CHAPTER 4

Paediatric Renal Biopsies

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4.1 Introduction

- Chapter 4 reports on renal biopsies done in children less than 15 years of age over from 2005-2017).
- A total of 1883 renal biopsies were performed in 1842 children.
- The majority of renal biopsies were performed in Ministry of Health hospitals. (96%)
- The average number of native renal biopsies is 120-180 per year but there appears to be a reduction in the number of biopsies performed over the recent 3-4 years. *(Table & Figure 4.1.1)*
- It was the first episode of renal biopsy in 89% of patients. *(Table 4.1.2)*
- Eighty-percent of the biopsies yielded 10 or more glomeruli; the minimum number deemed adequate for diagnosis. *(Table 4.1.3)*

Table 4.1.1: Number of patients from various hospitals, 2005-2017

Hospitals	2005-2009 (n=701)		2010-2014 (n=754)		2015 (n=130)		2016 (n=131)		2017 (n=126)		Total (n=1842)	
	n	%	n	%	n	%	n	%	n	%	n	%
Hospital Kuala Lumpur	173	24.7	160	21.2	28	21.5	31	23.7	32	25.4	424	23.0
Other MOH Hospitals	511	72.9	556	73.7	98	75.4	95	72.5	93	73.8	1353	73.5
Non MOH Hospitals	17	2.4	38	5.0	4	3.1	5	3.8	1	0.8	65	3.5

** University Hospital, Army Hospital, Private Hospital*

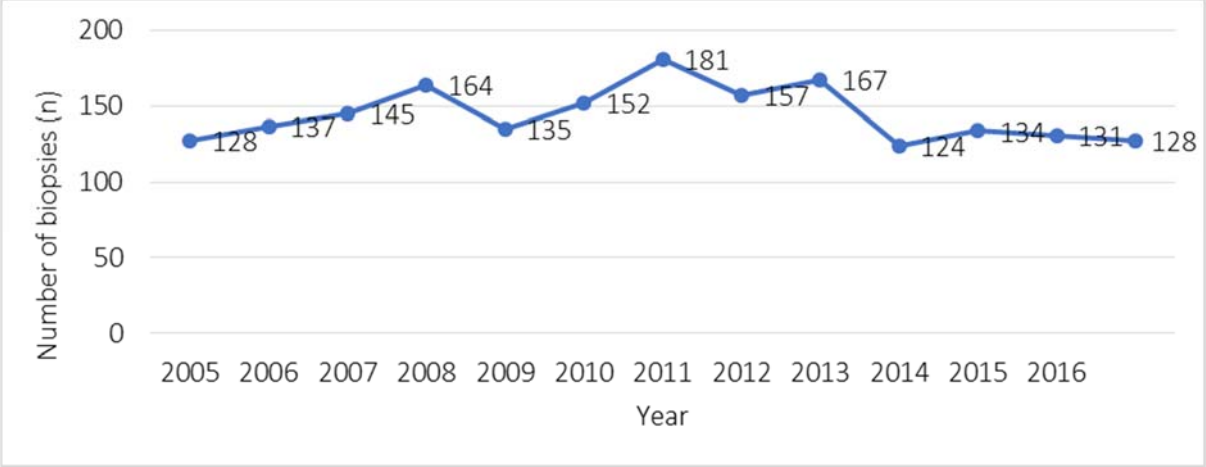

Figure 4.1.1: Number of renal biopsies, 2005-2017

Table 4.1.2: Distribution of native renal biopsy in patients by number of attempts, 2005-2017

Number of biopsy (s)	2005-2009 (n=701)		2010-2014 (n=754)		2015 (n=130)		2016 (n=131)		2017 (n=126)		Total (n=1842)	
	n	%	n	%	n	%	n	%	n	%	n	%
1st episode	605	86.3	680	90.2	121	93.1	119	90.8	112	88.9	1637	88.9
2nd episodes	74	10.6	62	8.2	6	4.6	12	9.2	13	10.3	167	9.1
3rd episodes	20	2.9	11	1.5	1	0.8	0	0	0	0	32	1.7
4th episodes	2	0.3	1	0.1	2	1.5	0	0	1	0.8	6	0.3

Table 4.1.3: Number of glomeruli obtained at each biopsy, 2005-2017

Number of glomeruli	2005-2009 (n=705)		2010-2014 (n=770)		2015 (n=133)		2016 (n=123)		2017 (n=127)		Total (n=1858)	
	n	%	n	%	n	%	n	%	n	%	n	%
< 10 Glomeruli	146	20.7	168	21.8	19	14.3	25	20.3	20	15.7	378	20.3
≥ 10 Glomeruli	559	79.3	602	78.2	114	85.7	98	79.7	107	84.3	1480	79.7

** 25 cases with missing number of glomeruli*

4.2 Patient Demographics

- The male to female ratio was equal
- The racial distribution was Malay 64%, Chinese 17%, Indian 6% and others 13%.
- The mean age at biopsy was 9.82 years.

Table 4.2.1: Gender and racial distribution, 2005-2017

Gender	2005-2009 (n=709)		2010-2014 (n=781)		2015 (n=134)		2016 (n=131)		2017 (n=128)		Total (n=1883)	
	n	%	n	%	n	%	n	%	n	%	n	%
Male	362	51.1	401	51.3	68	50.7	53	40.5	65	50.8	949	50.4
Female	347	48.9	380	48.7	66	49.3	78	59.5	63	49.2	934	49.6
Race												
Malay	426	60.1	527	67.5	87	64.9	75	57.3	90	70.3	1205	64.0
Chinese	145	20.5	120	15.4	23	17.2	25	19.1	15	11.7	328	17.4
Indian	58	8.2	34	4.4	5	3.7	9	6.9	2	1.6	108	5.7
Others*	80	11.3	100	12.8	19	14.2	22	16.8	21	16.4	242	12.9

** inclusive of 27 foreigners*

Table 4.2.2: Age distribution, 2005-2017

Year	2005 (n=128)	2006 (n=137)	2007 (n=145)	2008 (n=164)	2009 (n=135)	2010 (n=152)	2011 (n=181)
Mean	9.21	10.35	9.83	9.95	9.86	9.71	9.64
SD	4.32	3.57	3.61	3.74	3.99	3.94	4.33
Median	10.49	11.41	10.73	10.53	10.90	10.65	11.03
Minimum	0.59	1.06	2.41	0.25	0.53	0.86	0.23
Maximum	14.89	14.95	14.90	14.94	14.95	14.85	14.98
Year	**2012 (n=157)**	**2013 (n=167)**	**2014 (n=124)**	**2015 (n=134)**	**2016 (n=131)**	**2017 (n=128)**	**Total (n=1883)**
Mean	9.70	9.91	9.34	10.00	10.16	10.01	9.82
SD	4.26	3.83	4.13	4.04	4.09	3.69	3.97
Median	10.87	10.74	10.27	11.09	11.50	11.32	10.86
Minimum	0.13	0.10	0.37	1.65	1.36	1.95	0.10
Maximum	14.97	14.99	14.95	14.99	14.97	14.89	14.99

4.3: Clinical presentation

- The most frequent clinical presentation at biopsy was Nephrotic syndrome (50%), followed by asymptomatic urine abnormalities (19%) and mixed nephritic-nephrotic syndrome (13%). *(Table 4.3.1)*
- About two thirds (64.4%) of patients had normal renal function at the time of biopsy and one third (29%) had impaired renal function. *(Table 4.3.2)*
- Hypertension was found in 38% of patients and the most commonly used antihypertensive drugs were calcium channel blockers (56%) and angiotensin converting enzyme inhibitors (42%). *(Table 4.3.3(a) and (b))*

Table 4.3.1: Clinical presentation at biopsy, 2005-2017

Clinical Presentation	2005-2009 (n=709)		2010-2014 (n=781)		2015 (n=134)		2016 (n=131)		2017 (n=128)		Total (n=1883)	
	n	%	n	%	n	%	n	%	n	%	n	%
Nephrotic Syndrome	375	52.9	367	47.0	62	46.3	79	60.3	59	46.1	942	50.0
Asymptomatic urine abnormalities	120	16.9	156	20.0	21	15.7	22	16.8	32	25.0	351	18.6
Nephritic - Nephrotic	67	9.4	123	15.7	25	18.7	12	9.2	23	18.0	250	13.3
Nephritic syndrome	90	12.7	91	11.7	14	10.4	9	6.9	8	6.3	212	11.3
Not Available	57	80.4	44	56.3	12	9.0	9	6.9	6	4.7	128	6.8

Table 4.3.2: Renal function at biopsy, 2005-2017

Renal function	2005-2009 (n=709)		2010-2014 (n=781)		2015 (n=134)		2016 (n=131)		2017 (n=128)		Total (n=1883)	
	n	%	n	%	n	%	n	%	n	%	n	%
Impaired	209	29.5	239	30.6	40	29.9	29	22.1	37	28.9	554	29.4
Normal	453	63.9	497	63.6	84	62.7	90	68.7	88	68.8	1212	64.4
Not Available	47	6.6	45	5.8	10	7.5	12	9.2	3	2.3	117	6.2

Table 4.3.3(a): Hypertension at biopsy, 2005-2017

Hypertension	2005-2009 (n=709)		2010-2014 (n=781)		2015 (n=134)		2016 (n=131)		2017 (n=128)		Total (n=1883)	
	n	%	n	%	n	%	n	%	n	%	n	%
Present	217	30.6	346	44.3	48	35.8	44	33.6	56	43.8	711	37.8
Absent	467	65.9	388	49.7	72	53.7	77	58.8	63	49.2	1067	56.7
Not Available	25	3.5	47	6.0	14	10.4	10	7.6	9	7.0	105	5.6

Table 4.3.3(b): Type of antihypertensive drugs, 2005-2017

Type of anti-hypertensive	2005-2009 (n=217)		2010-2014 (n=346)		2015 (n=48)		2016 (n=44)		2017 (n=56)		Total (n=711)	
	n	%	n	%	n	%	n	%	n	%	n	%
Calcium Channel Blocker	115	53.0	183	52.9	30	62.5	30	68.2	38	67.9	396	55.7
ACEI	61	28.1	177	51.2	21	43.8	14	31.8	26	46.4	299	42.1
B Blocker	33	15.2	61	17.6	5	10.4	7	15.9	4	7.1	110	15.5
Alpha Blocker	32	14.7	30	8.7	2	4.2	6	13.6	3	5.4	73	10.3
ARB	7	3.2	12	3.5	0	0	1	2.3	1	1.8	21	3.0
Others	18	8.3	41	11.8	5	10.4	5	11.4	3	5.4	72	10.1
No drug available	70	32.3	16	4.6	4	8.3	2	4.5	3	5.4	95	13.4

**Patients may have more than one anti-hypertensive drug*

4.4: Diagnosis of paediatric renal biopsies

- Minimal change disease and FSGS together contribute the largest group of diagnosis 44%.
- Lupus nephritis was diagnosed in 26%, Post-infectious glomerulonephritis in 8%, IgA nephropathy 7% and Henoch Scholein Purpura 3%. *(Table 4.4)*

Table 4.4.1: Diagnosis of paediatric renal biopsies, 2005-2017

Diagnosis	2005-2009 (n=682)		2010-2014 (n=742)		2015 (n=128)		2016 (n=125)		2017 (n=120)		Total (n=1797)	
	n	%	n	%	n	%	n	%	n	%	n	%
Lupus Nephritis	176	25.8	192	25.9	38	29.7	26	20.8	34	28.3	466	25.9
Minimal Change	141	20.7	172	23.2	36	28.1	37	29.6	27	22.5	413	23.0
FSGS	176	25.8	119	16.0	21	16.4	31	24.8	23	19.2	370	20.6
Post Infectious GN	48	7.0	77	10.4	9	7.0	2	1.6	10	8.3	146	8.1
lg A nephropathy	36	5.3	66	8.9	7	5.5	9	7.2	12	10.0	130	7.2
Henoch Schonlein Purpura	22	3.2	14	1.9	6	4.7	7	5.6	1	0.8	50	2.8
Messangial Proliferative: non IgA	13	1.9	22	3.0	2	1.6	2	1.6	1	0.8	40	2.2
Advanced GN	18	2.6	12	1.6	2	1.6	0	0	1	0.8	33	1.8
Membranous nephropathy	9	1.3	14	1.9	2	1.6	1	0.8	4	3.3	30	1.7
Acute tubular Necrosis	10	1.5	4	0.5	2	1.6	0	0	0	0	16	0.9
Membrano-proliferative	8	1.2	6	0.8	0	0.0	0	0	1	0.8	15	0.8
Idiopathic Crescentic GN	5	0.7	2	0.3	0	0	1	0.8	1	0.8	9	0.5
Acute interstitial nephritis	1	0.1	6	0.8	1	0.8	0	0.0	0	0	8	0.4
Systemic vasculitis	4	0.6	1	0.1	0	0	0	0	1	0.8	6	0.3
Chronic interstitial nephritis	3	0.4	3	0.4	0	0	0	0	0	0	6	0.3
HUS / TTP	3	0.4	2	0.3	0	0	0	0	0	0	5	0.3
Crescentic ANCA	1	0.1	1	0.1	0	0	1	0.8	0	0	3	0.2
Thin Basement Membrane	1	0.1	2	0.3	0	0	0	0	0	0	3	0.2
Benign / Malignant Hypertension	0	0	1	0.1	0	0	0	0	1	0.8	2	0.1
Amyloidosis	0	0	1	0.1	0	0	0	0	0	0	1	0.1
Anti GBM disease	0	0	1	0.1	0	0	0	0	0	0	1	0.1
Malignancy	1	0.1	0	0	0	0	0	0	0	0	1	0.1
Other infection	0	0	0	0	0	0	1	0.8	0	0	1	0.1
Alport's syndrome	1	0.1	0	0	0	0	0	0	0	0	1	0.1
Other Hereditary	0	0	1	0.1	0	0	0	0	0	0	1	0.1
Others	3	0.4	16	2.2	1	0.8	4	3.2	1	0.8	25	1.4
Not Available	2	0.3	7	0.9	1	0.8	3	2.4	2	1.7	15	0.8

4.5: Nephrotic syndrome

- A total of 918 renal biopsies were performed in children with nephrotic syndrome.
- The commonest diagnosis was MCD (39%), FSGS (35%) and lupus nephritis (14%).
- The commonest histological finding for steroid resistant nephrotic syndrome was FSGS (45%) followed by MCD (44%). For the group with steroid sensitive nephrotic syndrome, MCD was found in 58% and FSGS in 32%.

Table 4.5.1: Renal histopathology diagnosis of children presenting with nephrotic syndrome, 2005-2017

Diagnosis	2005-2009 (n=368)		2010-2014 (n=355)		2015 (n=65)		2016 (n=73)		2017 (n=57)		Total (n=918)	
	n	%	n	%	n	%	n	%	n	%	n	%
FSGS	152	41.3	108	30.4	17	26.2	24	32.9	22	38.6	323	35.2
MCD	116	31.5	152	42.8	30	46.2	32	43.8	24	42.1	354	38.6
Lupus nephritis	58	15.8	43	12.1	10	15.4	9	12.3	4	7.0	124	13.5
IgA nephropathy	9	2.4	9	2.5	1	1.5	3	4.1	1	1.8	23	2.5
Mesangial prol- non-IgA	5	1.4	10	2.8	0	0	0	0	0	0	15	1.6
Post-infectious GN	4	1.1	5	1.4	0	0.0	0	0.0	1	1.8	10	1.1
Others**	24	6.5	28	7.9	7	10.8	5	6.8	5	8.8	69	7.5

**Patients may have more than 1 diagnosis classification (nephrotic n=943 but report conclusive for nephrotic n=909)*

*** Others – Henoch Schonlein Purpura, HUS/TTP, Systemic vasculitis, Malignancy, Membranous nephropathy, Membrano-proliferative, Idiopathic crescentic GN, Acute interstitial nephritis, Acute tubular necrosis, Chronic interstitial nephritis, Heredity (others), Advance GN, Others, Not available*

Table 4.5.2: The histopathological profile in different steroid response categories (nephrotic syndrome), 2005-2017

Diagnosis	Steroid resistant (n=410)		Steroid sensitive (n=172)		Not available (n=6)		Total (n=588)	
	n	%	n	%	n	%	n	%
FSGS	186	45.4	55	32.0	1	16.7	242	41.2
Minimal Change	182	44.4	99	57.6	4	66.7	285	48.5
Membranous nephropathy	14	3.4	1	0.6	0	0.0	15	2.6
lg A nephropathy	9	2.2	2	1.2	1	16.7	12	2.0
Mesangial Prol-non-IgA	4	1.0	7	4.1	0	0.0	11	1.9
Others**	11	2.7	12	5.6	0	0.0	23	3.9

**Patients may have more than 1 diagnosis classification*

***Others-Idiopathic Crescentic GN, Membrano-proliferative, Acute interstitial nephritis, Acute tubular necrosis, Chronic interstitial nephritis, Heredity, Not available*

4.6 Nephritic syndrome

- In children with presenting of nephritic syndrome; the commonest diagnosis was post-infectious GN (29%). Children with lupus nephritis 26% and IgA nephropathy 9% also presented with the similar syndrome.

Table 4.6: Renal histopathology diagnosis of children presenting with nephritic syndrome, 2005-2017

Diagnosis	2005-2009 (n=94)		2010-2014 (n=84)		2015 (n=14)		2016 (n=9)		2017 (n=6)		Total (n=207)	
	n	%	n	%	n	%	n	%	n	%	n	%
Post-infectious GN	21	22.3	30	35.7	4	28.6	1	11.1	3	50.0	59	28.5
Lupus nephritis	24	25.5	21	25.0	4	28.6	2	22.2	3	50.0	54	26.1
IgA nephropathy	7	7.4	9	10.7	1	7.1	1	11.1	0	0	18	8.7
Henoch Schonlein Purpura	5	5.3	1	1.2	1	7.1	1	11.1	0	0	8	3.9
FSGS	8	8.5	4	4.8	1	7.1	2	22.2	0	0	15	7.2
MCD	7	7.4	0	0	2	14.3	2	22.2	0	0	11	5.3
Mesangial prol non lgA	3	3.2	3	3.6	0	0	0	0	0	0	6	2.9
Acute tubular necrosis	9	9.6	2	2.4	0	0	0	0	0	0	11	5.3
Others**	10	10.6	14	16.7	1	7.1	0	0	0	0	25	12.1

**Patients may have more than 1 diagnosis classification (nephritic n=212 but report conclusive for nephrotic n=204)*

*** Others – Henoch Schonlein Purpura, HUS/TTP, Systemic vasculitis, Malignancy, Membranous nephropathy, Membrano-proliferative, Idiopathic crescentic GN, Acute interstitial nephritis, Acute tubular necrosis, Chronic interstitial nephritis, Heredity (others), Advance GN, Others, Not available*

4.7 Causes of severe renal failure (needed dialysis therapy)

- At the time of biopsy, 139 children (7.5%) needed dialysis therapy.
- The more common histological findings were post-infectious GN (23%), lupus nephritis (22%), advanced glomerulosclerosis (12%) and acute tubular necrosis (9%).

Table 4.7: Histology finding of children who had severe renal failure (needed dialysis therapy) who underwent renal biopsy, 2005-2017

Diagnosis	2005-2009 (n=40)		2010-2014 (n=76)		2015 (n=9)		2016 (n=4)		2017 (n=10)		Total (n=139)	
	n	%	n	%	n	%	n	%	n	%	n	%
Post-infectious GN	5	12.5	22	28.9	3	33.3	0	0	2	20.0	32	23.0
Lupus nephritis	9	22.5	16	21.1	2	22.2	0	0	4	40.0	31	22.3
FSGS	3	7.5	3	3.9	0	0	1	25.0	1	10.0	8	5.8
Advanced glomerulosclerosis (advance GN)	9	22.5	7	9.2	1	11.1	0	0	0	0	17	12.2
HUS/TTP	0	0	2	2.6	0	0	0	0	0	0	2	1.4
Acute tubular Necrosis	5	12.5	4	5.3	2	22.2	0	0	1	10.0	12	8.6
MCD	0	0	0	0	0	0	1	25.0	0	0	1	0.7
Acute interstitial nephritis	0	0	5	6.6	1	11.1	0	0	0	0	6	4.3
IgA nephropathy	1	2.5	5	6.6	0	0	0	0	0	0	6	4.3
Others	8	20.0	12	15.8	0	0	2	50.0	2	20.0	24	17.3

**Patients may have more than 1 diagnosis classification*

*** Others – HUS/TTP, Anti GBM disease, Advance GN, Systemic vasculitis, Membrano-proliferative, Idiopathic crescentic GN, Acute interstitial nephritis, Chronic interstitial nephritis, Alport's syndrome (needed dialysis therapy n=143 but report conclusive, n=133).*

4.8 Paediatric focal segmental glomerulosclerosis and minimal change disease

- Children with FSGS tend to be older, more likely to be female , had hypertension and lower eGFR compared to MCD. *(Table 4.8.1)*
- Patient survival was lower for children with FSGS; the survival rate at 5 years for MCD was 97% and FSGS was 92%. *(Table & Figure 4.8.2)*
- Children with FSGS showed a much poorer renal survival compared to MCD; 89% and 81% at 3 years and 5 years respectively. Renal survival for MCD at 3 years and 5 years was 95% and 92% respectively.

Table 4.8.1: Clinical characteristics of patients with MCD and FSGS

Clinical characteristics		FSGS		MCD		*p value*
Number		186	50.5	182	49.5	
Age/year (mean (SD))		7.8	3.92	6.7	4.02	0.005[a]
Age/year (median (IQR))		7.4	6.90	5.9	6.67	
Race	Malay	125	67.2	136	74.7	132[b]
	Chinese	20	10.8	13	7.1	
	Indian	12	6.50	16	8.80	
	Others	29	15.6	17	9.3	
BMI ((mean (sd))		19.01	3.71	18.97	4.58	0.0.294[c]
Gender	Male	114	61.3	131	72.0	0.030[d]
	Female	72	38.7	51	28.0	
Gross haematuria	Present	4	91.4	4	94.5	1.000[e]
	Absent	182	8.6	178	5.5	
Hypertension	Present	80	43.0	54	29.7	0.008[f]
	Absent	106	57.0	128	70.3	
Family history	Yes	7	3.8	7	3.8	0.967[g]
	No	179	96.2	175	96.2	
eGFR ml/min/1.73m²	< 30	8	4.3	2	2.7	0.002[h]
	30-60	19	10.2	4	6.3	
	60-90	22	11.8	15	10.1	
	≥90	114	61.3	127	65.5	
	Not available	23	12.4	34	15.5	
Dialysis required	Yes	5	2.7	1	0.5	0.002[h]
	No	181	97.3	181	99.5	
Albumin g/L (mean, sd)		20.55	10.60	20.87	10.04	0.256[l]
Tubulointerstitial disease	Yes	3	1.6	1	99.5	0.623[m]
	No	183	98.4	181	0.5	

a, c, l Mean Wintney U test
b, d, f,g,h Chi-square test
e, i, m Fisher's exact test

Interval (months)	Minimal Change Disease			Focal Segmental Glomerulosclerosis		
	n	% survival	SE	n	% survival	SE
0	413	100	-	370	100	-
12	381	99	0.006	338	97	0.008
24	341	98	0.008	302	95	0.011
36	304	97	0.008	280	95	0.012
48	269	97	0.008	266	94	0.013
60	236	97	0.009	234	92	0.015
72	208	96	0.012	206	92	0.015

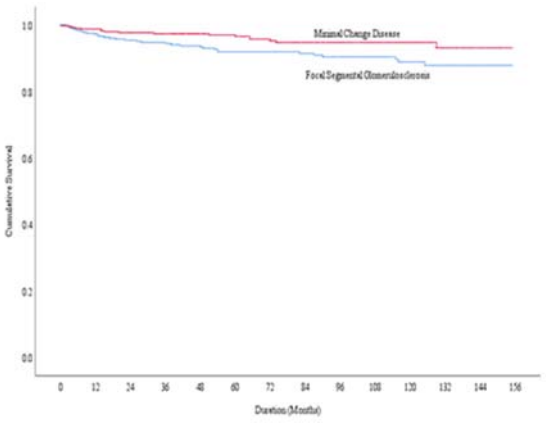

Table & Figure 4.8.2: Patient survival for focal segmental glomerulosclerosis and minimal change disease, 2005-2017

Interval (months)	Minimal Change Disease			Focal Segmental Glomerulosclerosis		
	n	% survival	SE	n	% survival	SE
0	413	100	-	370	100	-
12	381	100	-	318	94	0.013
24	337	98	0.007	278	92	0.015
36	289	95	0.012	248	89	0.018
48	253	94	0.013	223	84	0.021
60	221	93	0.014	190	81	0.023
72	195	92	0.015	157	77	0.025

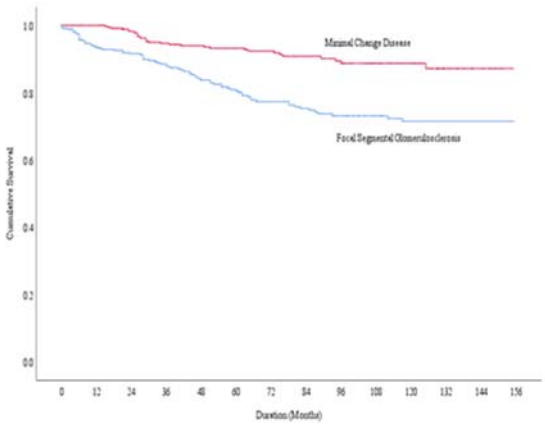

Table & Figure 4 8.3: Death-censored renal survival of patient with focal segmental glomerulosclerosis and minimal change disease, 2005-2017

4.9 Paediatric Lupus Nephritis

- There was a total of 435 renal biopsies performed for children with lupus. *(Figure 4.9.1)*
- Majority of children (85%) with lupus underwent first kidney. Sixty-four (15%) were repeat biopsies. *(Table 4.9.2)*
- The female: male ratio was 5.6:1. *(Table 4.9.3)*
- The racial distribution was Malay (65%), Chinese (23%), Indian (3%). (Table 4.9.3)
- Mean age at the time of biopsy was 11.8 years. *(Table 4.9.4)*
- About 6% of patients had severe renal failure and needed dialysis support while 43% had hypertension. *(Table 4.9.5 and Table 4.9.6))*
- The most frequent clinical presentation at biopsy was urinary abnormalities (34%) and nephrotic syndrome (28%). *(Table 4.9.7)*
- The most common extra renal manifestations were malar rash (43%), arthritis (28%) and hematological involvement (59%). Seventy-four percent of patients fulfilled 4 or more ARA criteria. *(Table 4.9.8 (a) and (b))*
- For patients who did not require dialysis therapy, the histology class was proliferative GN (III+V and IV+V) in 83% of biopsies. For those who needed dialysis, class IV or IV + V lupus nephritis was found in 61%. *(Table 4.9.9)*
- The patient survival was 92% at 3 years and 89% at 5 years from the time of diagnosis of lupus nephritis.
- The renal survival for lupus nephritis was 95% at 3 years and 94% at 5 years.

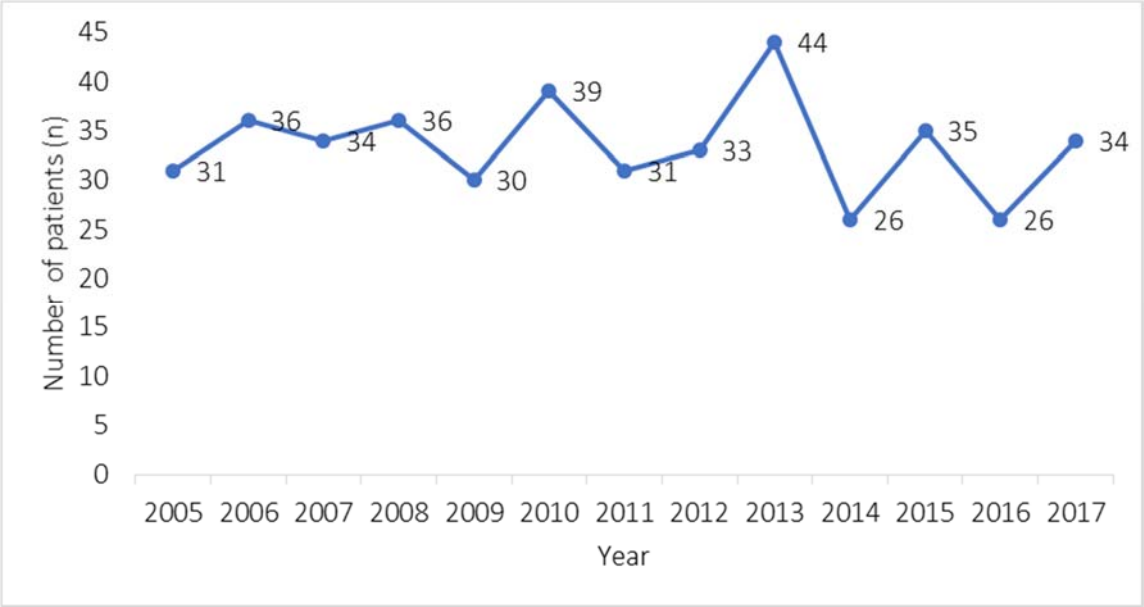

Figure 4.9.1: Total number biopsies (SLE), 2005-2017

Table 4.9.2: Distribution of renal biopsy in patient with lupus by number of episodes, 2005-2017

Year	2005-2009 (n=167)		2010-2014 (n=171)		2015 (n=35)		2016 (n=26)		2017 (n=33)		Total (n=432)	
	n	%	n	%	n	%	n	%	n	%	n	%
1st episode	145	86.8	142	83.0	29	82.9	24	92.3	28	84.8	368	85.2
2nd episodes	19	11.4	24	14.0	5	14.3	2	7.7	5	15.2	55	12.7
3rd episodes	3	1.8	5	2.9	0	0.0	0	0	0	0	8	1.9
4th episodes	0	0.0	0	0.0	1	2.9	0	0	0	0	1	0.2

Table 4.9.3: Gender and racial distribution of paediatric lupus nephritis, 2005-2017

Gender	2005-2009 (n=167)		2010-2014 (n=171)		2015 (n=35)		2016 (n=26)		2017 (n=33)		Total (n=435)	
	n	%	n	%	n	%	n	%	n	%	n	%
Male	24	14.4	24	13.9	6	17.1	7	26.9	6	17.6	67	15.4
Female	143	85.6	149	86.1	29	82.9	19	73.1	28	82.4	368	84.6
Race												
Malay	102	61.1	117	67.6	22	62.9	15	57.7	28	82.4	284	65.3
Chinese	43	25.7	34	19.7	9	25.7	8	30.8	4	11.8	98	22.5
Indian	7	4.2	3	1.7	1	2.9	1	3.8	0	0.0	12	2.8
Others*	15	9.0	19	11.0	3	8.6	2	7.7	2	5.9	41	9.4

Table 4.9.4: Age distribution of paediatric lupus nephritis, 2005-2017

Year	2005 (n=31)	2006 (n=36)	2007 (n=34)	2008 (n=36)	2009 (n=30)	2010 (n=39)	2011 (n=31)
Mean	12.46	12.08	12.24	11.16	11.34	11.76	12.08
SD	2.20	2.44	2.03	3.27	3.77	2.51	3.67
Median	13.16	12.93	12.65	11.70	11.89	12.19	13.22
Minimum	4.89	6.63	7.30	0.25	0.53	1.46	0.23
Maximum	14.80	14.76	14.89	14.94	14.95	14.82	14.98
Year	**2012 (n=33)**	**2013 (n=44)**	**2014 (n=26)**	**2015 (n=35)**	**2016 (n=26)**	**2017 (n=34)**	**Total (n=435)**
Mean	11.53	11.27	11.40	12.31	12.34	12.00	11.83
SD	3.88	3.36	2.74	2.15	2.71	2.18	2.90
Median	12.80	12.26	12.62	12.54	13.46	12.32	12.71
Minimum	0.27	0.10	4.08	6.15	3.14	6.22	0.10
Maximum	14.97	14.97	14.78	14.95	14.90	14.89	14.98

Table 4.9.5: Dialysis therapy for paediatric lupus nephritis at the time of biopsy, 2005-2017

Needed Dialysis therapy	2005-2009 (n=167)		2010-2014 (n=171)		2015 (n=35)		2016 (n=26)		2017 (n=33)		Total (n=435)	
	n	%	n	%	n	%	n	%	n	%	n	%
Yes	7	5.1	15	7.4	2	5.7	0	0	4	11.8	28	6.4
No	98	71.5	173	85.2	29	82.9	25	96.2	29	85.3	354	81.4
Not available	32	23.4	15	7.4	4	11.4	1	3.8	1	2.9	53	12.2

Table 4.9.6: Presence of hypertension of paediatric lupus nephritis, 2005-2017

Hypertension	2005-2009 (n=167)		2010-2014 (n=171)		2015 (n=35)		2016 (n=26)		2017 (n=33)		Total (n=435)	
	n	%	n	%	n	%	n	%	n	%	n	%
Present	64	38.3	79	45.7	14	40.0	11	42.3	20	58.8	188	43.2
Absent	94	56.3	84	48.6	19	54.3	13	50.0	11	32.4	221	50.8
Not Available	9	5.4	10	5.8	2	5.7	2	7.7	3	8.8	26	6.0

Table 4.9.7: Clinical presentation at biopsy of paediatric lupus nephritis, 2005-2017

Clinical Presentation	2005-2009 (n=167)		2010-2014 (n=171)		2015 (n=35)		2016 (n=26)		2017 (n=33)		Total (n=435)	
	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormalities	47	28.1	67	38.7	10	28.6	10	38.5	15	44.1	149	34.3
Nephrotic syndrome	57	34.1	41	23.7	10	28.6	9	34.6	4	11.8	121	27.8
Nephritic - Nephrotic	22	13.2	37	21.4	9	25.7	4	15.4	8	23.5	80	18.4
Nephritic syndrome	23	13.8	19	11.0	4	11.4	2	7.7	3	8.8	51	11.7
Not Available	18	10.8	9	5.2	2	5.7	1	3.8	4	11.8	34	7.8

Table 4.9.8 (a) ARA criteria at presentation, 2005-2017

ARA criteria	2005-2009 (n=167)		2010-2014 (n=171)		2015 (n=35)		2016 (n=26)		2017 (n=33)		Total (n=435)	
	n	%	n	%	n	%	n	%	n	%	n	%
Malar rash	80	47.9	71	41.0	12	34.3	15	57.7	10	29.4	188	43.2
Photosensitivity	41	24.6	40	23.1	6	17.1	7	26.9	3	8.8	97	22.3
Arthritis	50	29.9	56	32.4	6	17.1	6	23.1	4	11.8	122	28.0
Cerebral	15	9.0	23	13.3	2	5.7	4	15.4	4	11.8	48	11.0
Renal	139	83.2	149	86.1	27	77.1	18	69.2	30	88.2	363	83.4
Hematological	99	59.3	105	60.7	20	57.1	12	46.2	22	64.7	258	59.3
Discoid rash	9	5.4	19	11.0	3	8.6	4	15.4	6	17.6	41	9.4
Serositis	22	13.2	24	13.9	7	20.0	6	23.1	3	8.8	62	14.3
Oral ulcers	45	26.9	50	28.9	7	20.0	3	11.5	5	14.7	110	25.3
ANF* Positive	157	94.0	140	80.9	26	74.3	19	73.1	25	73.5	367	84.4
At least one positive in other labs*	112	67.1	115	66.5	28	80.0	20	76.9	28	82.4	303	69.7

**Anti-Nuclear Factor*
***dsDNA, ssDNA, Anti-cardiolipin antibody, Anti-phospholipid antibody, Histone, Nucleo, Ro, La or Sm*

Table 4.9.8(b): ARA criteria at presentation, 2005-2017

ARA criteria	2005-2009 (n=167)		2010-2014 (n=171)		2015 (n=35)		2016 (n=26)		2017 (n=33)		Total (n=435)	
	n	%	n	%	n	%	n	%	n	%	n	%
>4	39	23.4	47	27.2	10	28.6	8	30.8	9	26.5	113	26.0
≥4	128	76.6	126	72.8	25	71.4	18	69.2	25	73.5	322	74.0

Table 4.9.9: Classification of paediatric lupus nephritis, 2005-2017

Needed dialysis

WHO/ISN /RPS Class	2005-2009 (n=8)		2010-2014 (n=14)		2015 (n=2)		2016 (n=0)		2017 (n=4)		Total (n=28)	
	n	%	n	%	n	%	n	%	n	%	n	%
Class II	1	12.5	1	7.1	0	0	0	0	0	0	2	7.1
Class III or III + V	0	0	3	21.4	1	50.0	0	0	0	0	4	14.3
Class IV or IV + V	4	50.0	9	64.3	0	0	0	0	4	100	17	60.7
Class V or II + V	1	12.5	0	0	1	50.0	0	0	0	0	2	7.1
Class VI	2	25.0	0	0	0	0	0	0	0	0	2	7.1
Not Available	0	0	1	7.1	0	0	0	0	0	0	1	3.6

Not needed dialysis

WHO/ISN /RPS Class	2005-2009 (n=124)		2010-2014 (n=147)		2015 (n=29)		2016 (n=25)		2017 (n=29)		Total (n=354)	
	n	%	n	%	n	%	n	%	n	%	n	%
Class I	0	0	4	2.7	1	3.4	0	0.0	1	3.4	6	1.7
Class II	10	8.1	13	8.8	3	10.3	2	8.0	0	0	28	7.9
Class III or III + V	23	18.5	42	28.6	10	34.5	10	40.0	10	34.5	95	26.8
Class IV or IV + V	86	69.4	76	51.7	14	48.3	9	36.0	13	44.8	198	55.9
Class V or II + V	5	4.0	9	6.1	1	3.4	2	8.0	2	6.9	19	5.4
Not Available	0	0	3	2.0	0	0.0	2	8.0	3	10.3	8	2.3

Interval (months)	Lupus Nephritis patients		
	n	% survival	SE
0	435	-	-
12	383	96	0.009
24	345	94	0.012
36	307	92	0.014
48	281	91	0.015
60	237	89	0.017
72	198	86	0.019

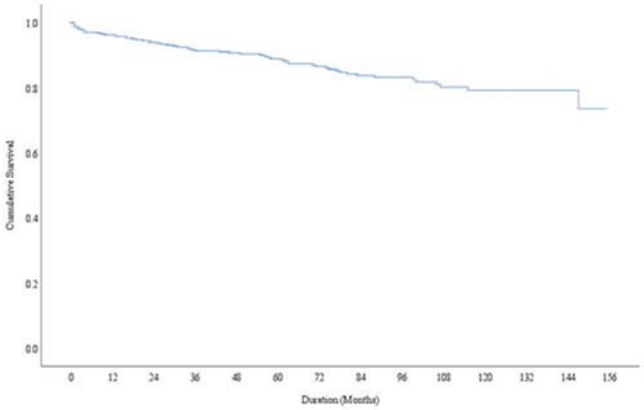

Table & Figure 4.9.10: Patients survival in lupus nephritis, 2005-2017

Interval (months)	Lupus Nephritis patients		
	n	% survival	SE
0	433	100	-
12	373	98	0.007
24	332	97	0.009
36	292	95	0.011
48	266	94	0.012
60	226	94	0.013
72	189	93	0.015

***Missing of 2 event case where the outcome date < date of 1st biopsy Event = ESRF; Status as at 31st Dec 2017 or died or last follow-up*

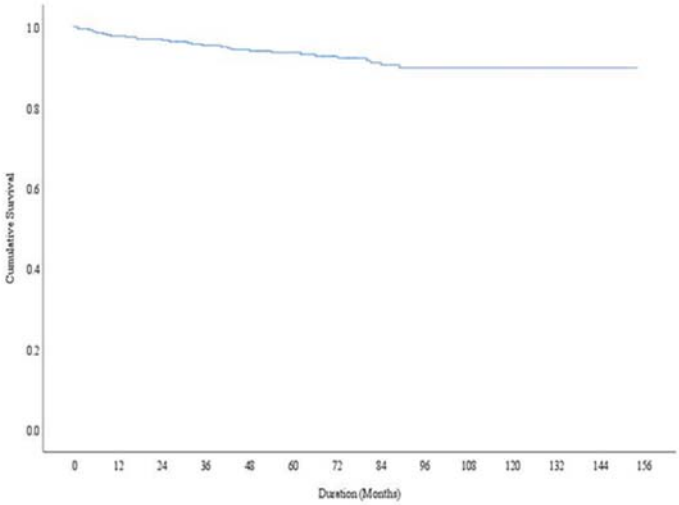

Table & figure 4.9.11: Death-censored Renal survival of patient with lupus nephritis, 2005-2017

4.10 Renal outcome

- Of the 1842 patients biopsied, 218 (11.8%) of these children were reported to the Malaysian Dialysis and Transplant Registry with end stage renal disease (ESRD*). (Table 4.10)*
- FSGS was the most common cause of ESRD accounting for 33%.
- Other causes of ESRD in children were lupus nephritis (17%), minimal change disease (13%), advance GN (9%) and IgA nephropathy(7%).

Table 4.10: Causes of end stage renal disease in children who underwent renal biopsy, 2005-2017

Causes	n=218	%
FSGS	71	32.6
Lupus Nephritis	36	16.5
Minimal Change	28	12.8
Advance GN	19	8.7
lg A nephropathy	16	7.3
Post Infectious GN	7	3.2
Chronic interstitial nephritis	4	1.8
Idiopathic Crescentic GN	3	1.4
Mesangial Proliferative GN-non IgA	3	1.4
Crescentic ANCA	2	0.9
Membranous nephropathy	2	0.9
Systemic vasculitis	2	0.9
Acute tubular necrosis	2	0.9
Membrano-proliferative	1	0.5
Henoch Schonlein Purpura	1	0.5
HUS / TTP	1	0.5
Other infection	1	0.5
Alport's syndrome	1	0.5
Other heredity	1	0.5
Benign / Malignant Hypertension	1	0.5
Others	6	2.8
Report Not conclusive	17	7.8

**Patients may have more than one cause of end stage renal disease*

4.11 Biopsy failure and complication

- Complication rate for the biopsy procedure was reported around 4%. *(Table 4.11.1)*
- The risk of bleeding was 3% and perinephric collection was 0.6%. *(Table 4.11.1)*
- The risk of complications post renal biopsy was higher in those with low GFR <30ml/min /1.72m^2 and needing dialysis therapy. *(Table 4.11.2)*
- The previous report found age less than 2 and a lower haemoglobin to be additional risk factors but it was not significant in this analysis.

Table 4.11.1: Frequency of complication, 2005-2017

Causes	n	%
Total number of biopsies	1883	
Total number of complications	67	3.6
- Bleeding	56	83.6
- Gross haematuria	49	73.1
- Haematoma	8	11.9
- Peri-renal collection	11	16.4
- Arteriovenous malformation	1	1.5
- Hypotension	3	4.5

Table 4.11.2: Risk factors for complication, 2005-2017

Factors		n	Number of complications	Odds ratio	95% CI	*p*-value
Age (years)	<2	59	4	2.279	0.779, 6.669	0.133
	>2-≤5	234	12	1.724	0.872, 3.407	0.117
	>5-≤10	481	20	1.398	0.788, 2.477	0.252
	>10 (ref*)	1042	31	1.00	-	-
Calculated GFR ml/min/1.73m²	<15	74	8	3.522	1.540, 8.055	0.003
	15-<30	90	9	3.258	1.481,7.168	0.003
	30-<60	173	10	1.883	0.892,3.976	0.097
	60- <90	226	11	1.586	0.772,3.258	0.210
	> 90 (ref*)	847	26	1.00	-	-
	Unknown	406	3	-	-	-
Renal failure	Needed dialysis	128	15	2.72	1.48,4.99	<0.001
	Not needed dialysis (ref*)	1476	47	1.00	-	-
	Unknown	212	5	-	-	-
SLE status	SLE	457	10	1.917	0.971,3.785	0.061
	Non SLE (ref*)	1359	57	-	-	-
Haemoglobin (Hb) level g/dl	<8	31	2	1.951	0.450, 8.450	0.372
	>8-≤10	486	24	1.493	0.886,2.516	0.132
	≥11 (ref*)	1149	38	1.00	-	-
	Unknown	150	3	-	-	-
Plug biopsy **	Yes	11	1	-	-	-
	No	1067	62	-	-	-
	Unknown	738	4	-	-	-
Ultrasound – guidance	Realtime	743	48	0.774	0.449,1.335	0.357
	Not Realtime	380	19	1.00	-	-
	Unknown	693	0	-	-	-
Needle size	14G	174	13	1.020	0.542,1.917	0.952
	16G (ref*)	696	51	1.00	-	-
	18G	323	3	0.127	0.039,0.409	0.001
	Unknown	623	0	-	-	-
Number of passes	≤2	722	35	0.671	0.410,1.100	0.113
	3-≤4 (ref*)	443	32	1.00	-	-
	≥ 5**	24	0	-	-	-
	Unknown	627	0	-	-	-

- *(ref*) Reference category*
- *CI-confidence interval*
  *** Not able to do compute due to the small sample size*
- *Unknown = No information*