% to 75.4%) of LN patients, followed by Chinese and then other races (Figure 3.2.2.3).
- The proportion of Indians at 3.1 to 4.9%, which was less compared to the overall ethnic distribution in Malaysia, where the proportion of Indians is around 6.5%.
- It appears that there were less proportion of Chinese affected by LN in the more recent years. Whether, this is a true decrease in the incidence among Chinese population is uncertain. Other possible explanation is that Chinese tend to visit private healthcare facilities, whereas this registry predominantly captured data in public hospitals.

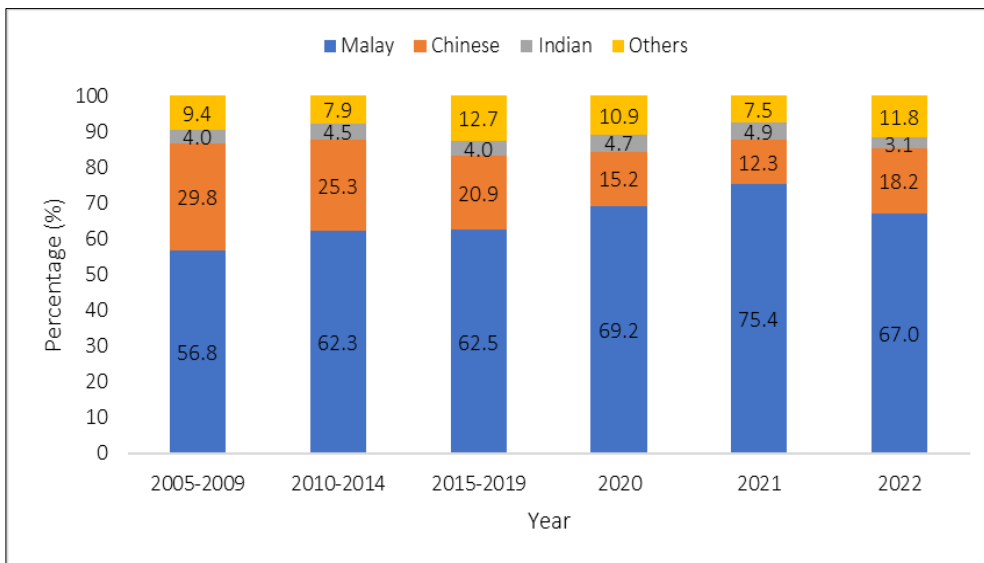


Figure 3.2.2.3: Ethnic distribution, 2005-2022

3.2.3: Clinical presentation

- The most common clinical presentation for LN was asymptomatic urinary abnormalities (where patients with extra-renal manifestations were screened for kidney involvement), followed by nephrotic syndrome and then nephrotic-nephritic syndrome (Figure 3.2.3).
- This trend was similarly observed among LN patients irrespective of age group or gender (Figure 3.2.3(a) and (b)).

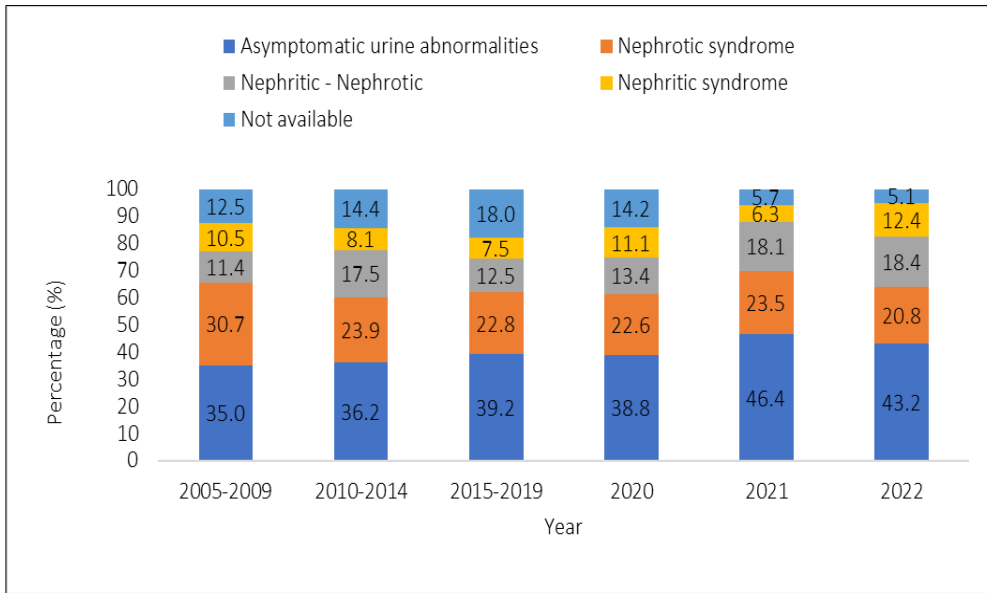


Figure 3.2.3: Clinical presentation by year, 2005-2022

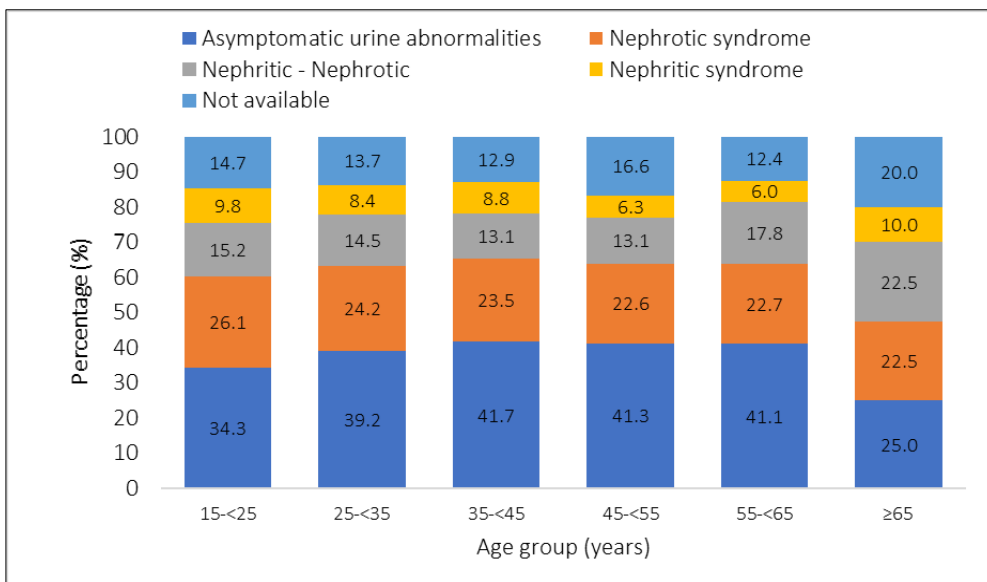


Figure 3.2.3(a): Clinical presentation by age group, 2005-2022

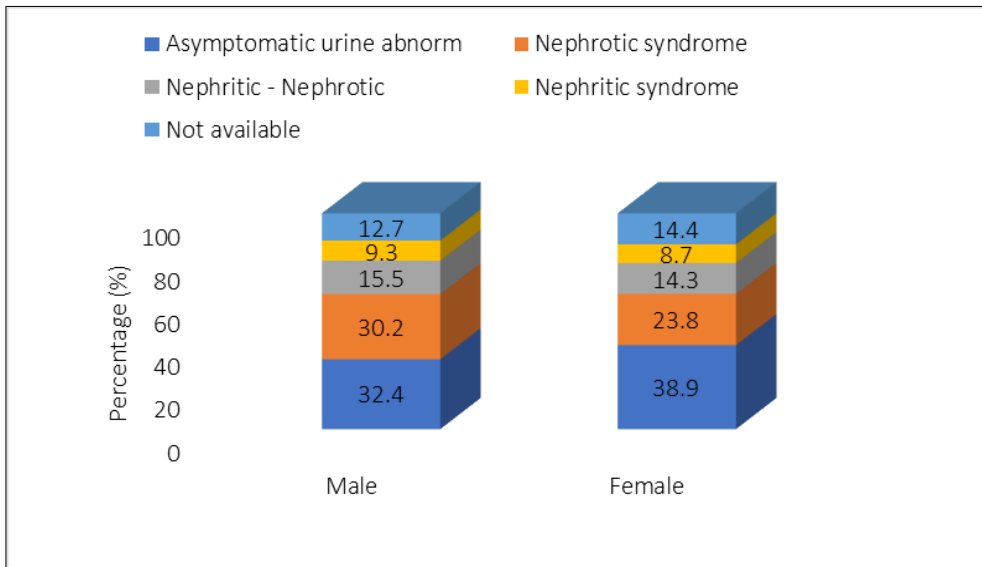


Figure 3.2.3(b): Clinical presentation by gender, 2005-2022

### 3.2.3.1 Hypertension

- Hypertension was observed between 40-50% of patients with biopsy proven LN between 2010 to 2022 (Figure 3.2.3.1).
- It was more common in males and in those who were above 55 years old (Figure 3.2.3.1(a) and (b)).

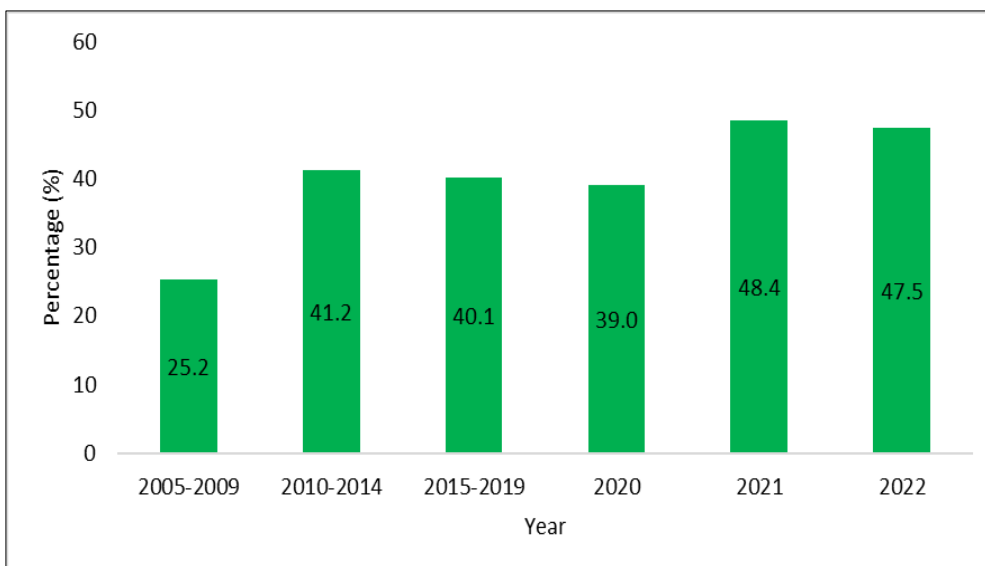


Figure 3.2.3.1: Hypertension by year, 2005-2022

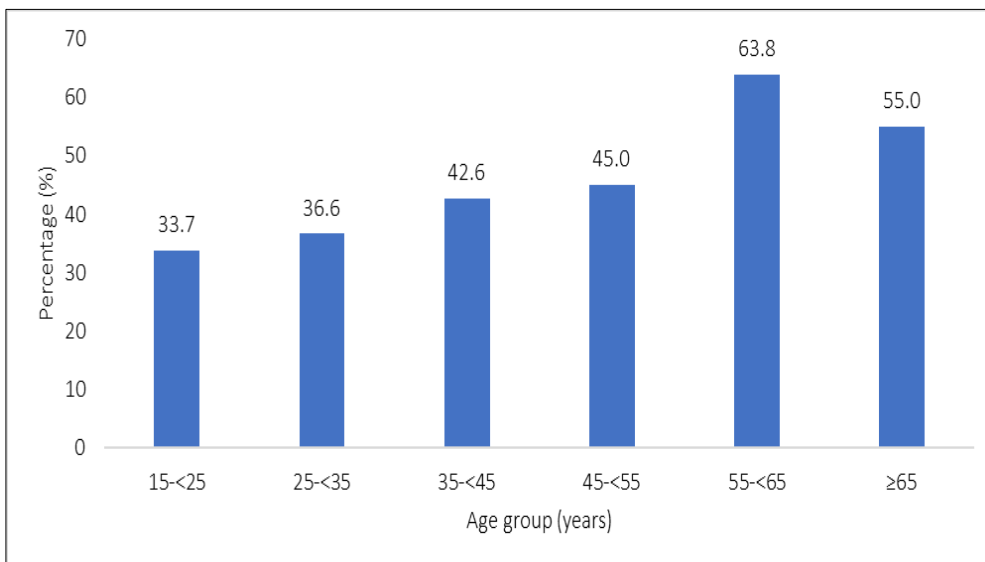


Figure 3.2.3.1(a): Hypertension by age group, 2005-2022

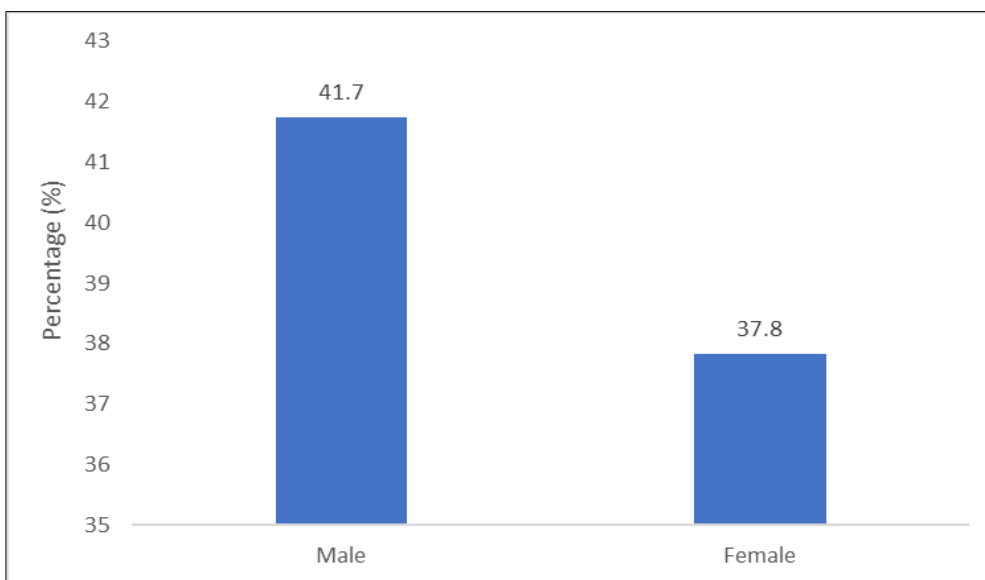


Figure 3.2.3.1(b): Hypertension by gender, 2005-2022

### 3.2.3.2 Renal function

- A greater proportion of patients (38.5%) had an initial eGFR >90ml/min/1.73m<sup>2</sup> at presentation (Table 3.2.3.2).
- The percentage of lupus nephritis patients with impaired renal function increased with age (Table 3.2.3.2(a)).
- For patients 45-65 years old, majority had eGFR 30 to 90 ml/min/1.73m<sup>2</sup> upon presentation; whereas for those aged ≥65, 70% of them had initial eGFR <60 ml/min/1.73m<sup>2</sup>.
- Renal function did not differ much between the two genders (Table 3.2.3.2(b)).

Table 3.2.3.2: Renal function by year, 2005-2022

eGFR (ml/min/1.73m <sup>2</sup> )	2005-2009 (n=1403)		2010-2014 (n=2111)		2015-2019 (n=2369)		2020 (n=487)		2021 (n=349)		2022 (n=451)		Total (n=7170)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<15	78	5.6	98	4.6	92	3.9	13	2.7	16	4.6	34	7.5	331	4.6
15 to <30	119	8.5	149	7.1	161	6.8	37	7.6	20	5.7	31	6.9	517	7.2
30 to <60	281	20.0	345	16.3	353	14.9	80	16.4	67	19.2	70	15.5	1196	16.7
60 to <90	343	24.4	471	22.3	449	19.0	90	18.5	70	20.1	92	20.4	1515	21.1
≥90	474	33.8	779	36.9	986	41.6	197	40.5	131	37.5	190	42.1	2757	38.5
Not available	108	7.7	269	12.7	328	13.8	70	14.4	45	12.9	34	7.5	854	11.9

Table 3.2.3.2(a): Renal function by age group, 2005-2022

eGFR (ml/min/1.73m <sup>2</sup> )	15-<25 (n=2570)		25-<35 (n=2340)		35-<45 (n=1372)		45-<55 (n=663)		55-<65 (n=185)		≥65 (n=40)		Total (n=7170)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<15	105	4.1	97	4.1	70	5.1	43	6.5	12	6.5	4	10.0	331	4.6
15-29	135	5.3	167	7.1	126	9.2	61	9.2	16	8.6	12	30.0	517	7.2
30-59	307	11.9	371	15.9	288	21.0	167	25.2	51	27.6	12	30.0	1196	16.7
60-89	438	17.0	500	21.4	348	25.4	174	26.2	48	25.9	7	17.5	1515	21.1
≥90	1,230	47.9	950	40.6	390	28.4	151	22.8	33	17.8	3	7.5	2757	38.5
Not Available	355	13.8	255	10.9	150	10.9	67	10.1	25	13.5	2	5.0	854	11.9

Table 3.2.3.2(b): Renal function by gender, 2005-2022

eGFR (ml/min/1.73m <sup>2</sup> )	Male (n=884)		Female (n=6286)		Total (n=7170)	
	n	%	n	%	n	%
<15	44	5.0	287	4.6	331	4.6
15-29	80	9.0	437	7.0	517	7.2
30-59	146	16.5	1,050	16.7	1196	16.7
60-89	178	20.1	1,337	21.3	1515	21.1
≥90	337	38.1	2,420	38.5	2757	38.5
Not Available	99	11.2	755	12.0	854	11.9

### 3.2.4 Histopathological diagnosis

- The most common histopathological finding was class III and IV, with or without a membranous component, consisting of almost 80% of all biopsy proven LN (Table 3.2.4).
- Class V, with or without class II, was the second most commonly observed histopathological finding, accounting for 10% of all LN cases.
- This trend was similar irrespective of age groups and gender (Table 3.2.4(a) and (b)).

Table 3.2.4: Histopathological diagnosis in lupus nephritis by year, 2005-2022

Histo-pathological diagnosis	2005-2009 (n=1403)		2010-2014 (n=2111)		2015-2019 (n=2369)		2020 (n=487)		2021 (n=349)		2022 (n=451)		Total (n=7170)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
I	9	0.6	19	0.9	20	0.8	4	0.8	1	0.3	1	0.2	54	0.8
II	121	8.6	127	6.0	117	4.9	27	5.5	15	4.3	26	5.8	433	6.0
III & III+V	290	20.7	538	25.5	749	31.6	150	30.8	107	30.7	145	32.2	1979	27.6
IV & IV+V	802	57.2	1126	53.3	1192	50.3	233	47.8	165	47.3	206	45.7	3724	51.9
V & II+V	144	10.3	230	10.9	229	9.7	59	12.1	43	12.3	60	13.3	765	10.7
VI	9	0.6	28	1.3	6	0.3	3	0.6	3	0.9	2	0.4	51	0.7
Others	9	0.6	2	0.1	3	0.1	0	0.0	0	0.0	0	0.0	14	0.2
Not available	19	1.4	41	1.9	53	2.2	11	2.3	15	4.3	11	2.4	150	2.1

Table 3.2.4(a): Histopathological diagnosis by age group in lupus nephritis, 2005-2022

Histo-pathological diagnosis	15-<25 (n=2570)		25-<35 (n=2340)		35-<45 (n=1372)		45-<55 (n=663)		55-<65 (n=185)		≥65 (n=40)		Total (n=7170)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
I	27	1.1	12	0.5	8	0.6	4	0.6	2	1.1	1	2.5	54	0.8
II	158	6.1	136	5.8	88	6.4	42	6.3	9	4.9	0	0.0	433	6.0
III & III+V	643	25.0	680	29.1	388	28.3	196	29.6	59	31.9	13	32.5	1,979	27.6
IV & IV+V	1,463	56.9	1,198	51.2	673	49.1	288	43.4	84	45.4	18	45.0	3,724	51.9
V & II+V	209	8.1	253	10.8	173	12.6	106	16.0	19	10.3	5	12.5	765	10.7
VI	18	0.7	17	0.7	9	0.7	6	0.9	1	0.5	0	0.0	51	0.7
Others	5	0.2	3	0.1	2	0.1	3	0.5	1	0.5	0	0.0	14	0.2
Not available	47	1.8	41	1.8	31	2.3	18	2.7	10	5.4	3	7.5	150	2.1

Table 3.2.4(b): Histopathological diagnosis by gender, 2005-2022

Histo-pathological diagnosis	Male (n=884)		Female (n=6286)		Total (n=7170)	
	n	%	n	%	n	%
I	6	0.7	48	0.8	54	0.8
II	49	5.5	384	6.1	433	6.0
III & III+V	249	28.2	1,730	27.5	1,979	27.6
IV & IV+V	448	50.7	3,276	52.1	3,724	51.9
V & II+V	107	12.1	658	10.5	765	10.7
VI	6	0.7	45	0.7	51	0.7
Others	1	0.1	13	0.2	14	0.2
Not available	18	2.0	132	2.1	150	2.1

### 3.2.4.1: Clinical Presentation by histopathology

- Across all LN classes, the most common clinical presentation was asymptomatic urinary abnormalities, followed by nephritic syndrome and then nephritic-nephrotic syndrome (Figure 3.2.4.1).
- Interestingly, nephrotic syndrome was an uncommon presentation in patients with class V LN, with or without class II, possibly indicating a less severe pathology or diagnosis at an early stage.
- Hypertension was a feature in 35-43% of patients with class III/ IV LN, with or without class V (Figure 3.2.4.1(a)).
- About 53% of patients with class VI LN were hypertensive upon diagnosis (Figure 3.2.4.1(a)).
- The prevalence of impaired renal function also correlated with histopathological findings. Impaired eGFR (<60ml/min/1.73m<sup>2</sup>) occurred most frequently in Class VI LN (55.0%), followed by class IV/ IV+V (39.1%) and Class III/III+V (16.6%) (Figure 3.2.4.1(b)).

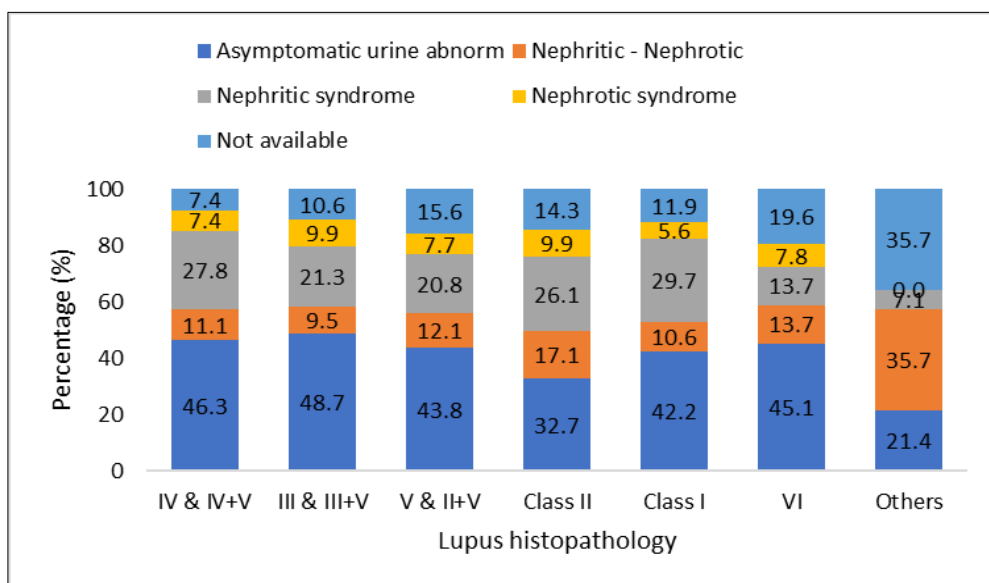


Figure 3.2.4.1: Clinical presentation by histopathology in lupus nephritis, 2005-2022

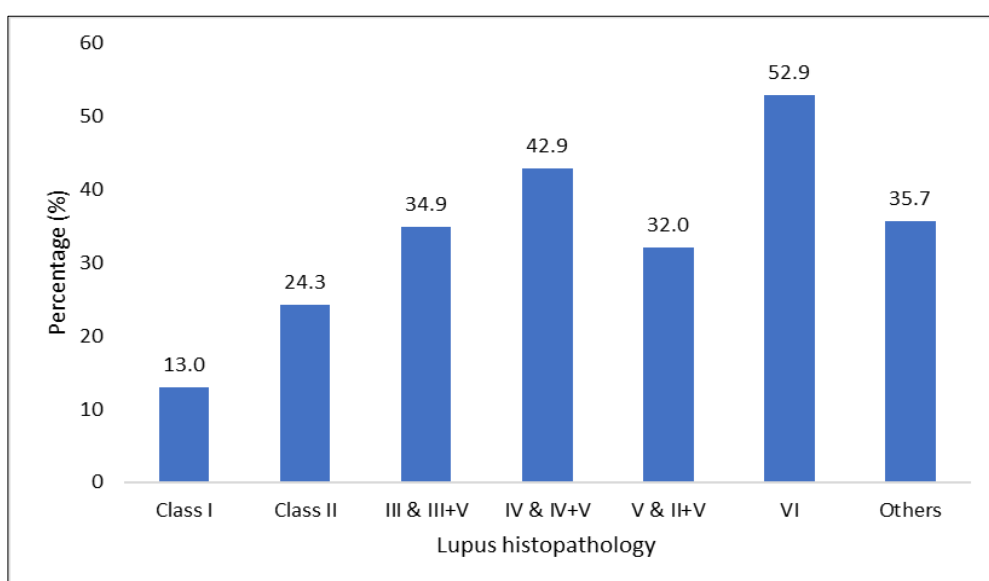


Figure 3.2.4.1(a): Hypertension by histopathology in lupus nephritis, 2005-2022

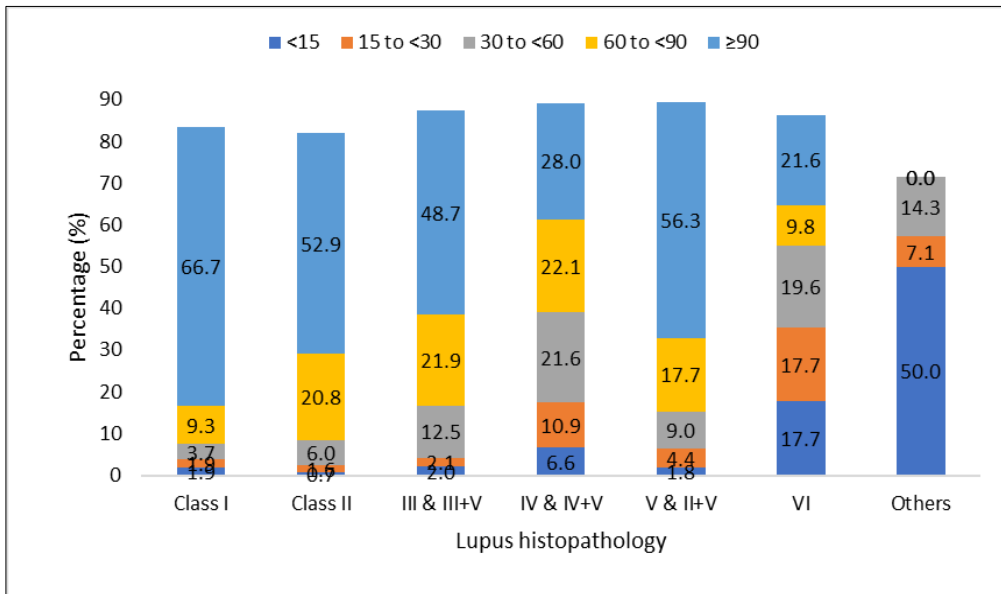


Figure 3.2.4.1(b): Renal function by histopathology, 2005-2022

### 3.2.5 Survival in lupus nephritis

- Patient survival rates were at 92% at 1 year, 85% at 5 years and 80% at 10 years (Figure 3.2.5(a)).
- Death-censored renal survival rates were 92% at 1 year, 87% at 5 years and 80% at 10 years (Figure 3.2.5(b)).
- Our result was much lower than the reported data from Hong Kong, in which patient survival rates were 98.6% and 98.2%, at 5 and 10 years respectively. And the renal survival rates were 99.5% and 98%, at 5 and 10 years respectively (Reference 1).
- Another cohort at China reported an overall patient survival rates at 88% and 77%, at 5 and 10 years respectively (Reference 2).

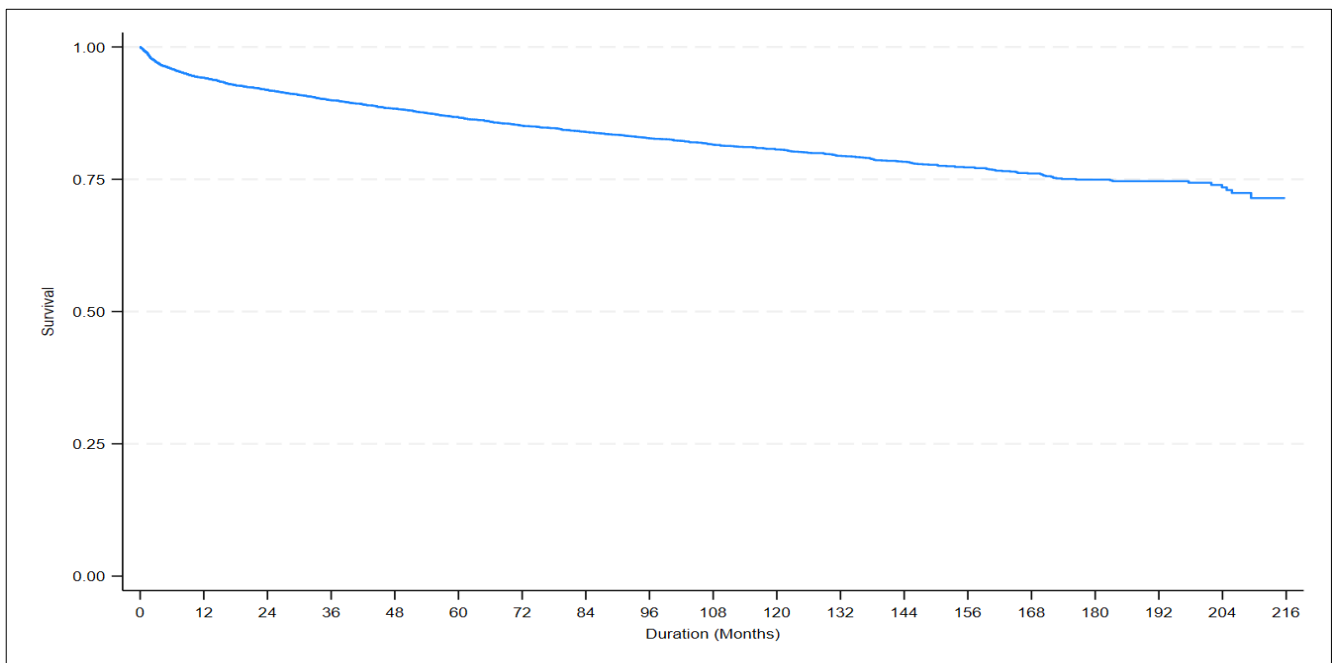


Figure 3.2.5(a): Patients Survival estimates for death in lupus nephritis, 2005-2022

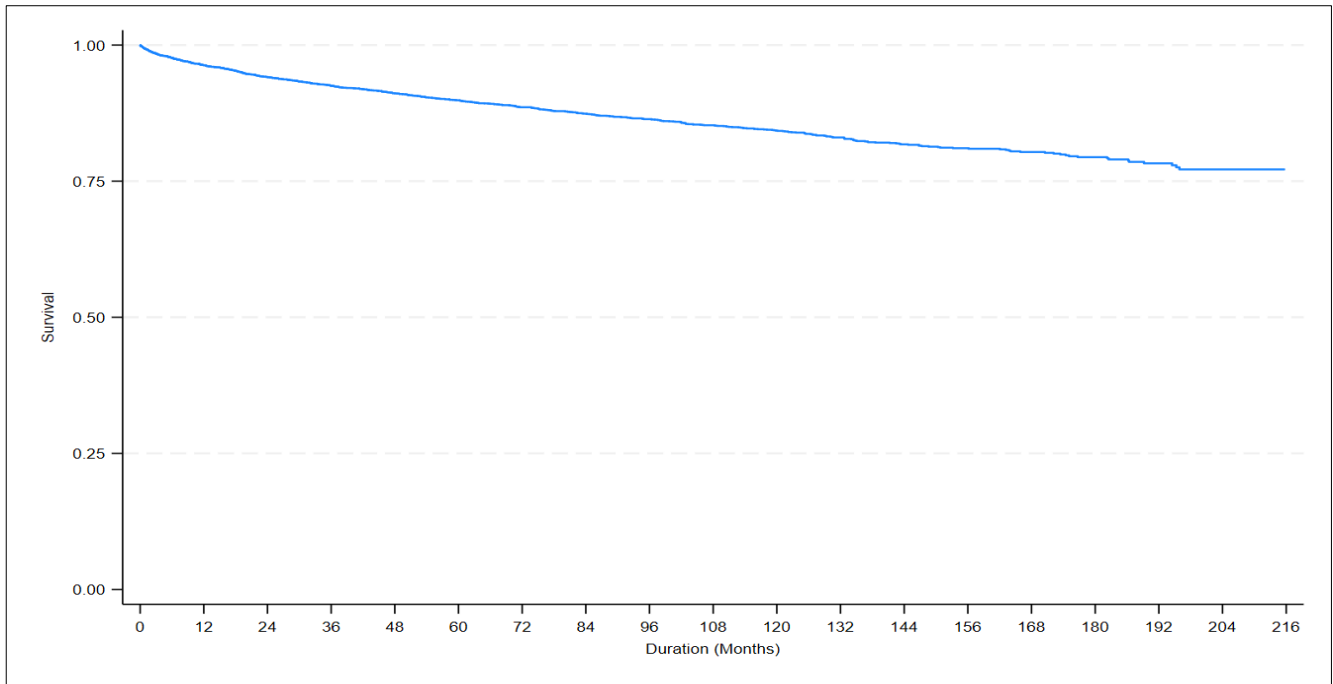


Figure 3.2.5(b): Death-censored Renal Survival estimates for lupus nephritis, 2005-2022

**Reference:**

1. Yap DYH, Tang CSO, Ma MKM, et al. Survival analysis and causes of mortality in patients with lupus nephritis. *Nephrology Dialysis Transplantation* 2012; 27: 3248–3254.
2. Zheng Z, Zhang L, Liu W, et al. Predictors of survival in Chinese patients with lupus nephritis. *Lupus*. 2012;21(10):1049-1056.