

# **CHAPTER 4**

# **PAEDIATRIC RENAL BIOPSIES**

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### 4.1 Introduction

- Chapter 4 reports on renal biopsies done in children and young people less than 15 years of age over a span of 18 years. Yearly data is available from 2020 to 2022.
- A total of 2491 renal biopsies were performed in 2463 children.
- The majority of renal biopsies were performed in the Ministry of Health hospital (96.6%).
- The average number of renal biopsies yearly was 110-140 (Table and Figure 4.1.1).
- It was the first episode of renal biopsy in 89.9% of patients (Table 4.1.2).
- Eighty-percent of the biopsies yielded 10 or more glomeruli; the minimum number deemed adequate for histopathological diagnosis (Table 4.1.3).

Table 4.1.1: Number of patients from various hospitals, 2005-2022

Hospitals	2005-2009 (n=701)		2010-2014 (n=769)		2015-2019 (n=654)		2020 (n=112)		2021 (n=113)		2022 (n=114)		Total (n=2463)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Hospital Kuala Lumpur	173	24.7	160	20.8	145	22.2	32	28.6	20	17.7	16	14.0	546	22.2
Other MOH Hospitals	511	72.9	567	73.7	492	75.2	77	68.8	91	80.5	94	82.5	1832	74.4
Non MOH* Hospitals	17	2.4	42	5.5	17	2.6	3	2.7	2	1.8	4	3.5	85	3.5

\* University Hospital, Army Hospital, Private Hospital

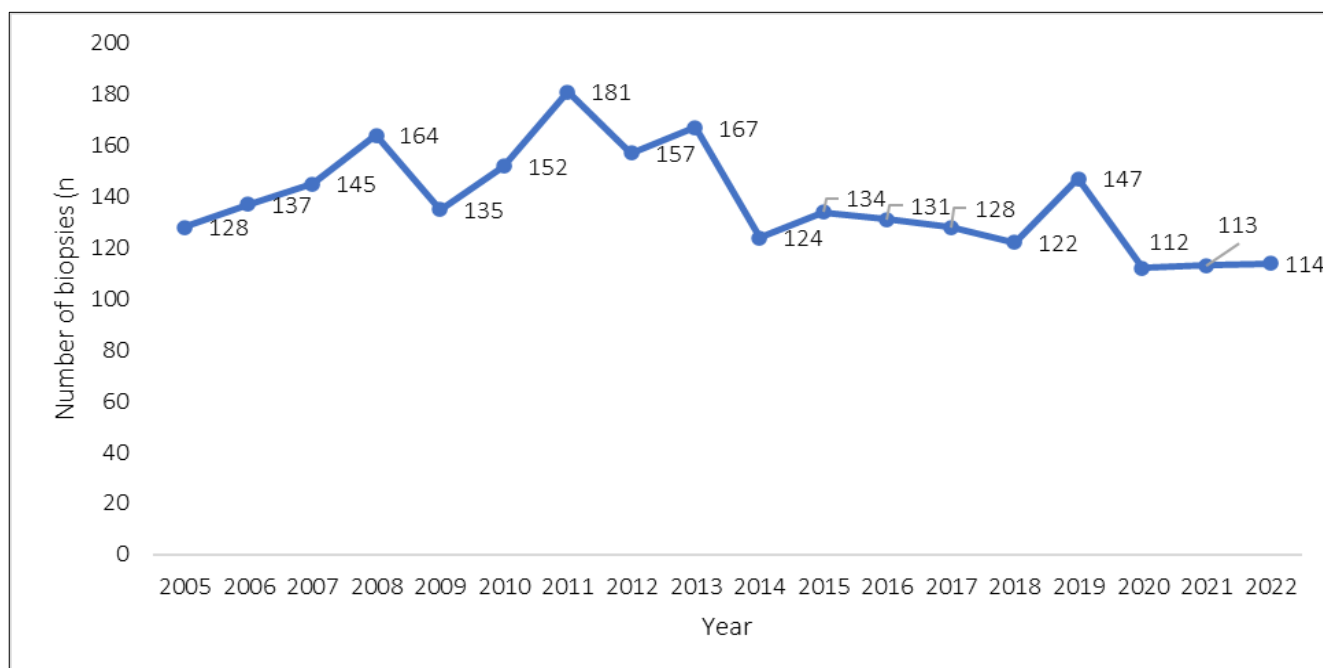


Figure 4.1.1: Number of renal biopsies, 2005-2022

Table 4.1.2: Distribution of native renal biopsy in patients by number of attempts, 2005-2022

Number of biopsy(s)	2005-2009 (n=701)		2010-2014 (n=769)		2015-2019 (n=654)		2020 (n=112)		2021 (n=113)		2022 (n=114)		Total (n=2463)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
1st episode	605	86.3	694	90.2	595	91.3	104	95.4	107	94.7	104	91.2	2214	89.9
2nd episode	74	10.6	64	8.3	53	8.1	5	4.6	6	5.3	9	7.9	211	8.6
3rd episode	20	2.9	9	1.2	1	0.2	0	0.0	0	0	1	0.9	31	1.3
4th episode	2	0.3	2	0.3	3	0.5	0	0	0	0	0	0	7	0.3

Table 4.1.3: Number of glomeruli obtained at each biopsy, 2005-2022

Number of glomeruli	2005-2009 (n=705)		2010-2014 (n=770)		2015-2019 (n=638)		2020 (n=109)		2021 (n=109)		2022 (n=105)		Total (n=2436)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
< 10	146	20.7	168	21.8	119	18.7	9	8.3	16	14.7	22	21.0	480	19.7
≥ 10	559	79.3	602	78.2	519	81.3	100	91.7	93	85.3	83	79.0	1956	80.3

\* 55 cases with missing number of glomeruli

## 4.2 Patient demographics

- There was an equal male to female ratio.
- The ethnic distribution was Malay 66.1%, Chinese 15.9%, Indian 5.5% and others 12.5%. This pattern followed the demographic composition of the country.
- The mean age at biopsy was 9.91 years.

Table 4.2.1: Gender and racial distribution, 2005-2022

	2005-2009 (n=709)		2010-2014 (n=781)		2015-2019 (n=662)		2020 (n=112)		2021 (n=113)		2022 (n=114)		Total (n=2491)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<b>Gender</b>														
Male	347	48.9	380	48.7	350	52.9	63	56.3	60	53.1	54	47.4	1254	50.3
Female	362	51.1	401	51.3	312	47.1	49	43.8	53	46.9	60	52.6	1237	49.7
<b>Race</b>														
Malay	426	60.1	527	67.5	451	68.1	76	67.9	84	74.3	83	72.8	1647	66.1
Chinese	145	20.5	120	15.4	94	14.2	19	17.0	8	7.1	9	7.9	395	15.9
Indian	58	8.2	34	4.4	25	3.8	6	5.4	10	8.8	4	3.5	137	5.5
Others*	80	11.3	100	12.8	92	13.9	11	9.8	11	9.7	18	15.8	312	12.5

Table 4.2.2: Age distribution, 2005-2022

Year	2005 (n=128)	2006 (n=137)	2007 (n=145)	2008 (n=164)	2009 (n=135)	2010 (n=152)	2011 (n=181)	2012 (=157)	2013 (n=167)	2014 (n=124)
Mean	9.21	10.35	9.83	9.95	9.86	9.71	9.64	9.70	9.91	9.34
SD	4.32	3.57	3.61	3.74	3.99	3.94	4.33	4.26	3.83	4.13
Median	10.49	11.41	10.73	10.53	10.90	10.65	11.03	10.87	10.74	10.27
Minimum	0.59	1.06	2.41	0.25	0.53	0.86	0.23	0.13	0.10	0.37
Maximum	14.89	14.95	14.90	14.94	14.95	14.85	14.98	14.97	14.99	14.95

Year	2015 (n=134)	2016 (n=131)	2017 (n=128)	2018 (n=122)	2019 (=147)	2020 (n=112)	2021 (n=113)	2022 (n=114)	Total (n=2491)
Mean	10.0	10.16	10.1	9.76	10.14	10.42	9.94	10.70	9.91
SD	4.04	4.09	3.69	3.94	3.84	3.97	4.13	3.77	3.97
Median	11.09	11.50	11.32	10.58	10.77	11.62	11.47	12.03	10.97
Minimum	1.65	1.36	1.95	0.96	0.68	1.90	1.38	1.78	0.10
Maximum	14.99	14.97	14.89	14.95	14.98	14.98	14.98	14.98	14.99

### 4.3 Clinical presentation

- The most frequent clinical presentation at biopsy was nephrotic syndrome (51.0%), followed by asymptomatic urine abnormalities (18.5%), mixed nephrotic-nephritic syndrome (12.7%) and nephritic syndrome (11.4%) (Table 4.3.1).
- About two-thirds (65.8%) of patients had normal renal function at the time of biopsy and one third (28.5%) had impaired renal function (Table 4.3.2).
- Hypertension was found in 36.6% of patients and the commonly used antihypertensive drugs were calcium channel blocker (56%) and ACEI / ARB (47.3%) (Table 4.3.3 (a) and (b)).

Table 4.3.1: Clinical presentation at biopsy, 2005-2022

Clinical Presentation	2005-2009 (n=709)		2010-2014 (n=781)		2015-2019 (n=662)		2020 (n=112)		2021 (n=113)		2022 (n=114)		Total (n=2491)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Nephrotic syndrome	375	52.9	367	47.0	330	49.8	67	59.8	66	58.4	66	57.9	1271	51.0
Asymptomatic urine abnormalities	120	16.9	156	20	133	20.1	20	17.9	21	18.6	12	10.5	462	18.5
Nephritic - Nephrotic	67	9.4	123	15.7	94	14.2	9	8.0	9	8.0	15	13.2	317	12.7
Nephritic syndrome	90	12.7	91	11.7	63	9.5	11	9.8	12	10.6	16	14.0	283	11.4
Not Available	57	80.4	44	56.3	42	6.3	5	4.5	5	4.4	5	4.4	158	6.3

Table 4.3.2: Renal function at biopsy, 2005-2022

Renal function	2005-2009 (n=709)		2010-2014 (n=781)		2015-2019 (n=662)		2020 (n=112)		2021 (n=113)		2022 (n=114)		Total (n=2491)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Impaired	209	29.5	239	30.6	169	25.5	24	21.4	30	26.5	40	35.1	711	28.5
Normal	453	63.9	497	63.6	455	68.7	85	75.9	79	69.9	70	61.4	1639	65.8
Not Available	47	6.6	45	5.8	38	5.7	3	2.7	4	3.5	4	3.5	141	5.7

Table 4.3.3(a): Hypertension at biopsy, 2005-2022

Hypertension	2005-2009 (n=709)		2010-2014 (n=781)		2015-2019 (n=662)		2020 (n=112)		2021 (n=113)		2022 (n=114)		Total (n=2491)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Yes	217	30.6	346	44.3	250	37.8	29	25.9	56	43.8	33	28.9	912	36.6
No	467	65.9	388	49.7	356	53.8	70	62.5	63	49.2	75	65.8	1424	57.2
Not Available	25	3.5	47	6.0	56	8.5	13	11.6	9	7.0	6	5.3	155	6.2

Table 4.3.3(b): Type of antihypertensive drugs, 2005-2022

Type of antihypertensives	2005-2009 (n=217)		2010-2014 (n=346)		2015-2019 (n=250)		2020 (n=29)		2021 (n=56)		2022 (n=33)		Total (n=841)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Calcium Channel Blocker	115	53.0	183	52.9	163	65.2	16	55.2	18	48.6	16	48.5	511	56.0
ACEI	61	28.1	177	51.2	112	44.8	15	51.7	22	59.5	16	48.5	403	44.2
B Blocker	33	15.2	61	17.6	30	12.0	4	13.8	2	5.4	4	12.1	110	12.1
Alpha Blocker	32	14.7	30	8.7	18	7.2	3	10.3	7	18.9	5	15.2	95	10.4
ARB	7	3.2	12	3.5	7	2.8	0	0	0	0	2	6.1	28	3.1
Others	18	8.3	41	11.8	17	6.8	4	13.8	6	16.2	5	15.2	91	10
No drug available	70	32.3	16	4.6	13	5.2	0	0	1	2.7	0	0	100	11.0

\*Patients may have more than one antihypertensives drug

#### 4.4 Diagnosis of paediatric renal biopsies

- Minimal change disease and FSGS together accounted for the largest diagnostic group, comprising 44.9%.
- Lupus nephritis was diagnosed in 25.1%, post-infectious glomerulonephritis in 7.2%, IgA nephropathy in 7.4% and Henoch-Schonlein Purpura in 3.0% (Table 4.4).

Table 4.4: Diagnosis of paediatric renal biopsies, 2005-2022

Diagnosis	2005-2009 (n=682)		2010-2014 (n=742)		2015-2019 (n=631)		2020 (n=110)		2021 (n=108)		2022 (n=106)		Total (n=2379)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Lupus Nephritis	176	25.8	192	25.9	152	24.1	26	23.6	28	25.9	22	20.8	596	25.1
Minimal Change	141	20.7	172	23.2	169	26.8	33	30	35	32.4	39	36.8	589	24.8
FSGS	176	25.8	119	16.0	118	18.7	25	22.7	24	22.2	15	14.2	477	20.1
Post Infectious GN	48	7.0	77	10.4	37	5.9	5	4.5	3	2.8	2	1.9	172	7.2
IgA nephropathy	36	5.3	66	8.9	53	8.4	7	6.4	7	6.5	7	6.6	176	7.4
Henoch- Schonlein Purpura	22	3.2	14	1.9	26	4.1	5	4.5	2	1.9	2	1.9	71	3.0
Mesangial Proliferative GN-non IgA	13	1.9	22	3.0	7	1.1	2	1.8	0	0	1	0.9	45	1.9
Advanced GN	21	3.1	12	1.6	7	1.1	1	0.9	0	0	3	2.8	44	1.8
Membranous nephropathy	9	1.3	14	1.9	11	1.7	0	0	0	0	1	0.9	35	1.5
Acute tubular necrosis	18	2.6	7	0.9	4	0.6	1	0.9	1	0.9	31	29.2	62	2.6
Membrano-proliferative	8	1.2	6	0.8	1	0.2	1	0.9	0	0	1	0.9	17	0.7
Idiopathic Crescentic GN	5	0.7	2	0.3	3	0.5	1	0.9	0	0	0	0	11	0.5
Acute interstitial nephritis	2	0.3	9	1.2	3	0.5	0	0	1	0.9	15	14.2	30	1.3
Systemic vasculitis	4	0.6	1	0.1	3	0.5	0	0	0	0	0	0	8	0.3
Chronic interstitial nephritis	7	1.0	3	0.4	1	0.2	0	0	0	0	11	10.4	22	0.9
HUS / TTP	3	0.4	2	0.3	0	0	1	0.9	0	0	0	0	6	0.3
Crescentic ANCA	1	0.1	1	0.1	1	0.2	0	0	0	0	2	1.9	5	0.2
Thin Basement Membrane disease	1	0.1	2	0.3	1	0.2	0	0	0	0	0	0	4	0.2
Benign / Malignant Hypertension	1	0.1	1	0.1	1	0.2	0	0	0	0	1	0.9	4	0.2
Amyloidosis	0	0	1	0.1	0	0	0	0	0	0	0	0	1	0
Anti GBM disease	0	0	1	0.1	0	0	0	0	0	0	0	0	1	0
Malignancy	1	0.1	0	0	0	0	0	0	0	0	0	0	1	0
Other infection	0	0	0	0	0	0	1	0.9	0	0	0	0	1	0
Alport's syndrome	1	0.1	0	0	0	0	0	0	0	0	0	0	1	0
Other Hereditary	0	0	1	0.1	0	0	0	0	0	0	0	0	1	0
Others	3	0.4	16	2.2	14	2.2	3	2.7	2	1.9	3	2.8	41	1.7
Not Available	2	0.3	9	1.2	10	1.6	2	1.8	0	0	0	0	23	1.0

\*Patients may have more than 1 diagnosis classification (total=2491 but report conclusive n=2379)

## 4.5 Nephrotic syndrome

- A total of 1109 renal biopsies were performed in children with nephrotic syndrome.
- The common diagnoses were MCD (41.9%), FSGS (33.5%) and lupus nephritis (12.4%) (Table 4.5.1).
- MCD was the commonest histological finding (43.6%) for steroid-resistant nephrotic syndrome, followed by FSGS (32.5%) (Table 4.5.2).

Table 4.5.1: Renal histopathology diagnosis of children presenting with nephrotic syndrome, 2005-2022

Diagnosis	2005-2009 (n=366)		2010-2014 (n=348)		2015-2019 (n=322)		2020 (n=65)		2021 (n=63)		2022 (n=64)		Total (n=1109)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
	Minimal Change	116	31.7	152	43.7	148	46.0	30	46.2	31	49.2	37	57.8	514
FSGS	152	41.5	108	31.0	96	29.8	19	29.2	22	34.9	14	21.9	411	33.5
Lupus nephritis	58	15.8	43	12.4	34	10.6	7	10.8	6	9.5	4	6.3	152	12.4
IgA nephropathy	9	2.5	9	2.6	12	3.7	2	3.1	1	1.6	1	1.6	34	2.8
Mesangial proliferative GN non-IgA	5	1.4	10	2.9	1	0.3	2	3.1	0	0	1	1.6	19	1.5
Post-infectious GN	4	1.1	5	1.4	3	0.9	1	1.5	1	1.6	0	0	14	1.1
Others**	30	8.2	22	6.3	28	8.7	5	7.7	1	1.6	7	10.9	93	7.6

\*Patients may have more than 1 diagnosis classification (nephrotic n=1271 but report conclusive for nephrotic n=1228)

\*\* Others – Henoch-Schonlein Purpura, HUS/TTP, Systemic vasculitis, Malignancy, Membranous nephropathy, Membranoproliferative, 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), 2005-2022

Diagnosis	Steroid resistant (n=1009)		Steroid sensitive (n=43)		Not available (n=219)		Total (n=1271)	
	n	%	n	%	n	%	n	%
FSGS	328	32.5	5	11.6	78	35.6	411	32.3
Minimal Change	440	43.6	10	23.3	64	29.2	514	40.4
Lupus Nephritis	101	10	8	18.6	43	19.6	152	12.0
Membranous nephropathy	19	1.9	2	4.7	1	0.5	22	1.7
IgA nephropathy	21	2.1	3	7.0	10	4.6	34	2.7
Mesangial Proliferative GN-non-IgA	14	1.4	2	4.7	3	1.4	19	1.5
Others**	62	6.1	13	30.2	13	5.9	88	6.9

\*Patients may have more than 1 diagnosis classification

\*\* Others – Henoch-Schonlein Purpura, Membranoproliferative, Idiopathic crescentic GN, Acute interstitial nephritis, Acute tubular necrosis, Chronic interstitial nephritis, Post Infectious GN, Heredity (others), Advance GN, Others, Not available

## 4.6 Nephritic syndrome

- In children presenting with nephritic syndrome; the common diagnoses were lupus nephritis (28.6%) and post-infectious GN (26.4%).
- IgA nephropathy was diagnosed in 11.2% and Henoch-Schonlein Purpura in 4.5%.

Table 4.6: Renal histopathology diagnosis of children presenting with nephritic syndrome, 2005-2022

Diagnosis	2005-2009 (n=88)		2010-2014 (n=87)		2015-2019 (n=58)		2020 (n=11)		2021 (n=12)		2022 (n=13)		Total (n=269)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Post-infectious GN	21	23.9	30	34.5	14	24.1	3	27.3	1	8.3	2	15.4	71	26.4
Lupus nephritis	24	27.3	21	24.1	15	25.9	5	45.5	6	50	6	46.2	77	28.6
IgA nephropathy	7	8.0	9	10.3	9	15.5	1	9.1	2	16.7	2	15.4	30	11.2
Henoch-Schonlein Purpura	5	5.7	1	1.1	4	6.9	1	9.1	0	0	1	7.7	12	4.5
FSGS	8	9.1	4	4.6	5	8.6	1	9.1	1	8.3	0	0	19	7.1
MCD	7	8.0	0	0	5	8.6	0	0	2	16.7	1	7.7	15	5.6
Mesangial proliferative GN-non IgA	3	3.4	3	3.4	1	1.7	0	0	0	0	0	0	7	2.6
Acute tubular necrosis	9	10.2	2	2.3	0	0	0	0	0	0	0	0	11	4.1
Others**	15	17.0	19	21.8	8	13.8	1	9.1	0	0	4	30.8	47	17.5

\*Patients may have more than 1 diagnosis classification

\*\* Others – Systemic vasculitis, Anti GBM disease, Alport's syndrome, Thin Basement Membrane disease, Advanced GN, Membrano-proliferative, Crescentic ANCA, Idiopathic crescentic GN, Chronic interstitial nephritis, not available

^nephritic n=283 but report conclusive for nephrotic n=269

#### 4.7 Causes of severe renal failure (needed dialysis therapy)

- At the time of the biopsy, 165 children (6.7%) needed dialysis therapy.
- Common histological findings in patients presenting with severe kidney injury (requiring dialysis) were lupus nephritis (25.5%), post-infectious GN (23.6%) and advanced glomerulosclerosis (12.7%).

Table 4.7: Histology finding of children who had severe renal failure (needed dialysis therapy) who underwent renal biopsy, 2005-2022

Diagnosis	2005-2009 (n=38)		2010-2014 (n=73)		2015-2019 (n=39)		2020 (n=4)		2021 (n=6)		2022 (n=5)		Total (n=165)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Post-infectious GN	5	13.2	22	30.1	10	25.6	1	25.0	1	16.7	0	0	39	23.6
Lupus nephritis	9	23.7	16	21.9	9	23.1	2	50	4	66.7	2	40	42	25.5
FSGS	3	7.9	3	4.1	2	5.1	0	0	1	16.7	1	20	10	6.1
Advanced glomerulosclerosis (advanced GN)	9	23.7	7	9.6	4	10.3	0	0	0	0	1	20	21	12.7
HUS/TTP	0	0	2	2.7	0	0	1	25.0	0	0	0	0	3	1.8
Acute tubular necrosis	5	13.2	4	5.5	3	7.7	0	0	0	0	0	0	12	7.3
MCD	0	0	0	0	1	2.6	0	0	0	0	1	20	2	1.2
Acute interstitial nephritis	0	0	5	6.8	1	2.6	0	0	0	0	0	0	6	3.6
IgA nephropathy	1	2.6	5	6.8	0	0	0	0	0	0	0	0	6	3.6
Others	8	21.1	12	16.4	9	23.1	0	0	0	0	2	40	31	18.8

\*Patients may have more than 1 diagnosis classification

\*\* Other – Anti GBM disease, Systemic vasculitis, Membrano-proliferative, Idiopathic crescentic GN, Henoch-Schonlein Purpura, Crescentic ANCA, Chronic interstitial nephritis, Mesangial Proliferative GN-non IgA, Other infection, Heredity, Malignancy, Others, Not available

^needed dialysis therapy n=183 but report conclusive, n=165

#### 4.8 Paediatric focal segmental glomerulosclerosis and minimal change disease

- Children with FSGS had hypertension and lower eGFR compared to MCD (Table 4.8.1).
- Both FSGS and MCD exhibited similar patient survival rates (Table 4.8.2 and Figure 4.8.1).
- Children with FSGS showed much poorer renal survival compared to MCD; 77.9% versus 91.0% and 72.3% versus 87.9% at 3 and 5 years respectively (Table 4.8.3 and Figure 4.8.2).

Table 4.8.1: Clinical characteristics of children with MCD and FSGS, 2005-2022

Clinical characteristics	FSGS		MCD		p-value
	n	%	n	%	
<b>Number</b>	328	42.7	440	57.3	
<b>Age/year (mean (SD))</b>	8.6	3.98	8.0	4.29	0.83 <sup>a</sup>
<b>Age/year (median (IQR))</b>	8.5	6.80	8.1	8.1	
<b>Race</b>					
Malay	226	68.9	322	73.2	0.121 <sup>b</sup>
Chinese	37	11.3	45	10.2	
Indian	22	6.7	37	8.4	
Others	43	13.1	36	8.2	
<b>Gender</b>					
Male	215	65.5	312	70.9	0.113 <sup>b</sup>
Female	113	34.5	128	29.1	
<b>Gross haematuria</b>					
Present	7	2.1	5	1.1	0.270 <sup>e</sup>
Absent	321	97.9	435	98.9	
<b>Hypertension</b>					
Present	136	41.5	112	25.5	<0.01 <sup>b</sup>
Absent	192	58.5	328	74.5	
<b>Family history</b>					
Yes	11	3.4	10	2.3	0.364 <sup>b</sup>
No	317	96.6	430	97.7	
<b>eGFR ml/min/1.73m<sup>2</sup></b>					
<15	4	1.2	0	0	<0.01 <sup>b</sup>
15-30	10	3.0	2	0.5	
30-60	30	9.1	6	1.4	
60-90	34	10.4	38	8.6	
≥90	195	59.5	286	65.0	
Not available	55	16.8	108	24.5	
<b>Dialysis required</b>					
Yes	8	2.4	2	0.5	0.22 <sup>c</sup>
No	320	97.6	438	99.5	

a two sample t test

b Chi-square test

c Fisher's exact test

Table 4.8.2 Patient survival by focal segmental glomerulosclerosis and minimal change disease, 2005-2022 (overall)

Time (Months)	Focal segmental glomerulosclerosis		Minimal change disease	
	Survival (%)	SE	Survival (%)	SE
12	95.8	0.0094	98.0	0.0061
36	94.8	0.0106	97.1	0.0075
60	94.2	0.0114	95.2	0.0102
84	93.2	0.0127	94.5	0.0111
108	93.2	0.0127	94.5	0.0111
120	92.7	0.0134	93.6	0.0128

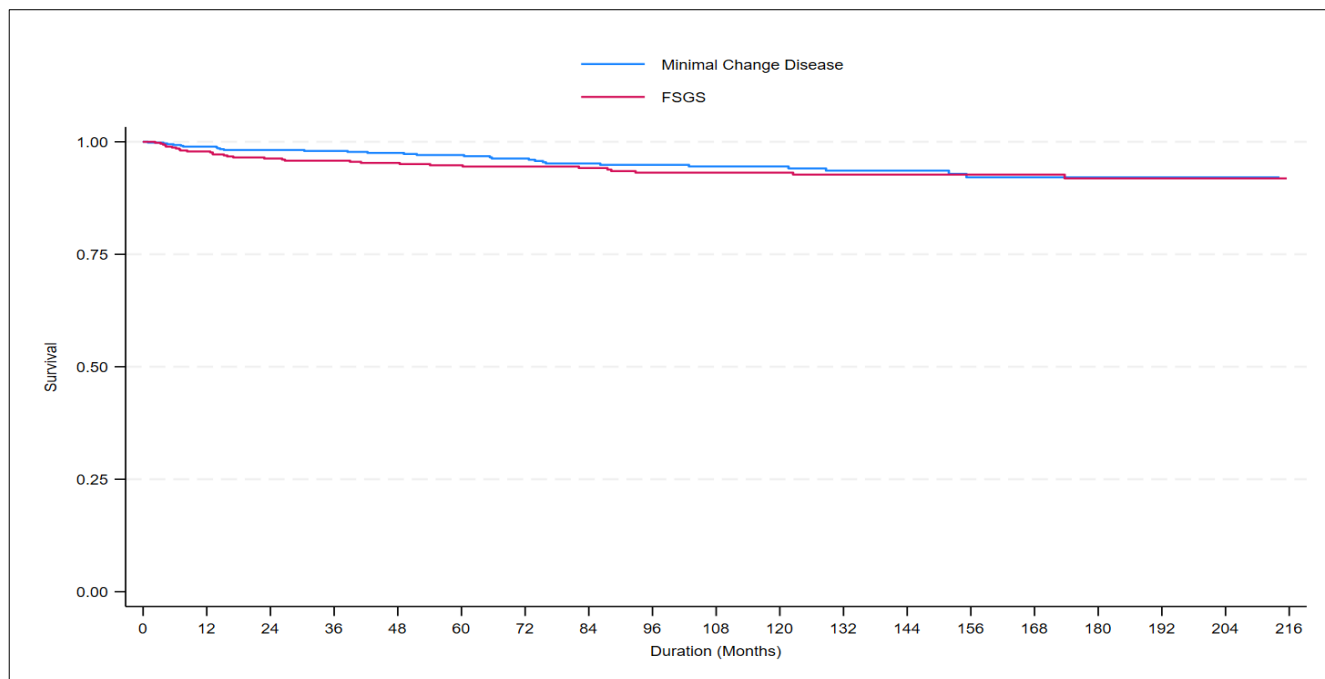


Figure 4.8.1: Patient survival by focal segmental glomerulosclerosis and minimal change disease, 2005-2022 (overall)

Table 4.8.3: Renal survival by focal segmental glomerulosclerosis and minimal change disease, 2005- 2022 (overall)

Time (Months)	Focal segmental glomerulosclerosis		Minimal change disease	
	Survival (%)	SE	Survival (%)	SE
12	85.9	0.0169	93.9	0.0109
36	77.9	0.0209	91.0	0.0133
60	72.3	0.0233	87.9	0.0158
84	70.1	0.0243	84.7	0.0184
108	69.2	0.0248	83.9	0.0193
120	68.7	0.0251	81.8	0.0214

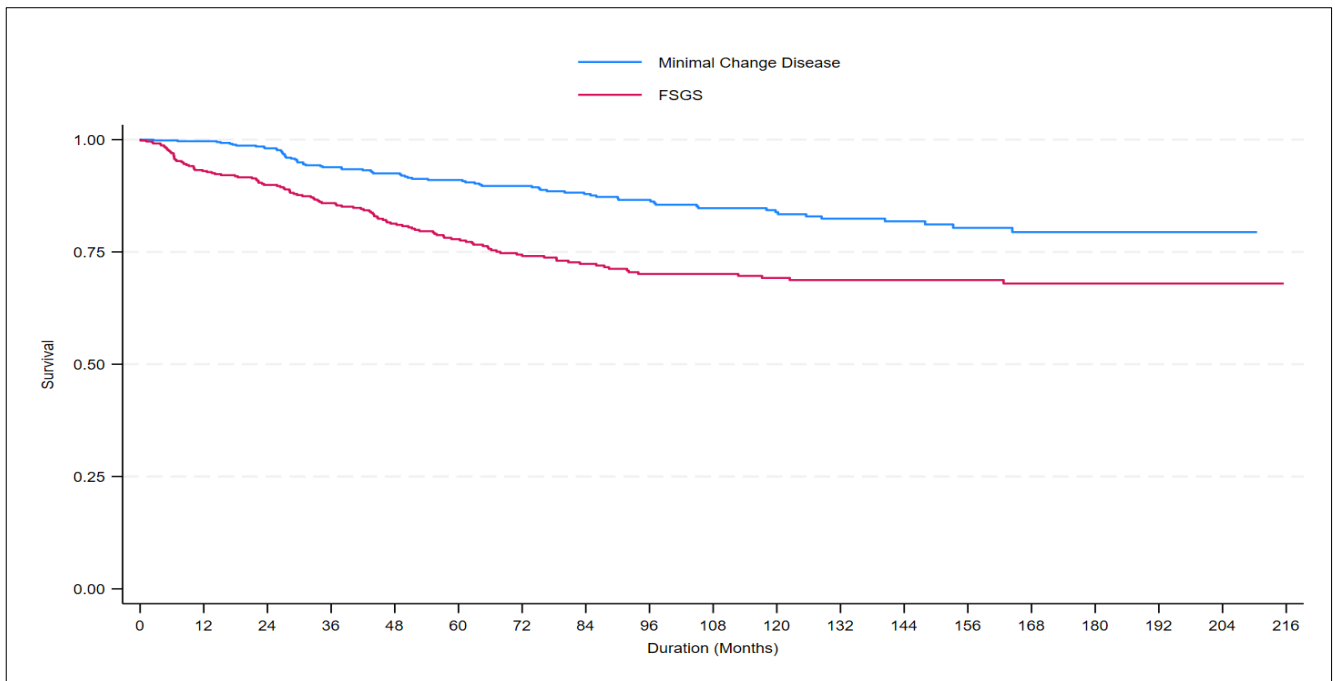


Figure 4.8.2: Renal survival by focal segmental glomerulosclerosis and minimal change disease, 2005- 2022 (overall)

### 4.9 Paediatric Lupus Nephritis

- There were a total of 558 renal biopsies performed for children with lupus nephritis (Figure 4.9.1).
- Most children (86.4%) with lupus received only one renal biopsy. Seventy-six (13.6%) had repeat biopsies (Table 4.9.2).
- The female: male ratio was 5.3:1 (Table 4.9.3).
- The racial distribution was Malay (67.1%), Chinese (20.1%), and Indian (2.8%). This observation may suggest a disproportionately lower prevalence of lupus nephritis among the Indian population (Table 4.9.3).
- The mean age at the time of the biopsy was 11.9 years (Table 4.9.4).
- About 39 (6.9%) of patients had severe kidney failure and needed dialysis support. The histologic class was proliferative GN (74.3%) and advanced sclerosing lupus nephritis (5.1%) (Table 4.9.5 and Table 4.9.9).
- The most frequent clinical presentation at biopsy was urinary abnormalities (34.2%) followed by nephrotic syndrome (Table 4.9.7)
- The common extra kidney manifestations were cutaneous features (malar rash 42.9%, photosensitivity (20.6%), discoid rash (8.9%), haematological involvement (59.1%), arthritis (26.5%), and oral ulcer (25.6%) (Table 4.9.8).
- ANF was positive in 85.1% of patients.
- For patients who did not require dialysis therapy, the histological class was proliferative GN (Class III/III+V and IV//IV+V) in 83.8% of biopsies (Table 4.9.9).
- The patient survival was 90.1% at 3 years and 87.1% at 5 years from the time of diagnosis of lupus nephritis (Table 4.9.10 and Figure 4.9.2).
- The renal survival for lupus nephritis was 90.6% at 3 years and 87.5% at 5 years (Table 4.9.11 and Figure 4.9.3).

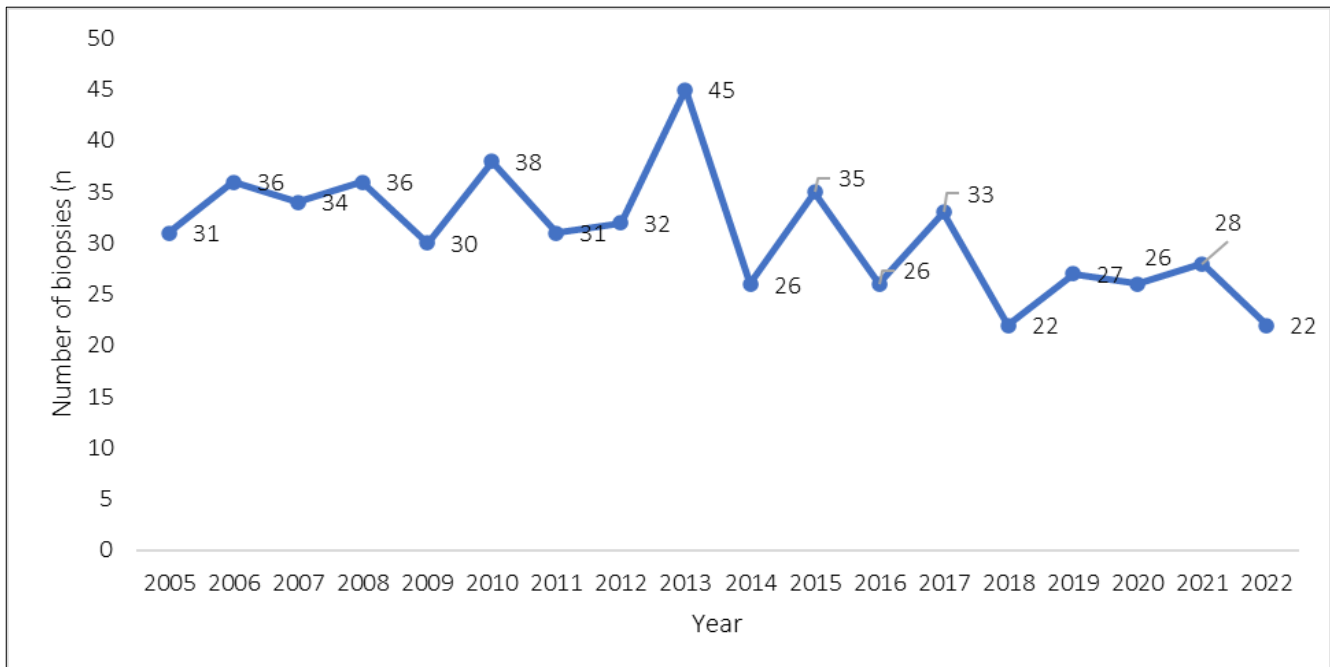


Figure 4.9.1: Total number of biopsies (SLE), 2005-2022

Table 4.9.2: Distribution of renal biopsy in patients with lupus by number of episodes, 2005-2022

Year	2005-2009 (n=167)		2010-2014 (n=172)		2015-2019 (n=143)		2020 (n=26)		2021 (n=28)		2022 (n=22)		Total (n=558)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
1st episode	145	86.8	143	83.1	124	86.7	25	96.2	27	96.4	18	81.8	482	86.4
2nd episode	19	11.4	24	14.0	18	12.6	1	3.8	1	3.6	4	18.2	67	12.0
3rd episode	3	1.8	5	2.9	0	0	0	0	0	0	0	0	8	1.4
4th episode	0	0	0	0	1	0.7	0	0	0	0	0	0	1	0.2

Table 4.9.3: Gender and racial distribution of paediatric lupus nephritis, 2005-2022

	2005-2009 (n=167)		2010-2014 (n=174)		2015-2019 (n=145)		2020 (n=26)		2021 (n=28)		2022 (n=22)		Total (n=562)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
<b>Gender</b>														
Male	24	14.4	25	14.4	30	20.7	5	19.2	3	10.7	2	9.1	89	15.8
Female	143	85.6	149	85.6	115	79.3	21	80.8	25	89.3	20	90.9	473	84.2
<b>Race</b>														
Malay	102	61.1	117	67.2	105	72.4	19	73.1	19	67.9	15	68.2	377	67.1
Chinese	43	25.7	34	19.5	27	18.6	3	11.5	4	14.3	2	9.1	113	20.1
Indian	7	4.2	3	1.7	2	1.4	2	7.7	1	3.6	1	4.5	16	2.8
Others*	15	9.0	20	11.5	11	7.6	2	7.7	4	14.3	4	18.2	56	10

Table 4.9.4: Age distribution of paediatric lupus nephritis, 2005-2022

Year	2005 (n=31)	2006 (n=36)	2007 (n=34)	2008 (n=36)	2009 (n=30)	2010 (n=39)	2011 (n=31)	2012 (=33)	2013 (n=45)	2014 (n=26)
Mean	12.46	12.08	12.24	11.16	11.34	11.76	12.08	11.53	11.34	11.40
SD	2.20	2.44	2.03	3.27	3.77	2.51	3.67	3.88	3.35	2.74
Median	13.16	12.93	12.65	11.70	11.89	12.19	13.22	12.80	12.36	12.62
Minimum	4.89	6.63	7.30	0.25	0.53	1.46	0.23	0.27	0.10	4.08
Maximum	14.80	14.76	14.89	14.94	14.95	14.82	14.98	14.97	14.97	14.78

Year	2015 (n=35)	2016 (n=26)	2017 (n=34)	2018 (n=23)	2019 (=27)	2020 (n=26)	2021 (n=28)	2022 (n=22)	Total (n=562)
Mean	12.31	12.34	12.00	12.00	11.78	13.28	12.35	12.17	11.94
SD	2.15	2.71	2.18	2.43	3.19	2.14	1.85	2.34	2.81
Median	12.54	13.46	12.32	12.84	12.61	13.99	12.73	12.49	12.81
Minimum	6.15	3.14	6.22	7.15	2.23	6.48	7.04	5.83	0.10
Maximum	14.95	14.90	14.89	14.95	14.98	14.92	14.80	14.98	14.98

Table 4.9.5: Dialysis therapy for paediatric lupus nephritis at the time of biopsy, 2005-2022

Needed dialysis therapy	2005-2009 (n=167)		2010-2014 (n=174)		2015-2019 (n=145)		2020 (n=26)		2021 (n=28)		2022 (n=22)		Total (n=562)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Yes	8	4.8	14	8.0	9	6.2	2	7.7	4	14.3	2	9.1	39	6.9
No	132	79.0	158	90.8	136	93.8	24	92.3	24	85.7	20	90.9	494	87.9
Not available	27	16.2	2	1.1	0	0	0	0	0	0	0	0	29	5.2

Table 4.9.6: Presence of hypertension of paediatric lupus nephritis, 2005-2022

Hypertension	2005-2009 (n=167)		2010-2014 (n=174)		2015-2019 (n=145)		2020 (n=26)		2021 (n=28)		2022 (n=22)		Total (n=562)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Present	64	38.3	79	45.4	69	47.6	8	30.8	13	46.4	9	40.9	242	43.1
Absent	103	61.7	95	54.6	76	52.4	18	69.2	15	53.6	13	59.1	320	56.9

Table 4.9.7: Clinical presentation at biopsy of paediatric lupus nephritis, 2005-2022

Clinical Presentation	2005-2009 (n=167)		2010-2014 (n=174)		2015-2019 (n=145)		2020 (n=26)		2021 (n=28)		2022 (n=22)		Total (n=562)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine abnormalities	47	28.1	67	38.5	56	38.6	8	30.8	8	28.6	6	27.3	192	34.2
Nephrotic syndrome	57	34.1	41	23.6	33	22.8	7	26.9	6	21.4	4	18.2	148	26.3
Nephritic - Nephrotic	22	13.2	37	21.3	30	20.7	4	15.4	8	28.6	4	18.2	105	18.7
Nephritic syndrome	23	13.8	19	10.9	15	10.3	5	19.2	6	21.4	6	27.3	74	13.2
Not Available	18	10.8	10	5.7	11	7.6	2	7.7	0	0	2	9.1	43	7.7

Table 4.9.8: Extra-kidney manifestation at presentation, 2005-2022

ARA criteria	2005-2009 (n=167)		2010-2014 (n=174)		2015-2019 (n=145)		2020 (n=25)		2021 (n=25)		2022 (n=25)		Total (n=511)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Malar rash	80	47.9	71	40.8	63	43.4	8	30.8	12	42.9	7	31.8	241	42.9
Photo-sensitivity	41	24.6	40	23.0	27	18.6	5	19.2	1	3.6	2	9.1	116	20.6
Arthritis	50	29.9	56	32.2	32	22.1	0	0	5	17.9	6	27.3	149	26.5
Cerebral	15	9.0	23	13.2	14	9.7	1	3.8	3	10.7	3	13.6	59	10.5
Renal	139	83.2	149	85.6	113	77.9	21	80.8	25	89.3	20	90.9	467	83.1
Hematological	99	59.3	105	60.3	78	53.8	16	61.5	21	75.0	13	59.1	332	59.1
Discoid rash	9	5.4	19	10.9	17	11.7	1	3.8	3	10.7	1	4.5	50	8.9
Serositis	22	13.2	24	13.8	24	16.6	4	15.4	9	32.1	8	36.4	91	16.2
Oral ulcers	45	26.9	50	28.7	30	20.7	6	23.1	6	21.4	7	31.8	144	25.6
ANF* Positive	157	94.0	140	80.5	111	76.6	19	73.1	24	85.7	27	122.7	478	85.1
At least one positive in other labs*	112	67.1	115	66.1	116	80	21	80.8	20	71.4	19	86.4	403	71.7

\*Anti-Nuclear Factor

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

Table 4.9.9: Classification of paediatric lupus nephritis, 2005-2022

Needed dialysis														
WHO/ISN /RPS Class	2005-2009 (n=8)		2010-2014 (n=14)		2015-2019 (n=9)		2020 (n=2)		2021 (n=4)		2022 (n=2)		Total (n=39)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Class II	1	12.5	1	7.1	0	0	0	0	0	0	0	0	2	5.1
Class III or III + V	0	0	3	21.4	2	22.2	0	0	0	0	0	0	5	12.8
Class IV or IV + V	4	50	9	64.3	6	66.7	1	50	4	100	0	0	24	61.5
Class V or II + V	1	12.5	0	0	1	11.1	0	0	0	0	2	100	4	10.3
Class VI	2	25	0	0	0	0	0	0	0	0	0	0	2	5.1
Not Available	0	0	1	7.1	0	0	1	50	0	0	0	0	2	5.1
Not needed dialysis														
WHO/ISN /RPS Class	2005-2009 (n=159)		2010-2014 (n=160)		2015-2019 (n=136)		2020 (n=24)		2021 (n=24)		2022 (n=20)		Total (n=523)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Class I	0	0	4	2.5	2	1.5	0	0	0	0	0	0	6	1.1
Class II	12	7.5	15	9.4	10	7.4	1	4.2	1	4.2	1	5.0	40	7.6
Class III or III + V	27	17.0	44	27.5	50	36.8	9	37.5	6	25.0	6	30	142	27.2
Class IV or IV + V	111	69.8	83	51.9	63	46.3	13	54.2	14	58.3	12	60	296	56.6
Class V or II + V	9	5.7	11	6.9	6	4.4	0	0	2	8.3	1	5.0	29	5.5
Not Available	0	0	3	1.9	5	3.7	1	4.2	1	4.2	0	0	10	1.9

Table 4.9.10: Patient survival in lupus nephritis, 2005-2022

Time (Months)	Lupus nephritis	
	Survival (%)	Survival (%)
12	91.4	0.0123
36	90.1	0.0133
60	87.1	0.0154
84	85.8	0.0164
108	85.2	0.0170
120	84.2	0.0180

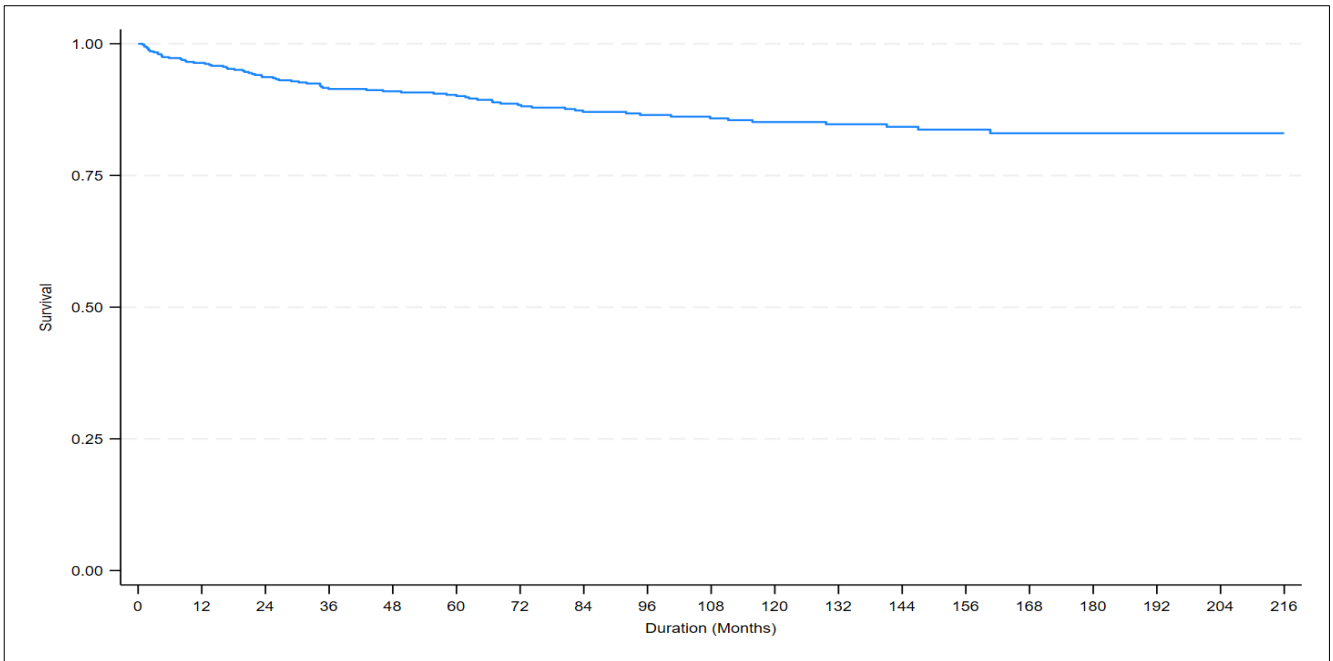


Figure 4.9.2: Patient survival in lupus nephritis, 2005-2022

Table 4.9.11: Death-censored renal survival in lupus nephritis, 2005-2022

Time (Months)	Lupus nephritis	
	Survival (%)	Survival (%)
12	93.3	0.0113
36	90.6	0.0135
60	87.5	0.0161
84	85.4	0.0177
108	85.4	0.0177
120	83.8	0.0197

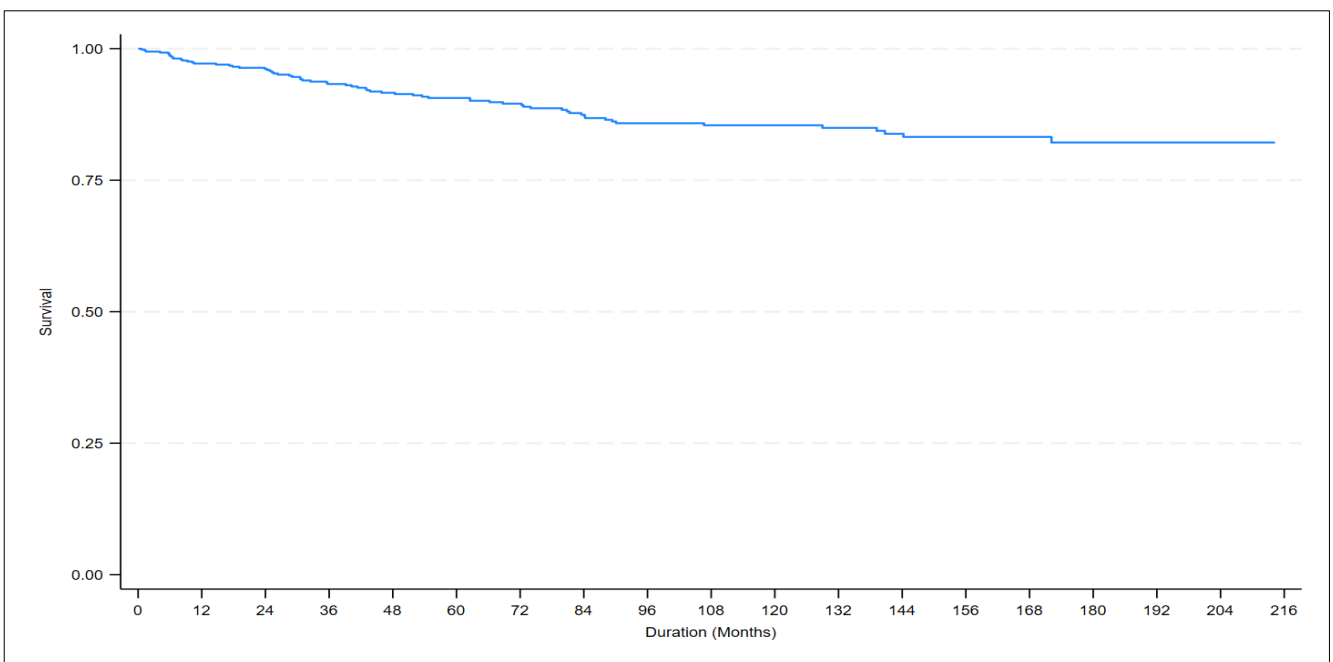


Figure 4.9.3: Death-censored renal survival in lupus nephritis, 2005-2022

#### 4.10 Overall Kidney outcome

- Of the 2463 children biopsied, 420 (17%) of these children were reported to the Malaysian Dialysis and Transplant Registry with End Stage Kidney Disease (ESKD) (Table 4.10.1).
- FSGS was the most cause of ESKD accounting for 28.6%.
- Other causes of ESKD in children were lupus nephritis (16.6%), MCD (16.9%), Advanced GN (10.5%), IgA nephropathy 6.4% and Henoch-Schonlein Purpura 1.2%.

Table 4.10.1: Causes of end-stage kidney disease in children who underwent renal biopsy, 2005-2022

Causes	n=420	%
FSGS	120	28.6
Lupus Nephritis	74	17.6
Minimal Change	71	16.9
Advance GN	44	10.5
IgA nephropathy	27	6.4
Post Infectious GN	11	2.6
Mesangial Proliferative GN-non IgA	8	1.9
Chronic interstitial nephritis	8	1.9
Membranous nephropathy	6	1.4
Idiopathic Crescentic GN	6	1.4
Henoch-Schonlein Purpura	5	1.2
HUS / TTP	4	1.0
Systemic vasculitis	4	1.0
Membrano-proliferative	3	0.7
Acute interstitial nephritis	3	0.7
Acute tubular necrosis	3	0.7
Crescentic ANCA	2	0.5
Benign / Malignant Hypertension	2	0.5
Others	1	0.2
Alport's syndrome	1	0.2
Others	10	2.4
Not available	4	1.0
Not Conclusive	31	7.4

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

#### 4.11 Biopsy failure and complication

- The complication rate for the biopsy procedure was reported to be 3.2% (Table 4.11.1).
- The overall risk of bleeding was 2.7% mainly gross hematuria. The risk of perinephric collection was 0.5%.
- The risk of complications post renal biopsy was higher in those less than 2 years of age, with low GFR <60ml/min/1.73m<sup>2</sup> and needing dialysis therapy at the time of biopsy.
- The use of a small diameter biopsy decreased the risk for complication (odds ratio 0.10, p=0.03) (Table 4.11.2).

Table 4.11.1: Frequency of complication, 2005-2022

Causes	n	%
<b>Total number of biopsies</b>	2491	
<b>Total number of complications</b>	80	3.2
Bleeding	68	2.73
Perirenal collection	13	0.52
Arteriovenous malformation	1	0.04
Hypotension	3	0.12

Table 4.11.2: Risk factors for complication, 2005-2022

Factors	n	Number of complications	Odds ratio	95% CI	p-value
<b>Age (years)</b>					
<2	70	5	2.69	1.03,7.03	0.044
>2-≤5	330	13	1.43	0.76,2.71	0.269
>5-≤10	654	22	1.22	0.72,2.06	0.469
>10 (ref*)	1,437	40	1.00	-	-
<b>Calculated GFR ml/min/1.73m<sup>2</sup></b>					
<15	92	9	3.94	1.82,8.52	0.001
15-<30	120	9	2.94	1.37,8.52	0.006
30-<60	220	13	2.28	1.18,4.42	0.015
60- <90	290	14	1.84	0.97,3.50	0.062
> 90 (ref*)	1,194	32	1.00	-	-
Unknown	575	3	-	-	-
<b>Renal failure</b>					
Needed dialysis	183	16	3.37	1.90,5.98	<0.001
Not needed dialysis(ref*)	2208	61	1.00	-	-
Unknown	100	3	-	-	-
<b>Needle size</b>					
14G	190	13	1.14	0.62,2.11	0.615
16G (ref*)	1058	64	1.00	-	-
18G	454	3	0.10	0.3,0.33	0.0322
Unknown	789	0	-	-	-

(ref\*) Reference category

CI-confidence interval

Unknown = No information