

## **CHAPTER 2**

### **Primary Glomerulonephritis**

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## 2.1 Introduction

- This chapter illustrates the main primary glomerulonephritis (GN) in adult (defined as age > 15 years old) from the years 2005-2017.
- The results are displayed over five-year time periods for 2005-2009 and 2010-2014. Data from 2015, 2016 and 2017 are reported independently.
- There has been changing trends that reflect changes in screening and renal biopsy practices.
- In previous reports, minimal change disease was the commonest GN in adults, focal segmental glomerulosclerosis seems to be catching up, closely followed by IgA nephropathy.
- Membranous nephropathy contributed to only 9.7% of all biopsy proven primary GN.
- The other types of primary glomerulonephritis were relatively uncommon. (*Table 2.1*).

Table 2.1: Primary Glomerulonephritis, 2005-2017

Histopathological Diagnosis	2005-2009 (n=1627)		2010-2014 (n=2639)		2015 (n=560)		2016 (n=505)		2017 (n=587)		Total (n=5918)	
	n	%	n	%	n	%	n	%	n	%	n	%
FSGS	489	30.1	782	29.6	174	31.1	139	27.5	182	31.0	1766	29.8
MCD	539	33.1	786	29.8	145	25.9	135	26.7	125	21.3	1730	29.2
IgAN	319	19.6	628	23.8	135	24.1	129	25.5	166	28.3	1377	23.3
MN	156	9.6	243	9.2	51	9.1	60	11.9	64	10.9	574	9.7
MPGN	54	3.3	79	3.0	19	3.4	15	3.0	12	2.0	179	3.0
Mes Prol GN	34	2.1	38	1.4	15	2.7	8	1.6	13	2.2	108	1.8
Idiopathic Crescentic	24	1.5	31	1.2	3	0.5	6	1.2	4	0.7	68	1.1
Crescentic ANCA	8	0.5	20	0.8	2	0.4	1	0.2	6	1.0	37	0.6
Not available/Missing	4	0.2	32	1.2	16	2.9	12	2.4	15	2.6	79	1.3
<b>Total</b>	<b>1627</b>	<b>100</b>	<b>2639</b>	<b>100</b>	<b>560</b>	<b>100</b>	<b>505</b>	<b>100</b>	<b>587</b>	<b>100</b>	<b>5918</b>	<b>100</b>

Abbreviation

*FSGS: Focal Segmental Glomerulosclerosis*

*MCD: Minimal Change Disease*

*IgAN: IgA Nephropathy*

*MN: Membranous Nephropathy*

*MPGN: Membranoproliferative GN*

*Mesangial Proliferative GN (non-IgA)*

## 2.2 Focal Segmental Glomerulosclerosis (FSGS)

### 2.2.1 Introduction

- Focal segmental glomerulosclerosis is a histological diagnosis and is defined by the presence of segmental glomerular capillary tufts obliteration with increased mesangial matrix deposition, intra-capillary hyaline deposits and focal adhesions of the capillary tuft to Bowman's capsule.
- Differentiating idiopathic FSGS changes from secondary FSGS clinically can be challenging and electron microscopy is not readily available to guide us.

### 2.2.2 Patient Population and Characteristics

- A total of 1766 FSGS cases were reported to the registry.
- FSGS was more common in males. (*Figure 2.2.2 (a)*)
- FSGS was mainly diagnosed in young patients, with a mean age of  $35.4 \pm 14.9$  years at the time of biopsy.

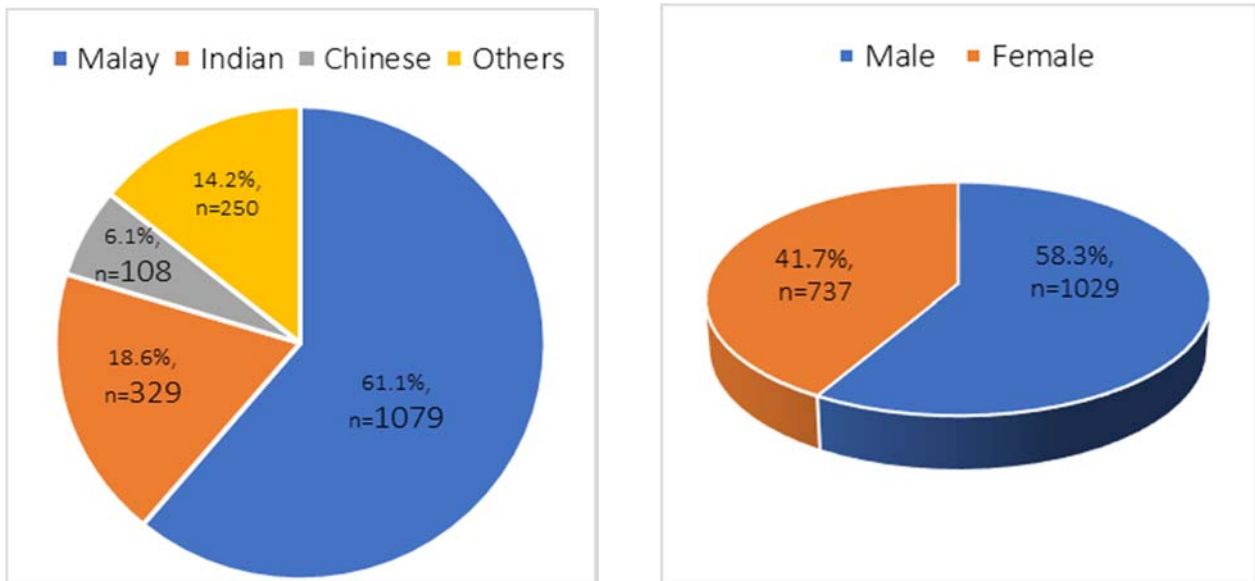


Figure 2.2.2(a): Demographic characteristics for FSGS, 2005-2017

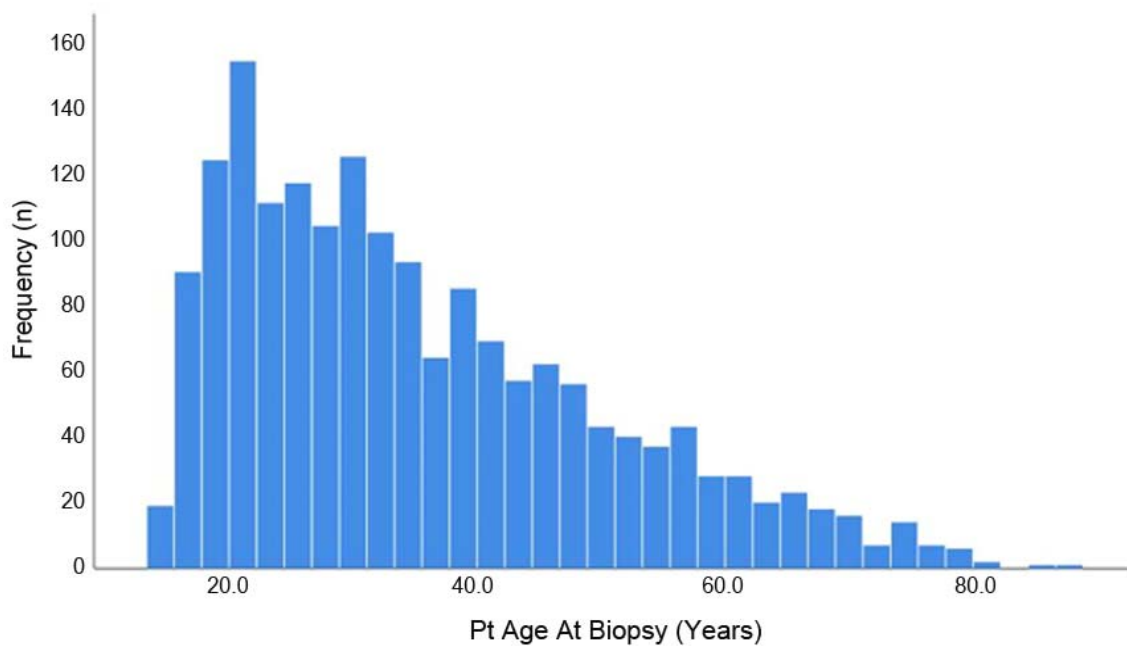


Figure 2.2.2(b): Age at time of biopsy (years) FSGS, 2005-2017

### 2.2.3 Clinical presentation

- Nephrotic syndrome is the most common clinical presentation (51%) followed by asymptomatic urine abnormalities (25%). (Table & Figure 2.2.3)
- Nephrotic syndrome still remains the commonest presentation of FSGS regardless of the gender (Table & Figure 2.2.3)
- In patients presenting with asymptomatic urine abnormalities, there seems to be a female preponderance compared to males. (Figure 2.2.3)

Table 2.2.3: Clinical presentation for FSGS, 2005-2017

Clinical Presentation	2005-2009 (n=489)		2010-2014 (n=782)		2015 (n=174)		2016 (n=139)		2017 (n=182)		Total (n=1766)	
	n	%	n	%	n	%	n	%	n	%	n	%
Nephrotic syndrome	298	60.9	379	48.5	81	46.6	54	38.8	87	47.8	899	50.9
Asymptomatic urine abnormalities	112	22.9	202	25.8	37	21.3	38	27.3	50	27.5	439	24.9
Nephritic-Nephrotic	22	4.5	61	7.8	8	4.6	16	11.5	18	9.9	125	7.1
Nephritic	24	4.9	30	3.8	15	8.6	6	4.3	8	4.4	83	4.7
Not available	33	6.7	110	14.1	33	19.0	25	18.0	19	10.4	220	12.5
<b>Total</b>	<b>489</b>	<b>100</b>	<b>782</b>	<b>100</b>	<b>174</b>	<b>100</b>	<b>139</b>	<b>100</b>	<b>182</b>	<b>100</b>	<b>1766</b>	<b>100</b>

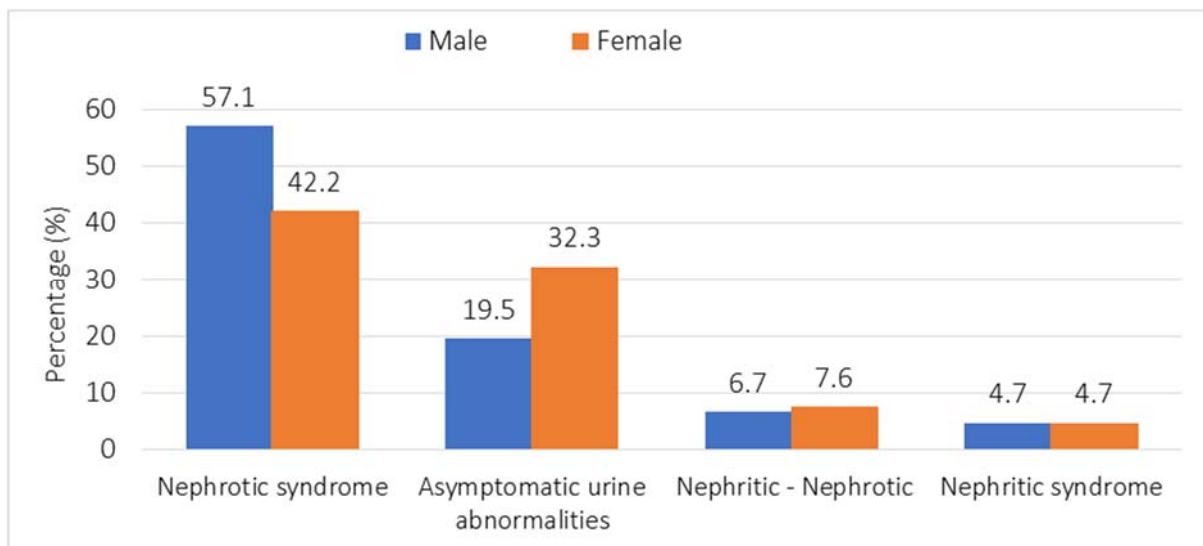


Figure 2.2.3(a): Clinical presentation by gender for FSGS, 2005-2017

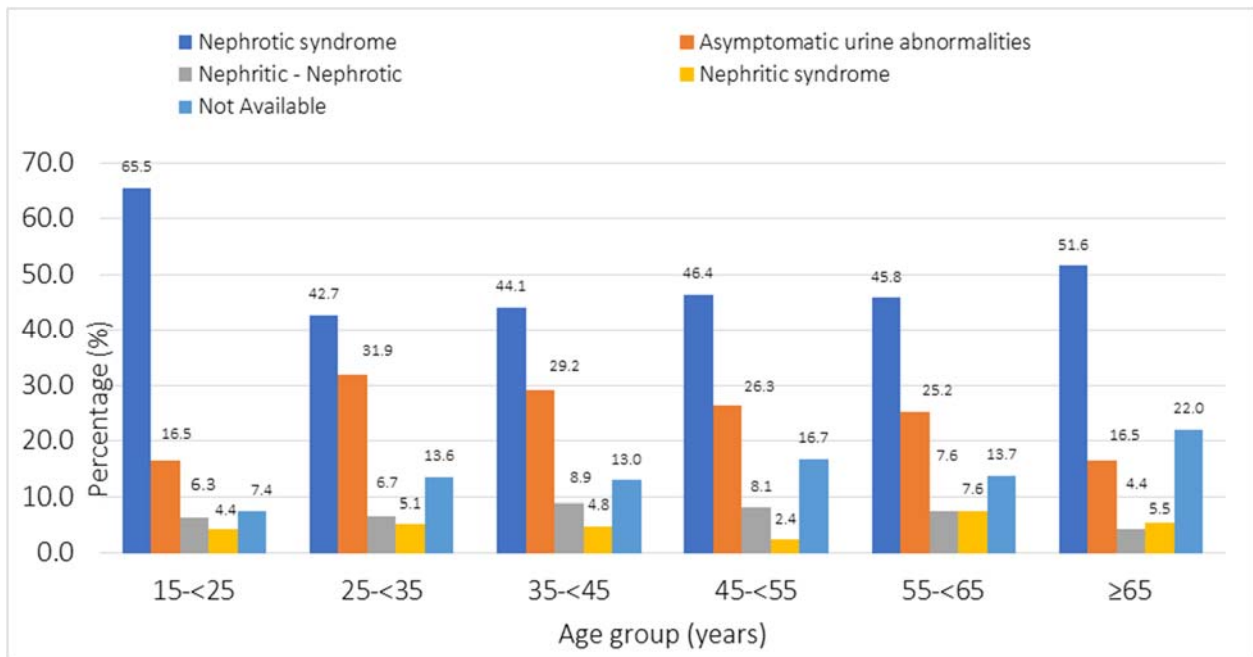


Figure 2.2.3(b): Clinical presentation by age group for FSGS, 2005-2017

## 2.2.4 Hypertension

- Seven hundred and four patients (39.9%) with FSGS had hypertension.
- Prevalence of hypertension in FSGS was higher in male.
- Older patients were more likely to have hypertension compared to younger patients. (*Figure 2.2.4 (b)*) which could be related to natural history of onset of hypertension and compounded by the decline in renal function in the older patients.

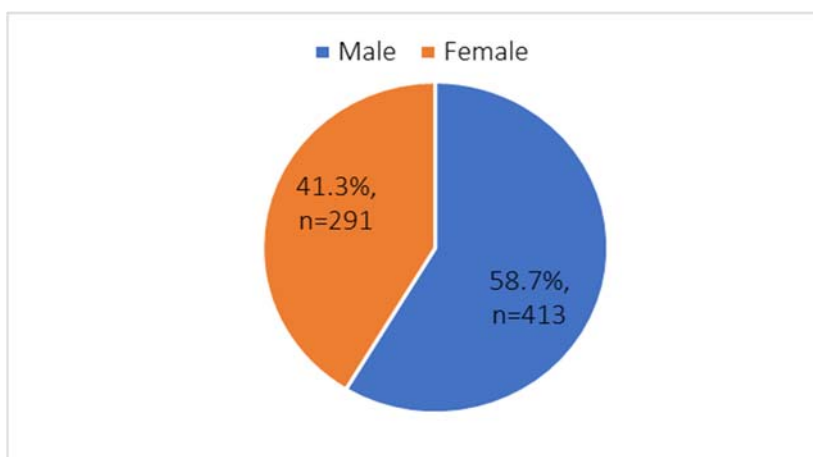


Figure 2.2.4 (a): Hypertension by gender for FSGS, 2005-2017

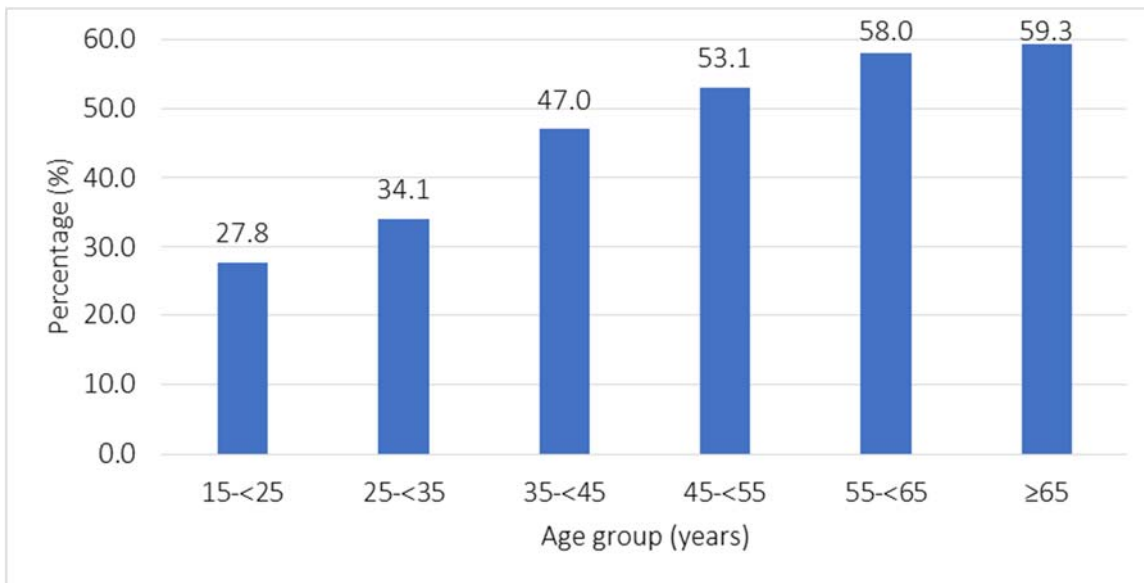


Figure 2.2.4(b): Hypertension by age group for FSGS, 2005-2017

### 2.2.5 Renal function

- Most patients had CKD stage II and below.
- There were no differences in renal function by gender. (Figure 2.2.5(a))
- Older patients had lower eGFR with majority being CKD stage III and above and this is in keeping with the prevalence of CKD in the general population. (Figure 2.2.5(b))

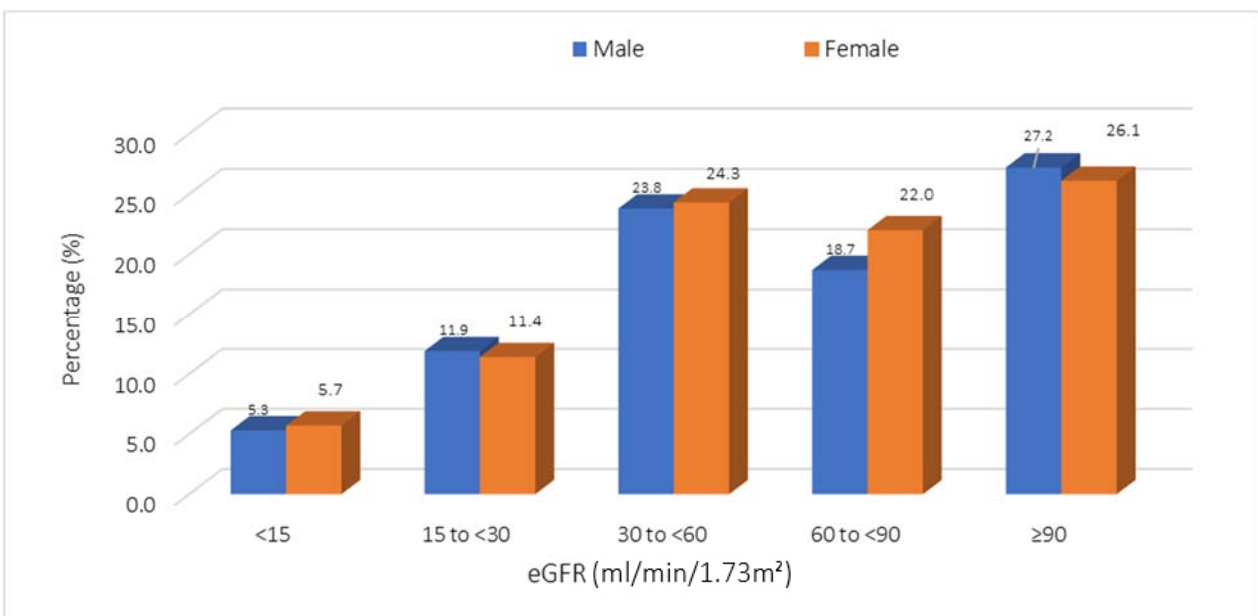


Figure 2.2.5(a): Renal function by gender for FSGS, 2005-2017

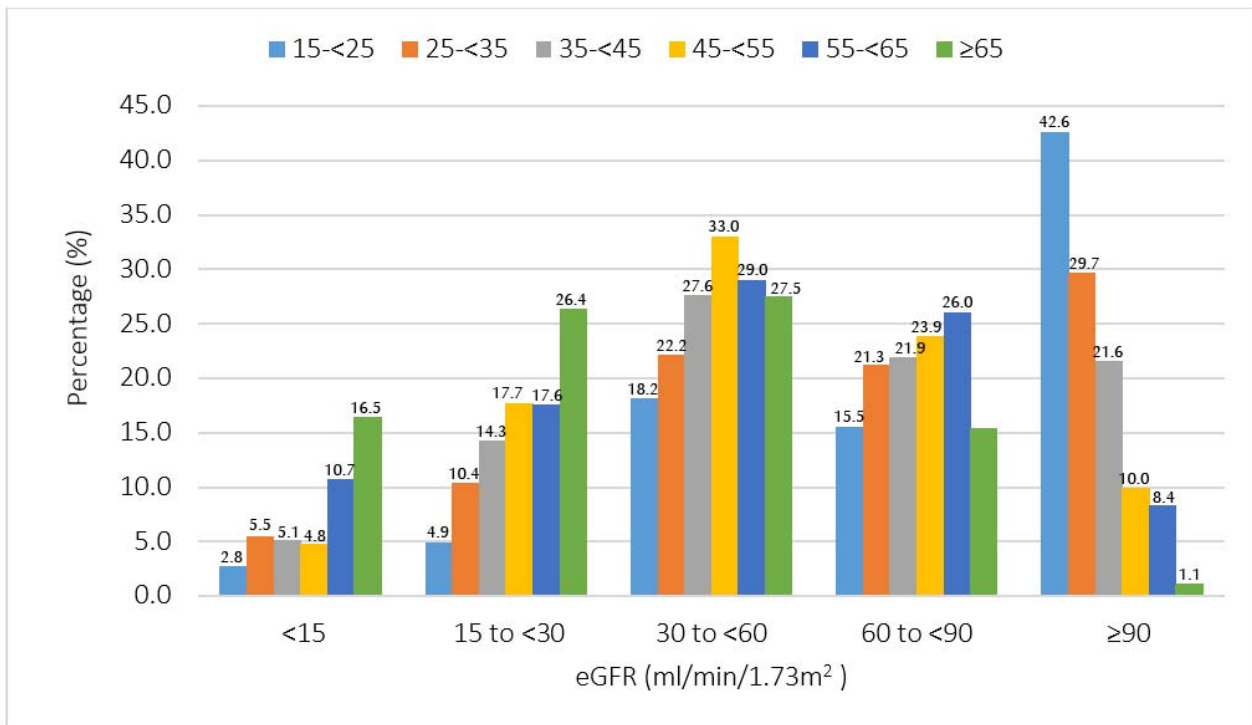


Figure 2.2.5(b): Renal function at presentation by age group for FSGS, 2005-2017

## 2.2.6 Outcome

- Renal survival at 5-year and 10-year was 88% and 80% respectively. (Figure 2.2.6(a))
- Patient survival at 5-year and 10-year was 88% and 80% respectively. (Figure 2.2.6(b))

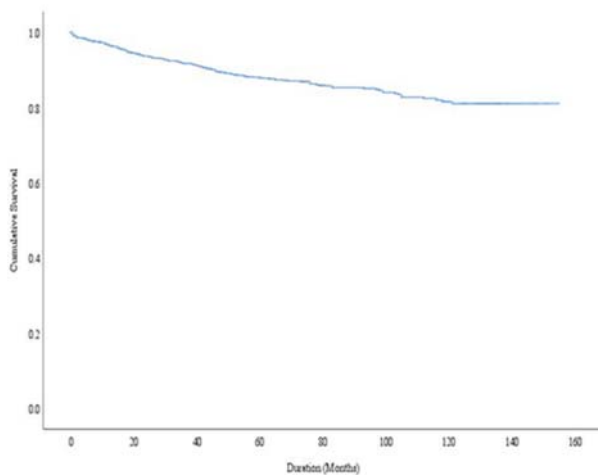


Figure 2.2.6(a): Renal Survival estimates for FSGS 2005-2017

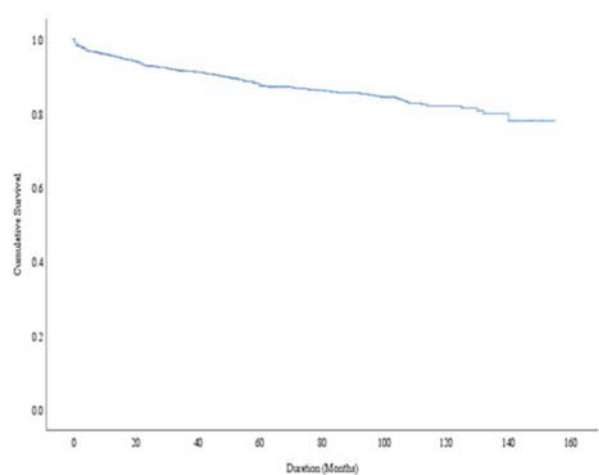


Figure 2.2.6(b): Patient Survival estimates for death in FSGS, 2005-2017

## 2.3 Minimal Change Disease

### 2.3.1 Introduction

- Minimal change disease (MCD) is a major cause of nephrotic syndrome in both children and adults.
- MCD is typically characterized by normal appearing glomeruli by light microscopy and absence of complement or immunoglobulin deposits on immunofluorescence microscopy. Glomerular size is usually normal by standard methods of light microscopy, although enlarged glomeruli may be observed. On electron microscopy, there is diffuse effacement ("fusion") of the epithelial foot processes.
- However, electron microscopy service is not readily available and not routinely done even in the available centers.

### 2.3.2 Patient Population and Characteristics

- A total of 1730 cases of MCD were reported to the registry.
- MCD was mainly diagnosed in young patients, with a mean age of  $31.5 \pm 14.1$  years at the time of biopsy.
- MCD was more common in males (63%).
- The racial distribution is shown in Figure 2.3.2(a).
- Traditionally MCD is known to have a bimodal distribution. This trend is not seen in our cohort with the higher proportion of younger patients presenting with MCD.

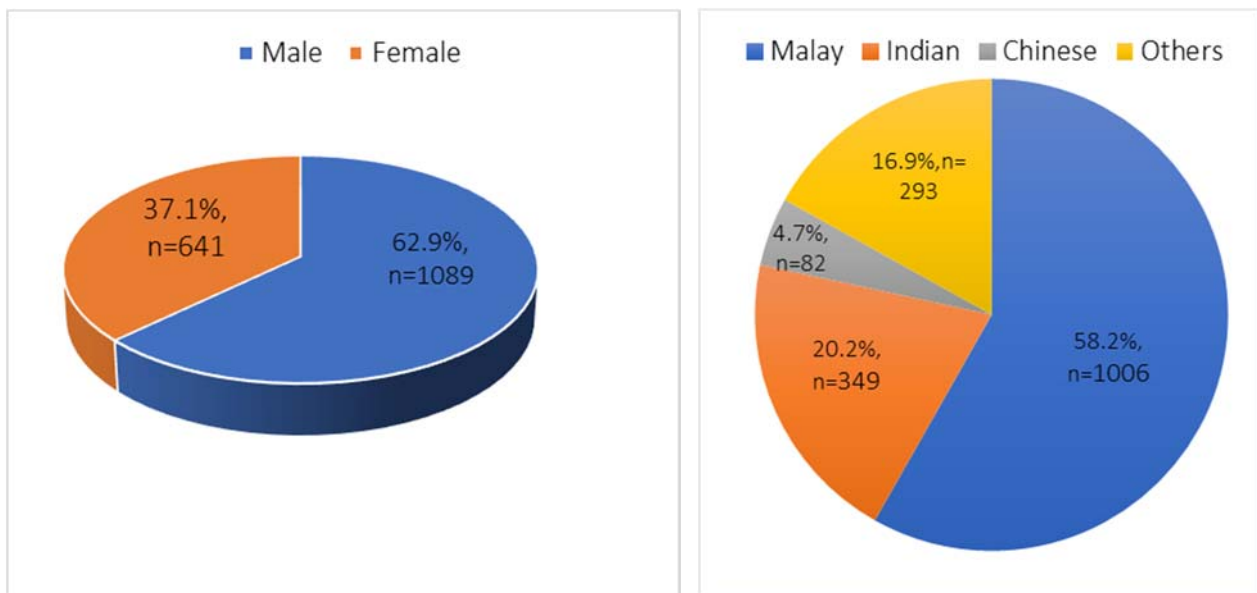


Figure 2.3.2(a): Demographic characteristics for MCD, 2005-2017



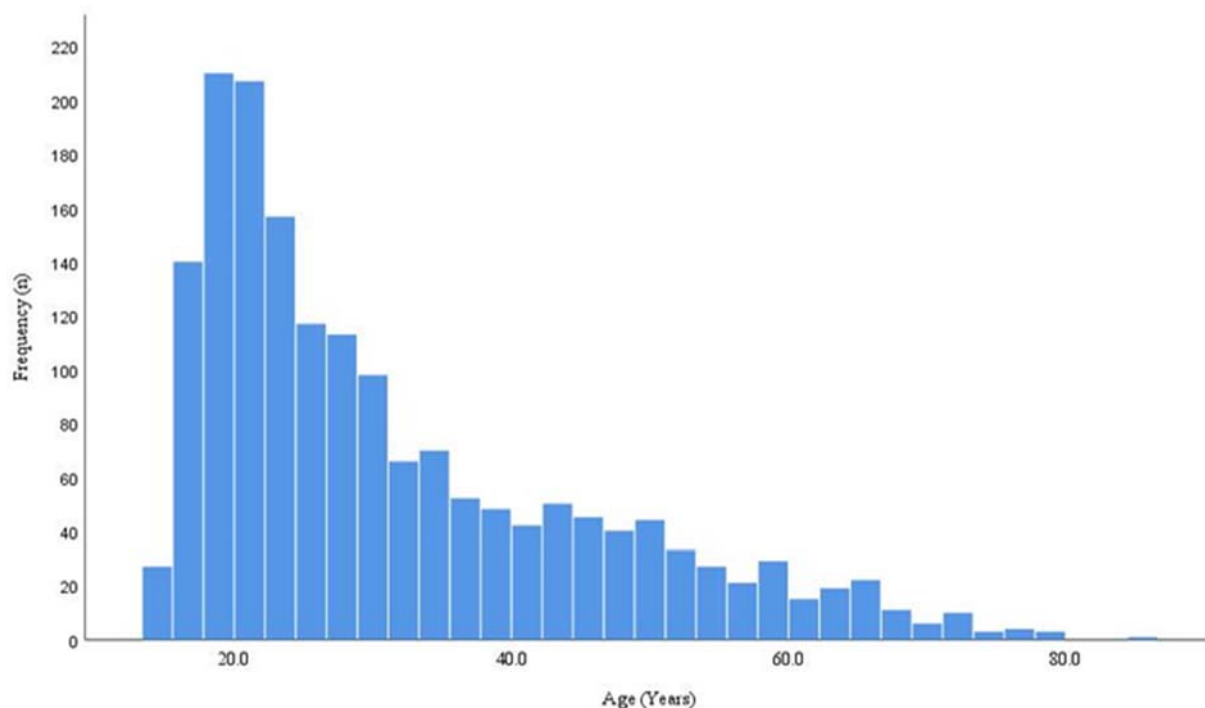


Figure 2.3.2(b): Age at time of biopsy (years) MCD, 2005-2017

### 2.3.3 Clinical presentation

- Nephrotic syndrome accounts for over two-thirds of clinical presentation of MCD (70%). (Table 2.3.3 (a))
- Nephrotic syndrome still remains the commonest presentation of MCD regardless of the gender (Figure 2.3.3(a)) and age. (Figure 2.3.3(b))

Table 2.3.3(a): Clinical presentation for MCD, 2005-2017

Clinical Presentation	2005-2009 (n=539)		2010-2014 (n=786)		2015 (n=145)		2016 (n=135)		2017 (n=125)		Total (n=1730)	
	n	%	n	%	n	%	n	%	n	%	n	%
Nephrotic syndrome	425	78.8	529	67.3	84	57.9	89	65.9	76	60.8	1203	69.5
Asymptomatic Urine abnormalities	60	11.1	132	16.8	25	17.2	23	17.0	18	14.4	258	14.9
Nephritic- Nephrotic	19	3.5	34	4.3	8	5.5	4	3.0	11	8.8	76	4.4
Nephritic	20	3.7	27	3.4	5	3.4	5	3.7	6	4.8	63	3.6
Not available	15	2.8	64	8.1	23	15.9	14	10.4	14	11.2	130	7.5
<b>Total</b>	<b>539</b>	<b>100</b>	<b>786</b>	<b>100</b>	<b>145</b>	<b>100</b>	<b>135</b>	<b>100</b>	<b>125</b>	<b>100</b>	<b>1730</b>	<b>100</b>

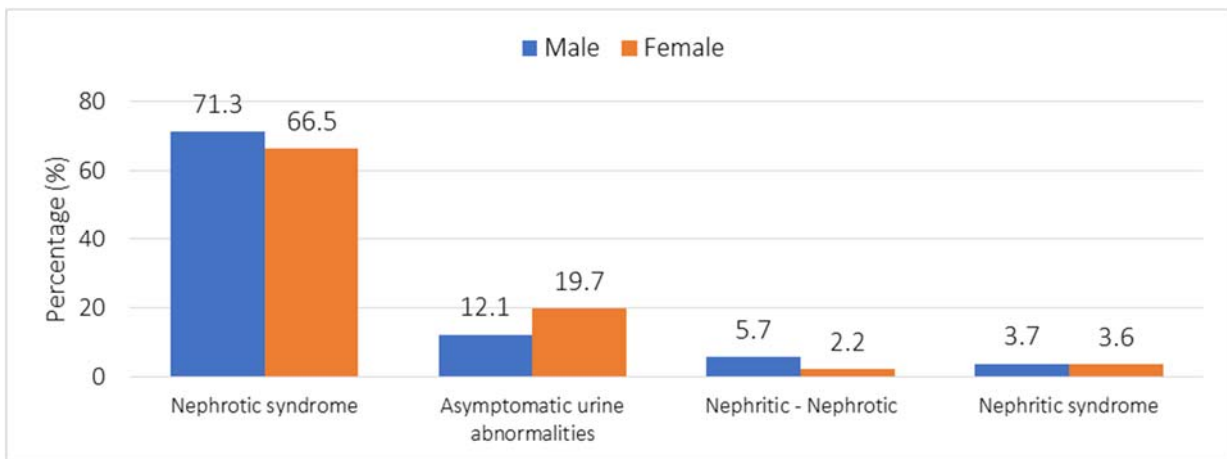


Figure 2.3.3(a): Clinical presentation by gender for MCD, 2005-2017

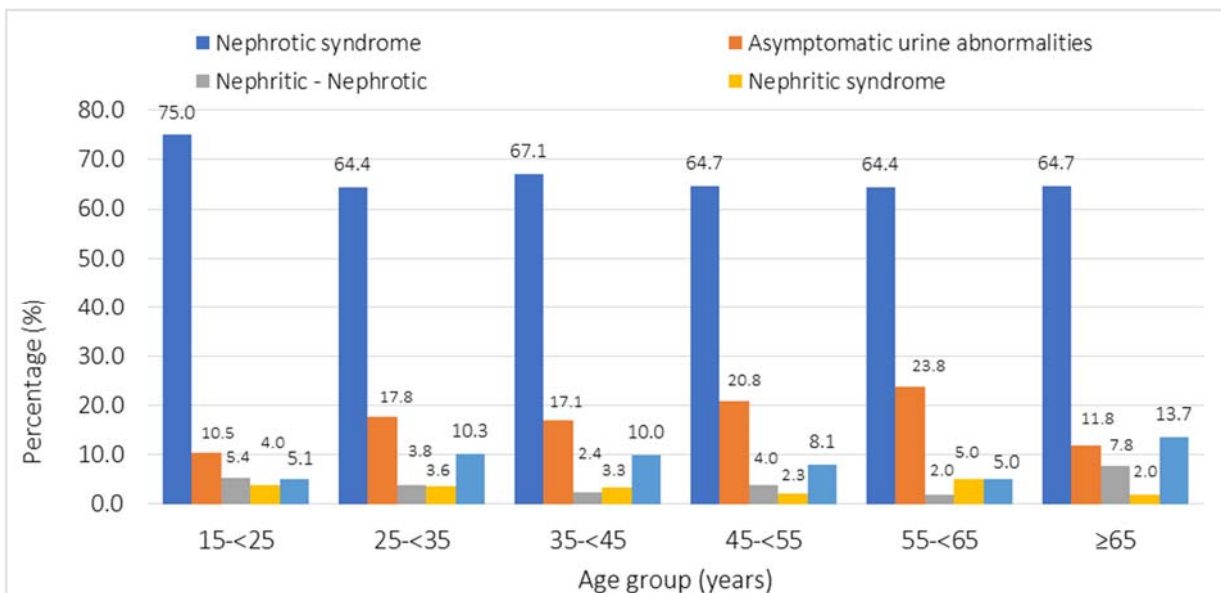


Figure 2.3.3(b): Clinical presentation by age group for MCD, 2005-2017

### 2.3.4 Hypertension

- Hypertension was present in 18.9% of patients with MCD.
- Prevalence of hypertension in MCD was higher in male.
- Older patients were more likely have hypertension with 1/3 of patients above the age of 45 years having hypertension. (Figure 2.3.4(b))
- This could be related to natural onset of hypertension and also decline in renal function in the older patients.

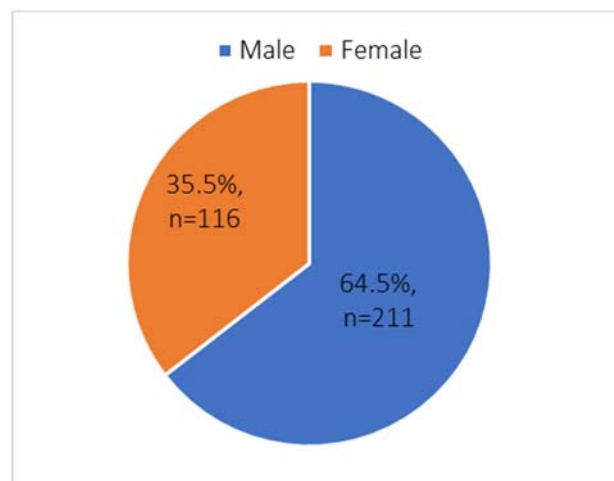


Figure 2.3.4(a) Hypertension by gender for MCD, 2005-2017

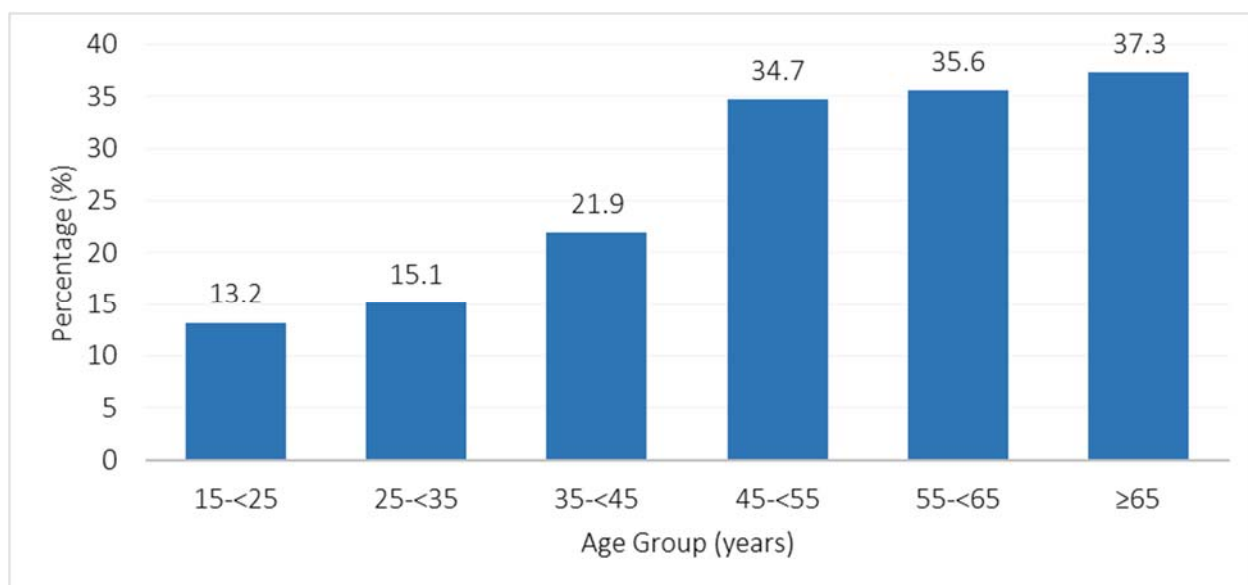


Figure 2.3.4(b): Hypertension by age group for MCD, 2005-2017

### 2.3.5 Renal function

- About 50% having eGFR more than 90mls/min/1.73m<sup>2</sup>. (Table 2.3.5(a))
- There were no differences in renal function by gender.
- Older patients had lower eGFR with majority being CKD stage III and above and in keeping with the prevalence of CKD in the general population. (Figure 2.3.5(a))

Table 2.3.5(a): Renal function in MCD, 2005-2017

eGFR (mls/ min/1.73m <sup>2</sup> )	2005-2009 (n=539)		2010-2014 (n=786)		2015 (n=145)		2016 (n=135)		2017 (n=125)		Total (n=1730)	
	n	%	n	%	n	%	n	%	n	%	n	%
< 15	7	1.3	16	2.0	3	2.1	4	3.0	2	1.6	32	1.8
15 to < 30	18	3.3	35	4.5	6	4.1	4	3.0	6	4.8	69	4.0
30 to < 60	69	12.8	98	12.5	15	10.3	9	6.7	9	7.2	200	11.6
60 to < 90	118	21.9	138	17.6	21	14.5	21	15.6	22	17.6	320	18.5
≥ 90	294	54.5	392	49.9	50	34.5	64	47.4	55	44.0	855	49.4
Not available	33	6.1	107	13.6	50	34.5	33	24.4	31	24.8	254	14.7
<b>Total</b>	<b>539</b>	<b>100</b>	<b>786</b>	<b>100</b>	<b>145</b>	<b>100</b>	<b>135</b>	<b>100</b>	<b>125</b>	<b>100</b>	<b>1730</b>	<b>100</b>

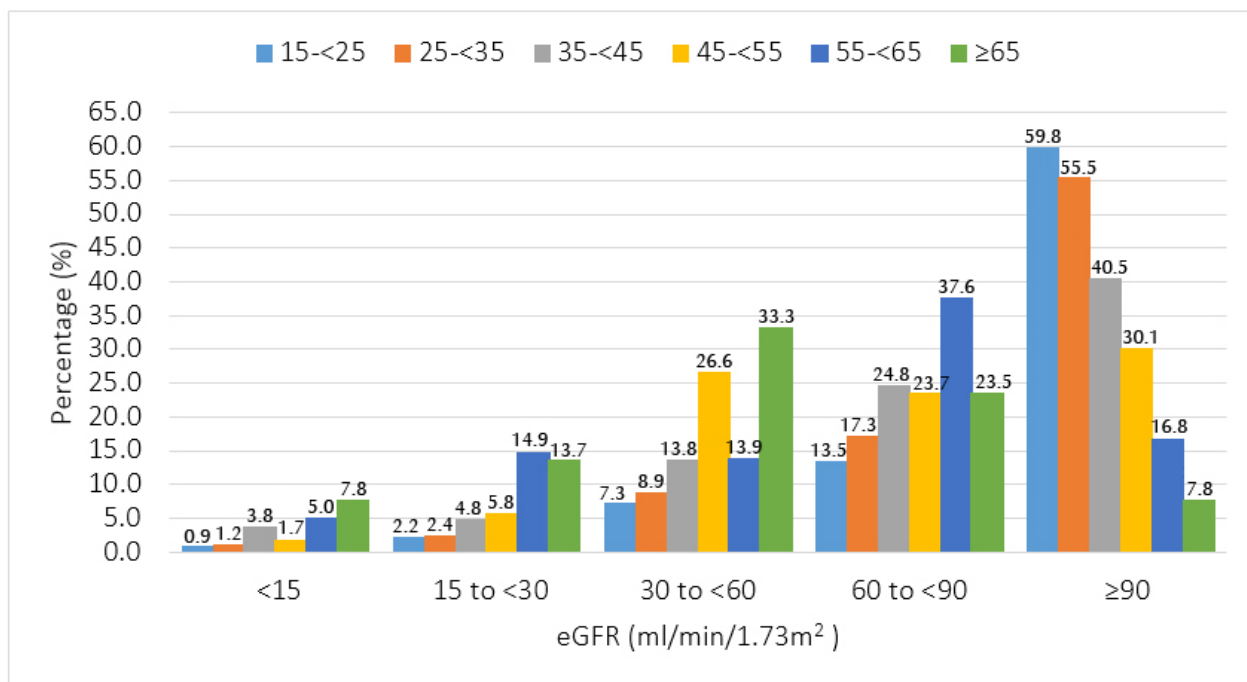


Figure 2.3.5(a): Renal function at presentation by age group for MCD, 2005-2017

### 2.3.6 Outcome

- Renal survival at 5-year and 10-year was 99% and 98% respectively. (Figure 2.3.6(a))
- Patient survival at 5-year and 10-year was 94% and 93% respectively. (Figure 2.3.6(b))
- These patients may have died due to complications of the disease or immunosuppressive treatment.

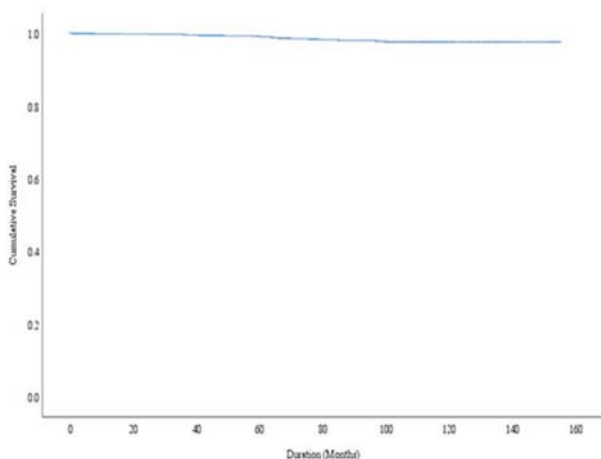


Figure 2.3.6(a): Renal Survival estimates for MCD 2005-2017

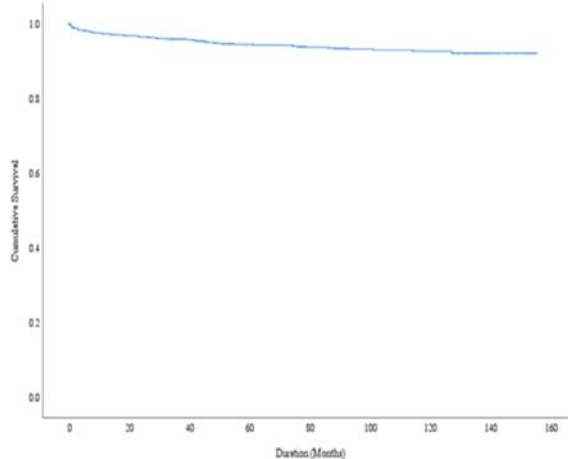


Figure 2.3.6(b): Patients' Survival estimates for death in MCD, 2005-2017

## 2.4 IgA Nephropathy (IgAN)

### 2.4.1 Introduction

- IgAN is defined by the predominant deposition of IgA in the glomerular mesangium although light microscopic appearances and clinical features can vary considerably due to the various patterns of histopathologic injury found in this glomerulonephritis.
- Over the years, there has been a significant increment in patients with IgAN and this may reflect changes in biopsy practices as well as earlier referral to nephrologist.

### 2.4.2 Patient Population and Characteristics

- There were 1377 reported cases of IgAN.
- The mean age at biopsy was  $34.0 \pm 12.2$  years and the majority of cases (81.8%) were between the ages 15 to 45 years. (Figure 2.4.2(b))
- There is slight female preponderance in our cohort (59.0% vs 41.0%) (Figure 2.4.2(a)). This is contrary to what has been reported in the literature.

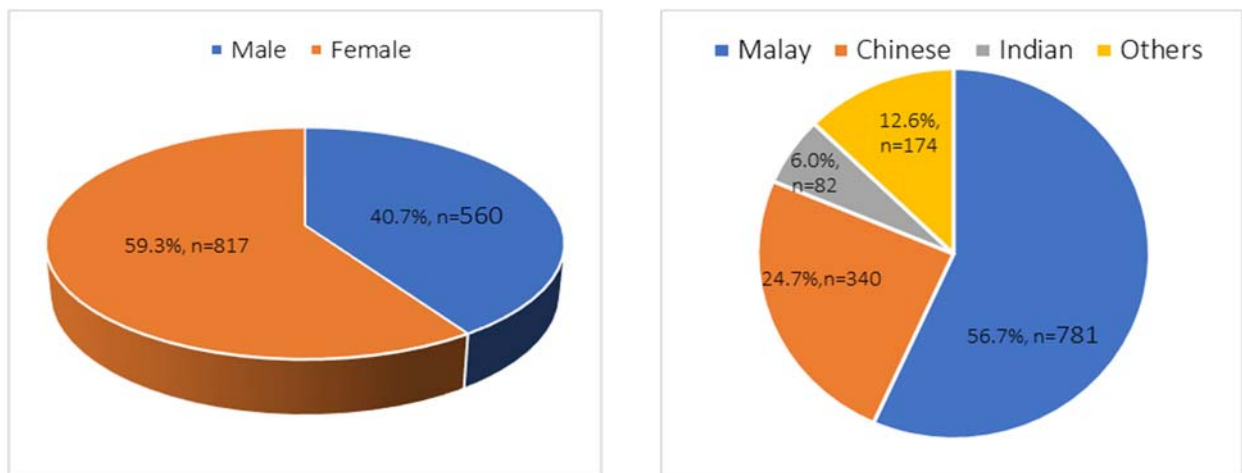


Figure 2.4.2(a): Demographic characteristics for IgAN, 2005-2017

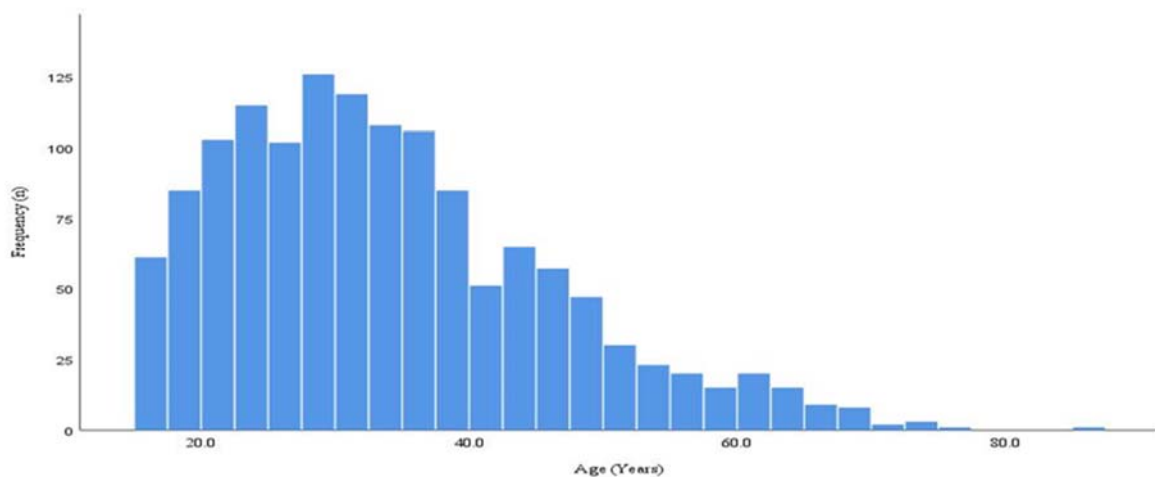


Figure 2.4.2(b) : Age at time of biopsy (year) IgAN, 2005-2017

**2.4.3 Clinical presentation**

- Asymptomatic urine abnormalities remain the most common presentation of IgAN (49.0%). Up to 21.0% of those who were biopsied had nephrotic syndrome. (Table 2.4.3(a))
- Males are more likely to present with nephrotic syndrome than females. (Figure 2.4.3(a))
- Asymptomatic urine abnormalities remained the most common presentation regardless of age group. (Figure 2.4.3(b))

Table 2.4.3(a): Clinical presentation for IgAN, 2005-2017

Clinical Presentation	2005-2009 (n=319)		2010-2014 (n=628)		2015 (n=135)		2016 (n=129)		2017 (n=166)		Total (n=1377)	
	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic urine Abnormalities	165	51.7	284	45.2	70	51.9	67	51.9	87	52.4	673	48.9
Nephrotic Syndrome	80	25.1	134	21.3	20	14.8	22	17.1	31	18.7	287	20.8
Nephritic-Nephrotic	22	6.9	60	9.6	10	7.4	16	12.4	13	7.8	121	8.8
Nephritic	22	6.9	47	7.5	9	6.7	6	4.7	11	6.6	95	6.9
Not available	30	9.4	103	16.4	26	19.3	18	14.0	24	14.5	201	14.6
<b>Total</b>	<b>319</b>	<b>100</b>	<b>628</b>	<b>100</b>	<b>135</b>	<b>100</b>	<b>129</b>	<b>100</b>	<b>166</b>	<b>100</b>	<b>1377</b>	<b>100</b>

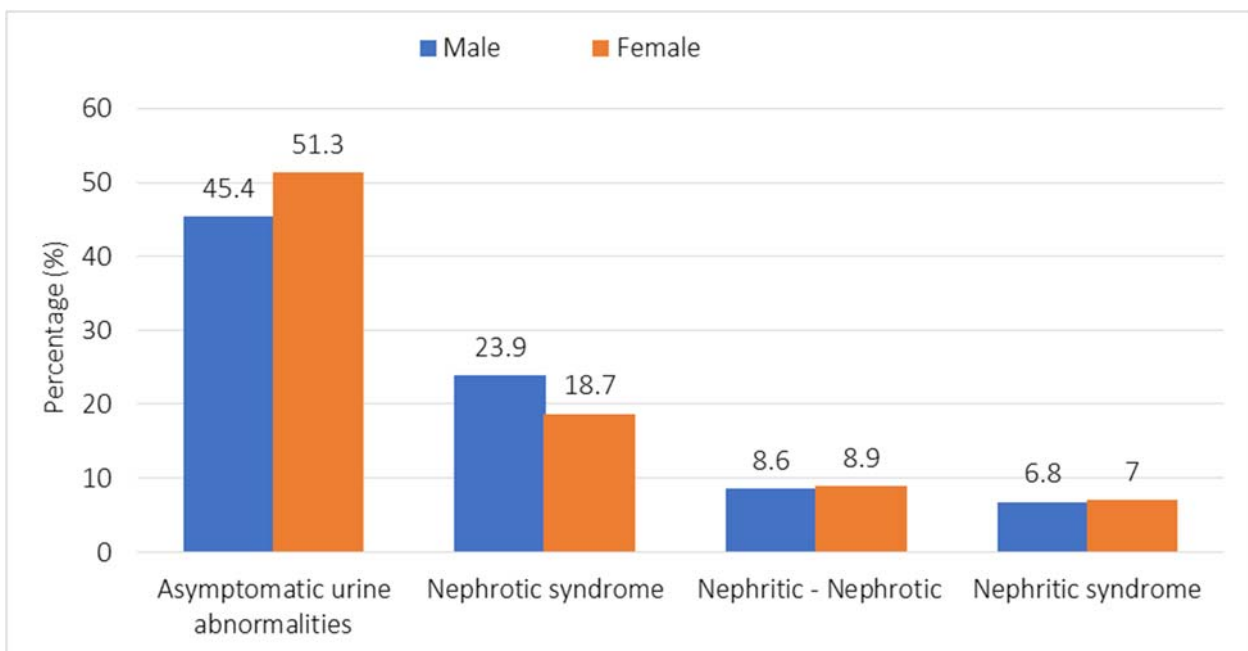


Figure 2.4.3(a): Clinical presentation by gender for IgAN, 2005-2017

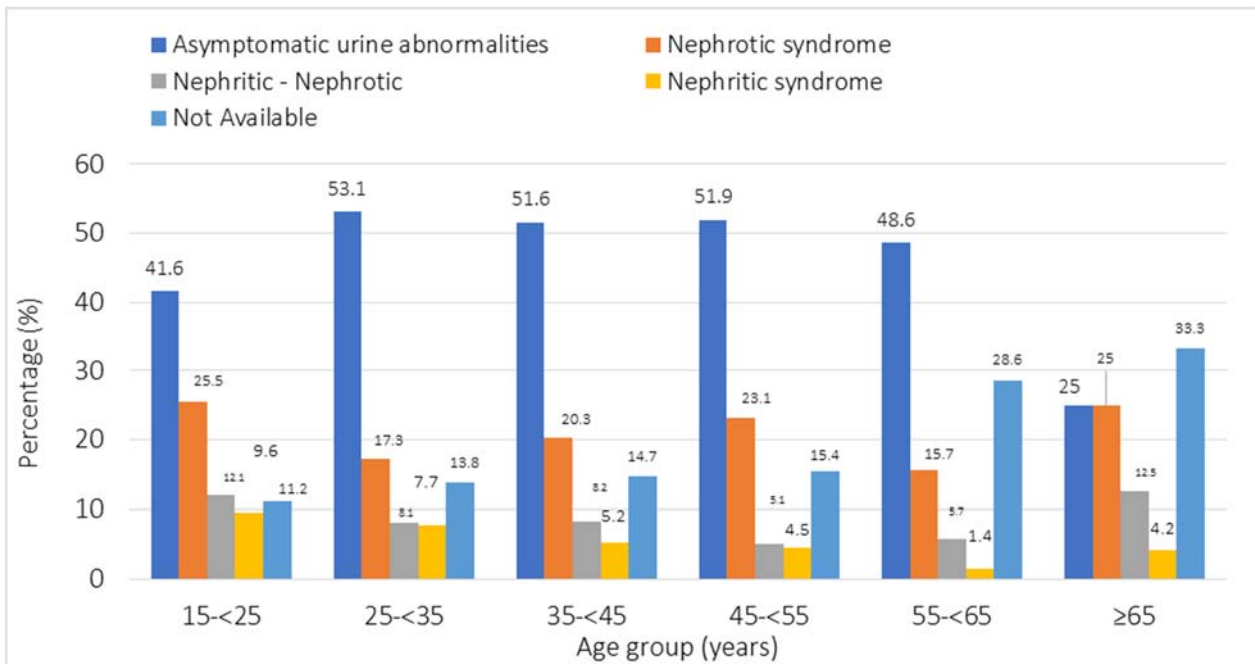


Figure 2.4.3(b): Clinical presentation by age group for IgAN, 2005-2017

#### 2.4.4 Hypertension

- The prevalence of hypertension was 46.3%.
- There was an increasing trend of hypertension over the last decade.
- Nearly 50% of the men with IgAN had hypertension whereas only 43.5% of women had hypertension. (Figure 2.4.4(a))
- More than two-thirds of patients over the age of 65 years had hypertension and about half (53%) were above the age of 35 years. (Figure 2.4.4(b))

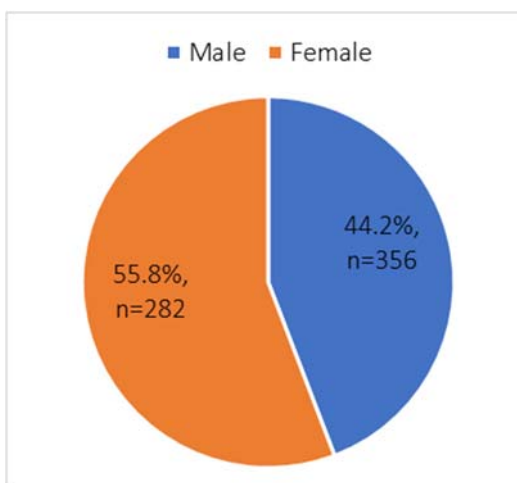


Figure 2.4.4(a): Hypertension by gender for IgAN, 2005-2017

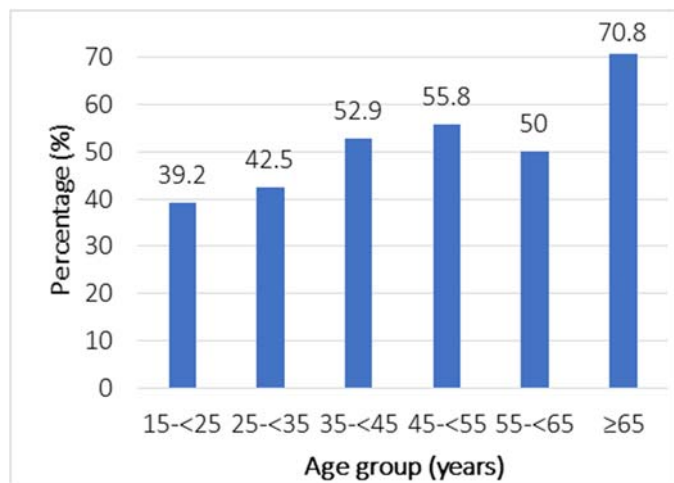


Figure 2.4.4(b): Hypertension by age group for IgAN, 2005-2017

**2.4.5 Renal function**

- Older patients (> 55 years old) had poorer eGFR with 1/3 to 1/2 having CKD stage IV and V. (Figure 2.4.5(a)). This may due to late presentation in these group of patients.

Table 2.4.5(a): Renal function in IgAN, 2005-2017

eGFR (mls/min/1.73m <sup>2</sup> )	2005-2009 (n=319)		2010-2014 (n=319)		2015 (n=135)		2016 (n=129)		2017 (n=166)		Total (n=1377)	
	n	%	n	%	n	%	n	%	n	%	n	%
< 15	31	9.7	70	11.1	8	5.9	13	10.1	13	7.8	135	9.8
15 to < 30	30	9.4	76	12.1	10	7.4	15	11.6	25	15.1	156	11.3
30 to < 60	85	26.6	140	22.3	32	23.7	31	24.0	36	21.7	324	23.5
60 to < 90	74	23.2	130	20.7	36	26.7	39	30.2	39	23.5	318	23.1
≥ 90	81	25.4	161	25.6	34	25.2	19	14.7	37	22.3	332	24.1
Not available	18	5.6	51	8.1	15	11.1	12	9.3	16	9.6	112	8.1
<b>Total</b>	<b>319</b>	<b>100</b>	<b>628</b>	<b>100</b>	<b>135</b>	<b>100</b>	<b>129</b>	<b>100</b>	<b>166</b>	<b>100</b>	<b>1377</b>	<b>100</b>

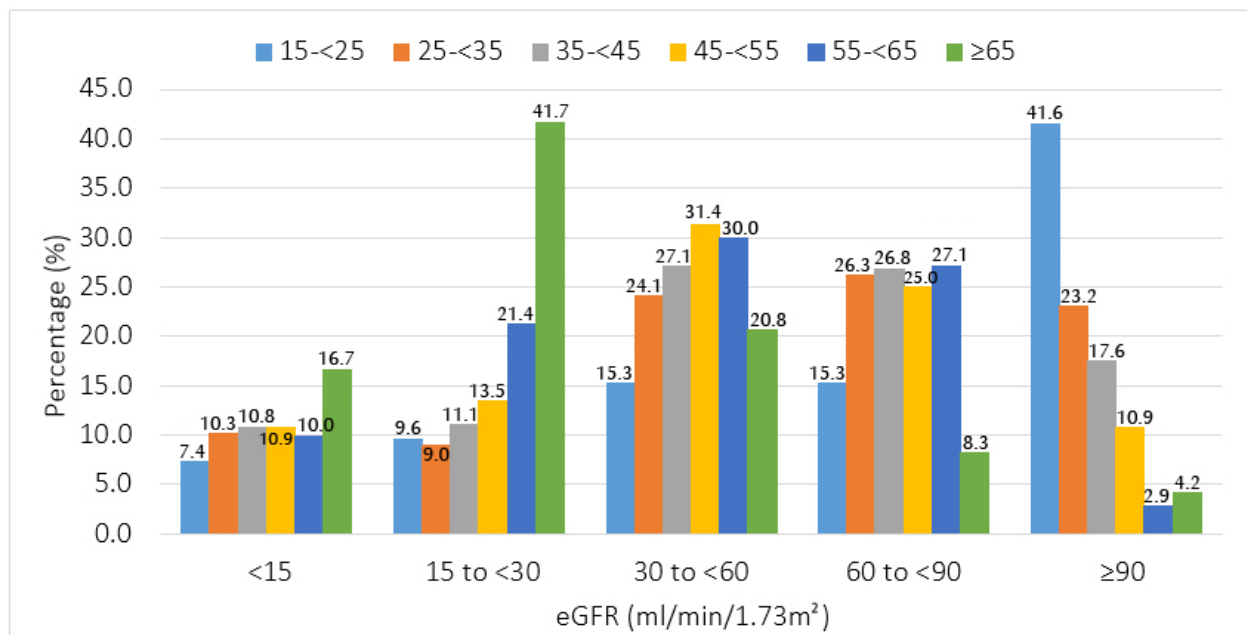


Figure 2.4.5(a): Renal function at presentation by age group for IgAN, 2005-2017



## 2.4.6 Outcome

- Renal survival for IgAN at 5-years and 10-years was 80% and 70% respectively.
- Patient survival at 5-years and 10- years was 96% and 93% respectively.
- The rate of progression to ESRD within 20 years is generally reported to be about 30% and however, our local rate measured over a shorter period of time seems to be higher.
- This suggests that IgAN in Malaysia has a different natural history and progression, especially when we have seen that close to 25% of patients present with nephrotic range proteinuria.

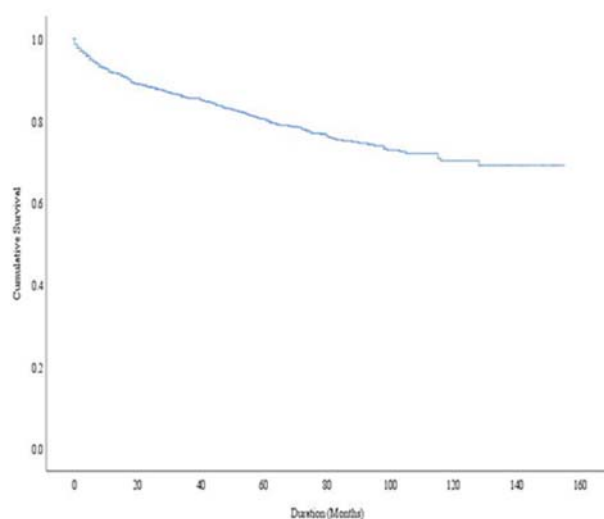


Figure 2.4.6(a): Renal Survival estimates for IgAN 2005-2017

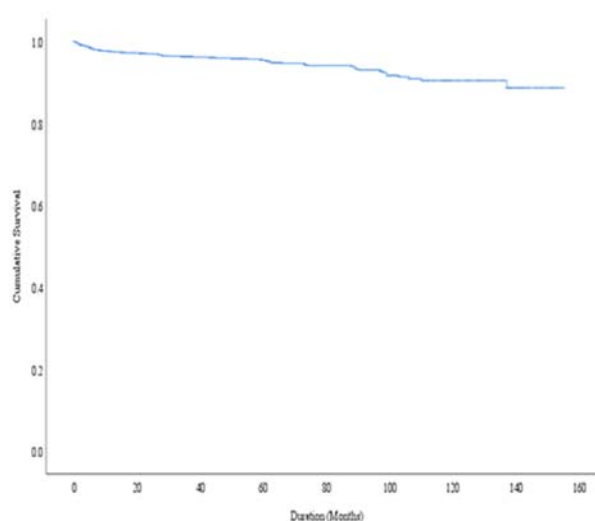


Figure 2.4.6(b): Patient Survival estimates for death in IgAN, 2005-2017

## 2.5 Membranous Nephropathy (MN)

### 2.5.1 Introduction

- MN is characterised by subepithelial immune deposits with spikes and thickening of the basement membrane. The absence of associated hypercellularity or glomerular inflammation confirms the diagnosis.
- MN is the fourth most commonly reported primary GN contributes to 9% of the total primary GN.
- There was no notable increment in the number of patients with membranous nephropathy over the past 5 years.

### 2.5.2 Patient Population and Characteristics

- There were 574 reported cases of MN.
- Patients with MN were older with a mean age of  $46.4 \pm 15.4$  years at biopsy and majority of cases (62%) were more than 45 years old. (Figure 2.5.2(b))
- There was a slight male preponderance in our cohort. (Figure 2.5.2 (a))
- There was a tendency towards more proportion of Indians and Chinese having membranous nephropathy as compared to the other GN. (Figure 2.5.2(a))

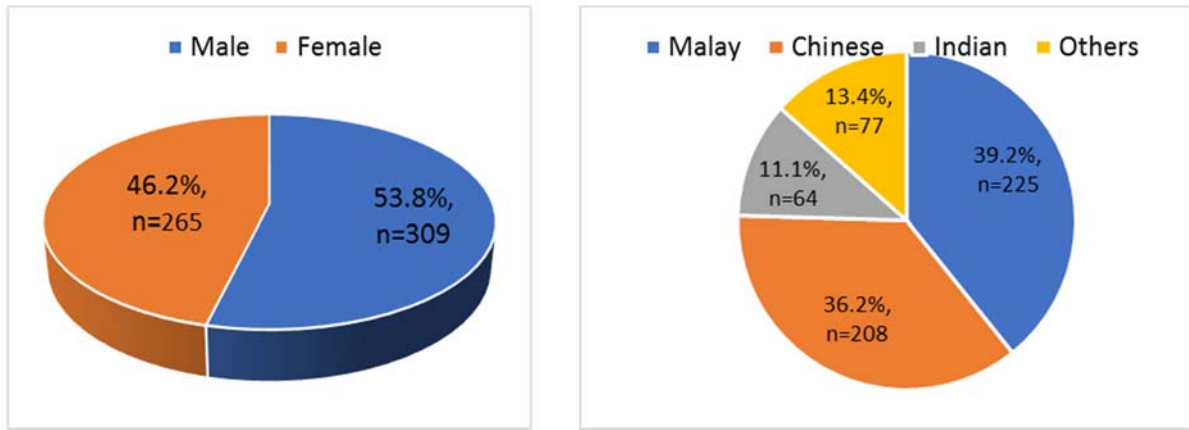


Figure 2.5.2(a): Demographic characteristics for MN, 2005 -2017

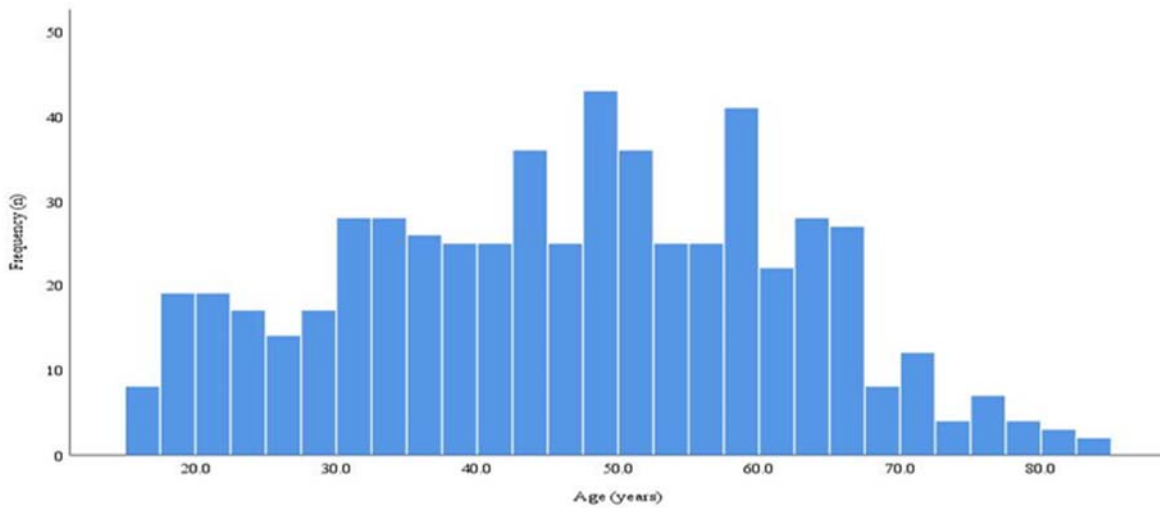


Figure 2.5.2(b): Age at time of biopsy (year) MN, 2005 -2017

**2.5.3 Clinical presentation**

- Nephrotic syndrome is the most common presentation. (Table 2.5.3(a))
- There were no differences in presentation with regards to gender (Figure 2.5.3(a)) and age group. (Figure 2.5.3(b))

Table 2.5.3(a): Clinical presentation for MN, 2005-2017

Clinical Presentation	2005-2009 (n=156)		2010-2014 (n=243)		2015 (n=51)		2016 (n=60)		2017 (n=64)		Total (n=574)	
	n	%	n	%	n	%	n	%	n	%	n	%
Nephrotic Syndrome	101	64.7	147	60.5	27	52.9	31	51.7	34	53.1	340	59.2
Asymptomatic urine abnormalities	41	26.3	53	21.8	12	23.5	17	28.3	15	23.4	138	24.0
Nephritic-Nephrotic	5	3.2	15	6.2	3	5.9	6	10.0	8	12.5	37	6.4
Nephritic	3	1.9	3	1.2	4	7.8	3	5.0	2	3.1	15	2.6
Not available	6	3.8	25	10.3	5	9.8	3	5.0	5	7.8	44	7.7
<b>Total</b>	<b>156</b>	<b>100</b>	<b>243</b>	<b>100</b>	<b>51</b>	<b>100</b>	<b>60</b>	<b>100</b>	<b>64</b>	<b>100</b>	<b>574</b>	<b>100</b>

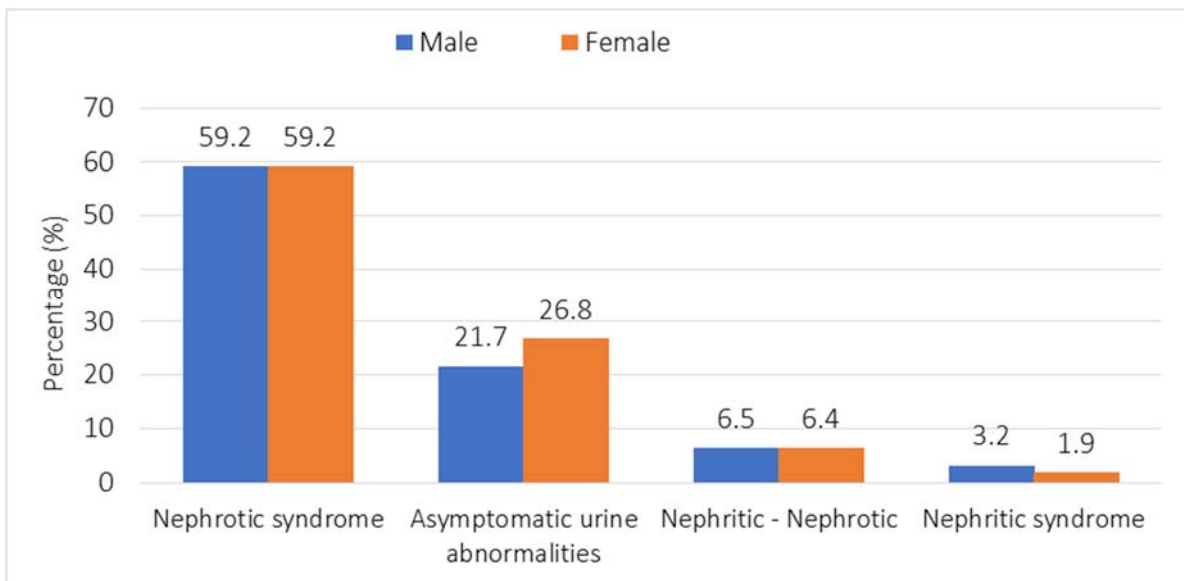


Figure 2.5.3(a): Clinical presentation by gender for MN, 2005-2017

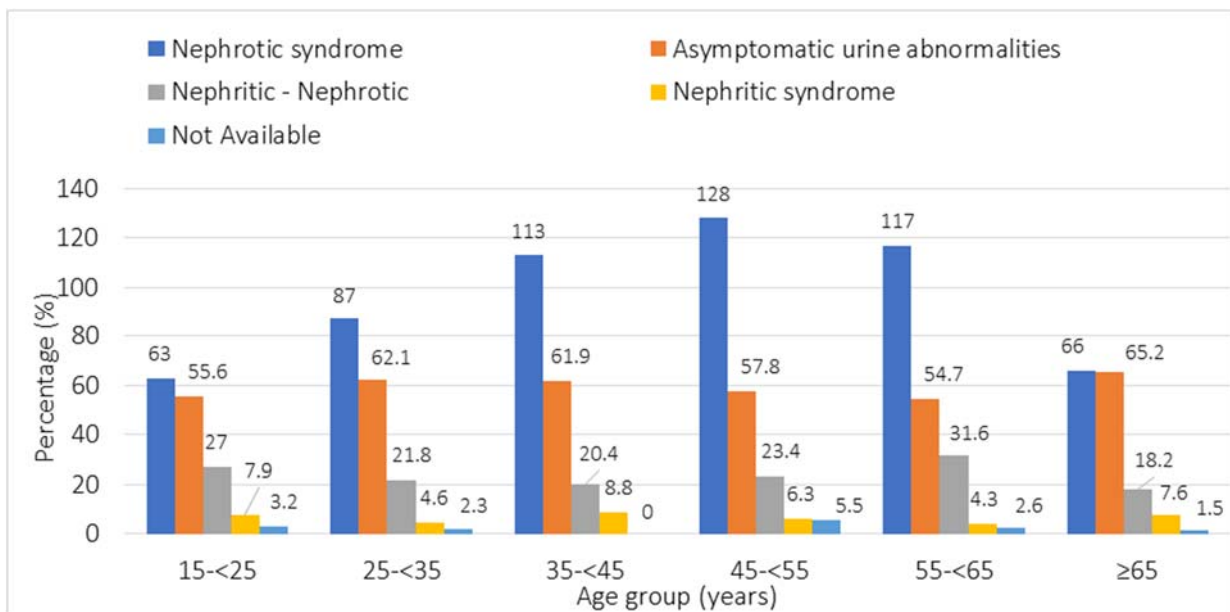


Figure 2.5.3(b): Clinical presentation by age group for MN, 2005-2017

### 2.5.4 Hypertension

- There was an increasing trend of hypertension over the last decade with over 50% of patients with MN having hypertension.
- Fifty- nine percent of patients over the age of 65 years and 35.3% above the age of 35 years were hypertensive.

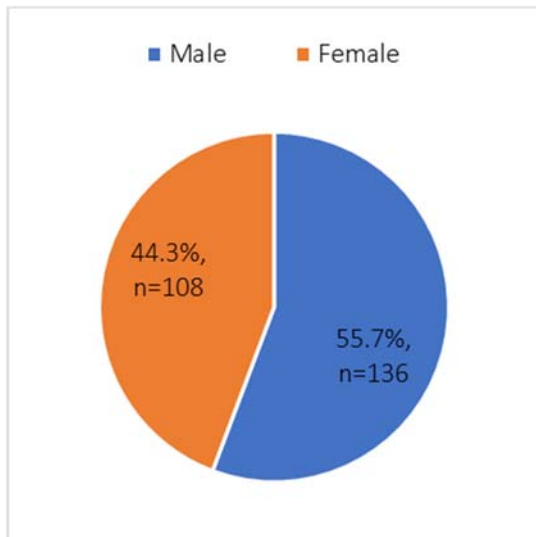


Figure 2.5.4(a): Hypertension by gender for MN, 2005-2017

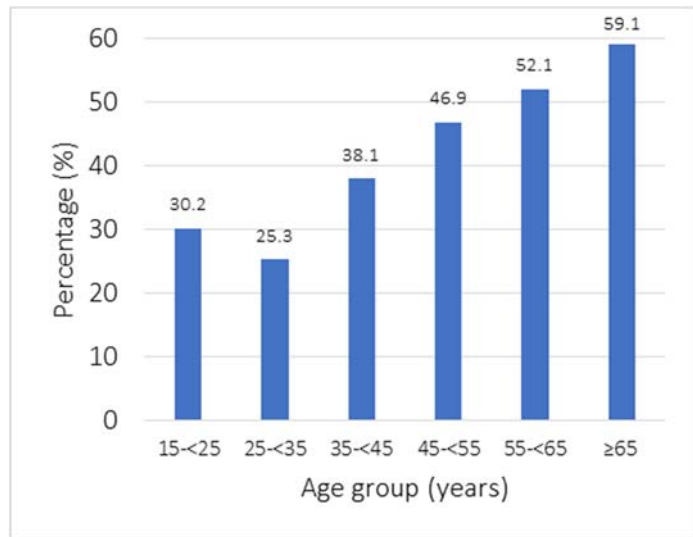


Figure 2.5.4(b): Hypertension by age group for MN, 2005-2017

### 2.5.5 Renal function

- Majority of the patients had preserved eGFR with 62% having CKD stage II and below.
- Older patients (age > 65 years old) predominantly presented with CKD stage III and above.

Table 2.5.5(a): Renal function in MN, 2005-2017

eGFR (mls/min/1.73m <sup>2</sup> )	2005-2009 (n=156)		2010-2014 (n=243)		2015 (n=51)		2016 (n=60)		2017 (n=64)		Total (n=574)	
	n	%	n	%	n	%	n	%	n	%	n	%
< 15	4	2.6	9	3.7	1	2.0	1	1.7	0	0.0	15	2.6
15 to < 30	10	6.4	15	6.2	4	7.8	4	6.7	6	9.4	39	6.8
30 to < 60	36	23.1	47	19.3	7	13.7	14	23.3	9	14.1	113	19.7
60 to < 90	48	30.8	50	20.6	10	19.6	11	18.3	16	25.0	135	23.5
≥ 90	47	30.1	92	37.9	24	47.1	26	43.3	26	40.6	215	37.5
Not available	11	7.1	30	12.3	5	9.8	4	6.7	7	10.9	57	9.9
<b>Total</b>	<b>156</b>	<b>100</b>	<b>243</b>	<b>100</b>	<b>51</b>	<b>100</b>	<b>60</b>	<b>100</b>	<b>64</b>	<b>100</b>	<b>574</b>	<b>100</b>

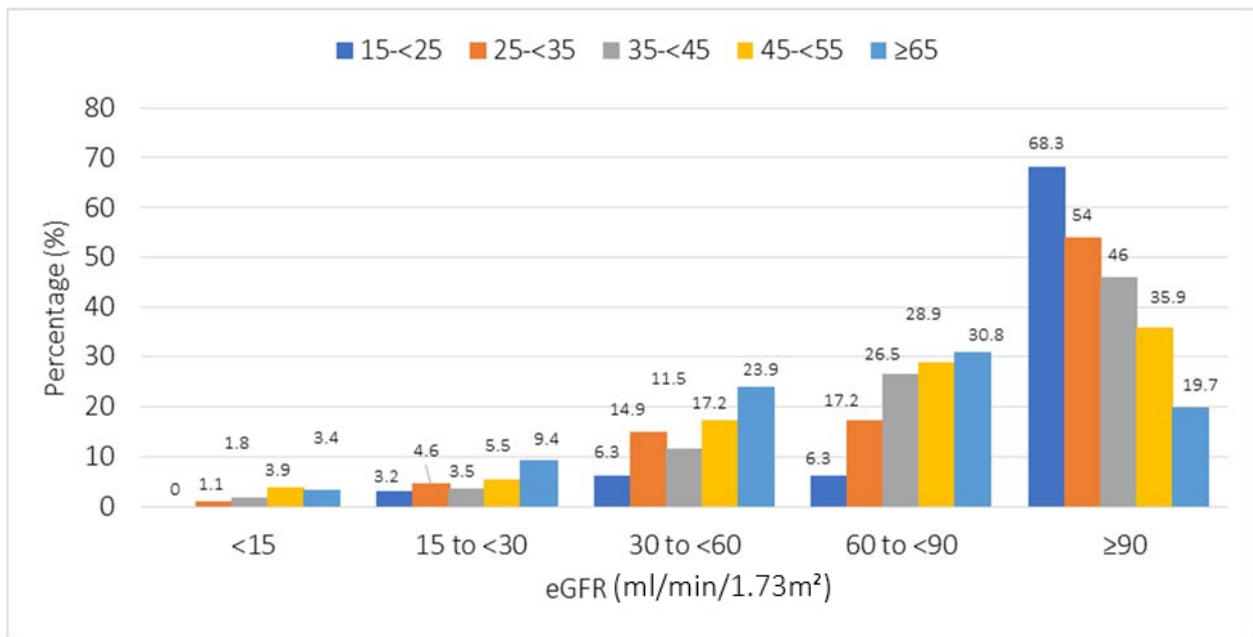


Figure 2.5.5(a): Renal function at presentation by age group for MN, 2005-2017

### 2.5.6 Outcome

- Renal survival at 5-year and 10-year for MN was 95% and 88% respectively. (Figure 2.5.6(a))
- Renal survival is good at 5-years in MN compared to other primary GN.
- Patient survival at 5-year and 10-year was 86% and 83% respectively. (Figure 2.5.6(b))

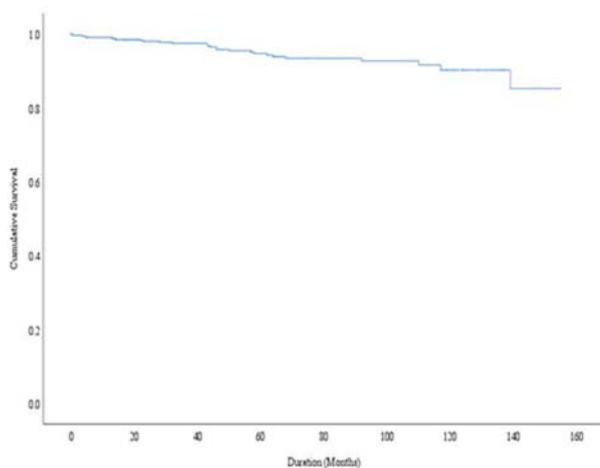


Figure 2.5.6(a): Renal Survival estimates for MN 2005-2017

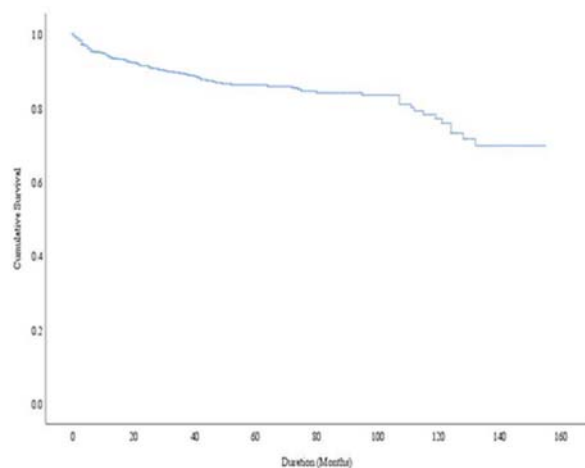


Figure 2.5.6(b): Patient Survival estimates for death in MN, 2005-2017