CHAPTER 5

Renal Allograft Biopsy

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5.1 Introduction

The systematic collection of renal allograft biopsy data was first started in the Department of Nephrology, Hospital Kuala Lumpur in 2004 and by 2005, has involved all the Ministry of Health hospitals in the country. The university hospitals joined in 2007 and the private hospitals began submitting data in 2008.

5.2: Number of renal allograft biopsy

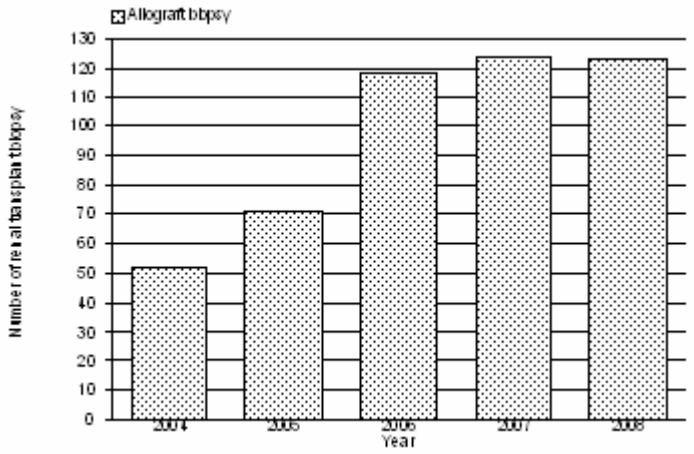
5.2.1: Number of renal allograft biopsy by year

There is an increasing trend in the number of renal allograft biopsy reported and the number has doubled over the last 5 years despite a decreased in the number of new transplant recipients (190 new transplant recipients in 2004 compared to 88 in 2008) and only a marginal increase in the number of functioning renal allograft (1595 functioning allograft in 2004 compared to 1730 in 2008) during the same period (Table & Figure 5.2.1). This marked increased in the number of renal allograft biopsies reported in recent years may be largely contributed by the marked increased in the number of participating centres (21 participating centres in 2005 compared to 43 centres in 2008) in the Malaysian Registry of Renal Biopsy.

Table 5.2.1: Number of renal allograft biopsy, 2004-2008

Year	2004	2005	2006	2007	2008	Total
Number of renal transplant biopsy	52	71	118	124	123	488

Figure 5.2.1: Number of renal allograft biopsy, 2004-2008



5.2.2: Number of renal allograft biopsy by year and site

In 2008, of the 43 participating centres, renal allograft biopsies were performed in only 12 centres with 90% of the biopsies performed in 5 centres (centre 1,7,19,20 & 24) in the Klang Valley (Table 5.2.2). These five centres have a very large number of renal transplant recipients and four of these centres are active renal transplant centres; performing most of the renal transplantation in this country.

Table 5.2.2: Number of renal allograft biopsy by centre, 2004-2008

Centre	2004 n	2004 %	2005 n	2005 %	2006 n	2006 %	2007 n	2007 %	2008 n	2008 %	Total n	Total %
1	47	90	28	39	50	42	43	35	37	30	205	42
2	0	0	0	0	0	0	0	0	3	2	3	1
3	0	0	12	17	11	9	2	2	4	3	29	6
4	0	0	0	0	1	1	0	0	0	0	1	0
5	0	0	1	1	2	2	2	2	0	0	5	1
6	0	0	0	0	0	0	0	0	0	0	0	0
7	0	0	5	7	11	9	12	10	10	8	38	8
8	0	0	0	0	1	1	1	1	1	1	3	1
9	0	0	0	0	0	0	0	0	0	0	0	0
10	0	0	0	0	2	2	1	1	1	1	4	1
11	0	0	0	0	2	2	0	0	1	1	3	1
12	0	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0
17	0	0	6	8	5	4	2	2	5	4	18	4
18	0	0	0	0	0	0	0	0	0	0	0	0
19	4	8	1	1	13	11	9	7	17	14	44	9
20	1	2	18	25	19	16	22	18	14	11	74	15
21	0	0	0	0	1	1	0	0	0	0	1	0
22	0	0	0	0	0	0	0	0	2	2	2	0
23	0	0	0	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	30	24	27	22	57	12
25	0	0	0	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	1	1	1	0
39	0	0	0	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0	0	0	0
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

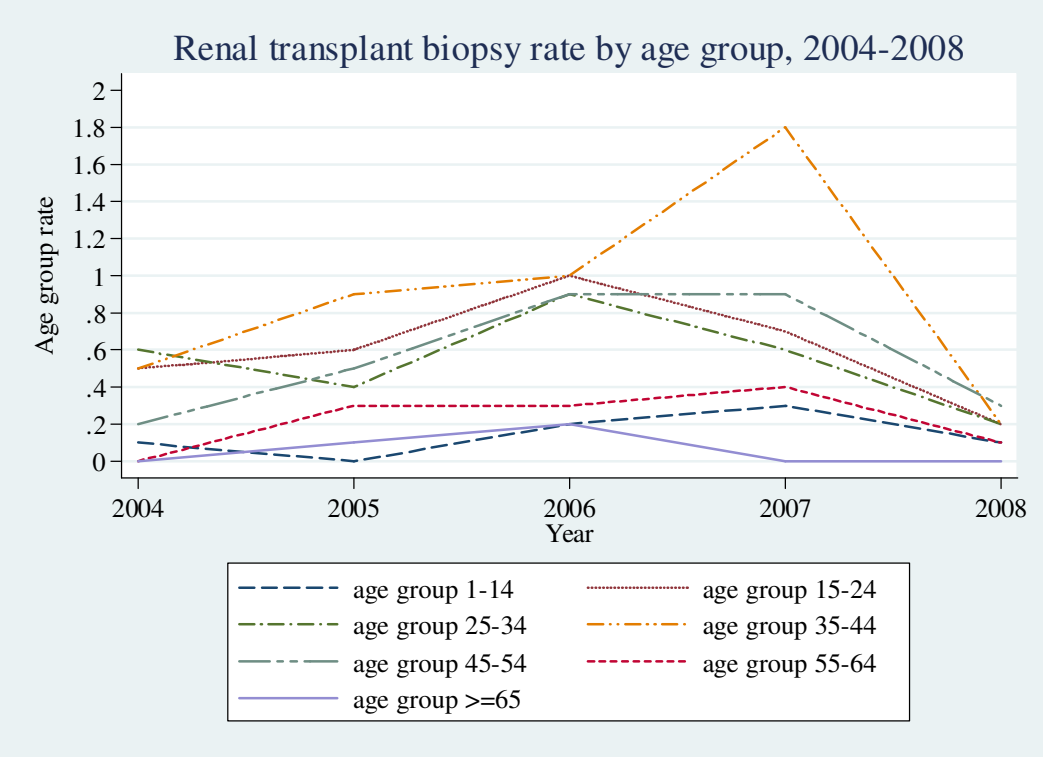
5.2.3: Number of renal allograft biopsy by year and age

Majority of the allograft renal biopsies were performed in the age group of 15 to 54 years and this pattern remained relatively unchanged over the last 5 years (Table 5.2.3). This probably reflects the transplant recipients' demography in this country. However in recent years, there is an increasing trend in the number of allograft biopsies performed in older transplant recipients. Allograft biopsies performed in the older age group (older than 54 years) has increased from 2% (2004) to 10% in 2008 (Table & Figure 5.2.3).

Table 5.2.3: Renal allograft biopsy by year and age group, rate per million population 2004-2008

Age group	2004			2005			2006			2007			2008			Total		
	n	%	Rate	n	%	Rate	n	%	Rate	n	%	Rate	n	%	Rate	n	%	Rate
<15	3	6	0.1	0	0	0	5	4	0.2	7	6	0.3	9	7	0.3	24	5	0.2
15-<25	14	27	0.5	15	21	0.6	26	22	1	19	15	0.7	22	18	0.8	96	20	0.7
25-<35	15	29	0.6	11	15	0.4	25	21	0.9	15	12	0.6	20	16	0.7	86	18	0.6
35-<45	14	27	0.5	23	32	0.9	26	22	1	49	40	1.8	25	20	0.9	137	28	1
45-<55	5	10	0.2	12	17	0.5	24	20	0.9	24	19	0.9	34	28	1.2	99	20	0.7
55-<65	1	2	0	8	11	0.3	8	7	0.3	10	8	0.4	9	7	0.3	36	7	0.3
≥65	0	0	0	2	3	0.1	4	3	0.2	0	0	0	4	3	0.1	10	2	0.1
Total	**52**	**101**	**1.9**	**71**	**99**	**2.8**	**118**	**99**	**4.5**	**124**	**100**	**4.7**	**123**	**99**	**4.3**	**488**	**100**	**3.6**

Figure 5.2.3 Renal allograft biopsy by year and age group, rate per million population 2004-2008



5.3: Clinical presentation at biopsy

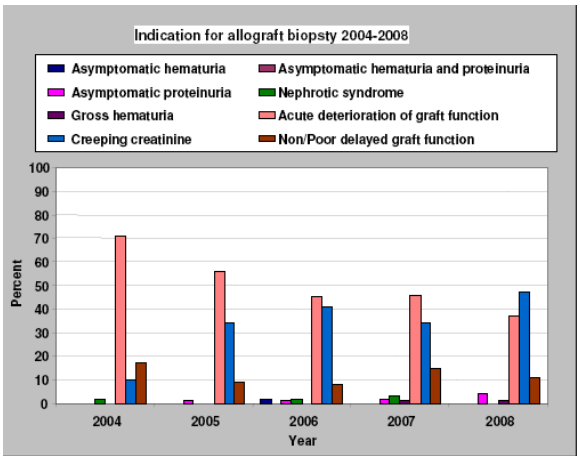
The most common indications for renal allograft biopsy were acute and chronic allograft dysfunction. This remained unchanged over the last 5 years and in 2008 accounted for 95% of the total number of renal allograft biopsies performed (Table 5.3). However there is a reversal in the pattern where the number of allograft biopsies performed for acute graft dysfunction has declined (71% in 2004 to 37% in 2008) by 50% while the number of allograft biopsies performed for chronic allograft dysfunction (creeping serum creatinine) has increased by nearly 5 folds (10% in 2004 to 47% in 2008).

Table 5.3: Indications for renal allograft biopsy, 2004-2008

Current clinical presentation	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Asymptomatic hematuria	0	0	0	0	2	2	0	0	0	0	2	0
Asymptomatic hematuria and proteinuria	0	0	0	0	0	0	0	0	0	0	5	1
Asymptomatic proteinuria	0	0	1	1	1	1	2	2	4	4	8	2
Nephrotic syndrome	1	2	0	0	3	2	3	3	0	0	7	1
Gross hematuria	0	0	0	0	0	0	1	1	1	1	2	0
Acute deterioration of graft function	34	71	39	56	55	45	55	46	42	37	225	47
Creeping creatinine	5	10	24	34	50	41	41	34	54	47	174	36
Non/Poor delayed graft function	8	17	6	9	10	8	18	15	13	11	55	12
Total	**48**	**100**	**70**	**100**	**121**	**100**	**120**	**100**	**114**	**100**	**478**	**100**

*** Patients may have one or more clinical presentation**

* 23 patients have no information on clinical presentation
For 2004, 1 patient has 2 indications
For 2006, 4 patients have 2 indications
For 2007, 2 patients have 2 indications
For 2008, 6 patients have 2 indications



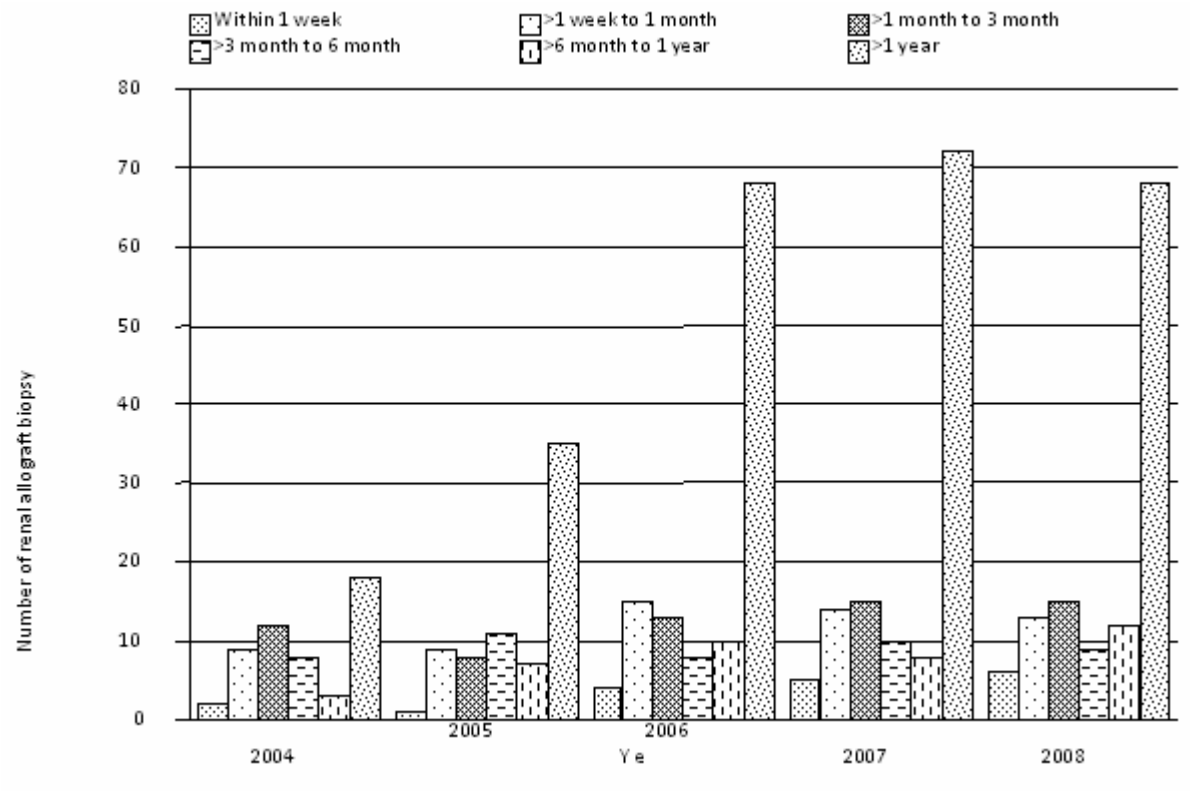
5.4: Timing of renal allograft biopsy

The number of renal allograft biopsies performed within the first six months post renal transplantation remained relatively unchanged over the last 5 years (Table & Figure 5.4). However in recent years, there has been a marked increased in the number of renal allograft biopsies performed in recipients after 1 year post transplant (35% in 2004 to 55% in 2008). This reflects the increasing importance of chronic allograft nephropathy among renal transplant recipients.

Table 5.4: Timing of renal allograft biopsy, 2004-2008

Timing of renal transplant biopsy	Within 1 week		>1 week to 1month		> 1month to 3 months		> 3 months to 6 months		> 6months to 1 year		>1 yr post transplant		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
2004	2	4	9	17	12	23	8	15	3	6	18	35	52	100
2005	1	1	9	13	8	11	11	15	7	10	35	49	71	100
2006	4	3	15	13	13	11	8	7	10	8	68	58	118	100
2007	5	4	14	11	15	12	10	8	8	6	72	58	124	100
2008	6	5	13	11	15	12	9	7	12	10	68	55	123	100
Total	**18**	**4**	**60**	**12**	**63**	**13**	**46**	**9**	**40**	**8**	**261**	**53**	**488**	**100**

Figure 5.4: Timing of renal allograft biopsy, 2004-2008



5.5: Renal allograft biopsy procedure

5.5.1: Renal allograft biopsy method

Over the last 5 years, nearly all renal allograft biopsies were performed under ultrasonographic guidance with real-time guidance accounting for at least 65% in 2008 (Table 5.5.1). When missing data are censored, ultrasonographic guidance with real-time renal allograft biopsy accounted for 96% in 2008 (Figure 5.5.1) and ultrasonography was used in all allograft biopsies.

Table 5.5.1: Biopsy method, 2004-2008

Method	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Blind (not US guided)	0	0	1	1	0	0	1	1	0	0	2	0
US guided: real-time	48	92	27	38	62	53	65	52	80	65	282	58
US guided: not real-time	3	6	32	46	33	28	5	4	3	2	76	16
Missing*	1	2	11	15	23	19	53	43	40	33	128	26
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

* Missing means no data on biopsy technique

Figure 5.5.1: Biopsy method, 2004-2008

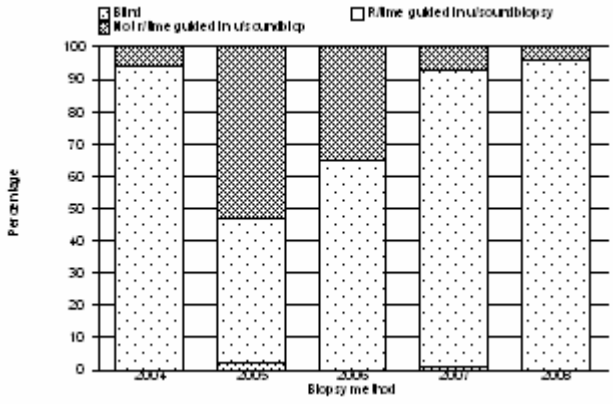
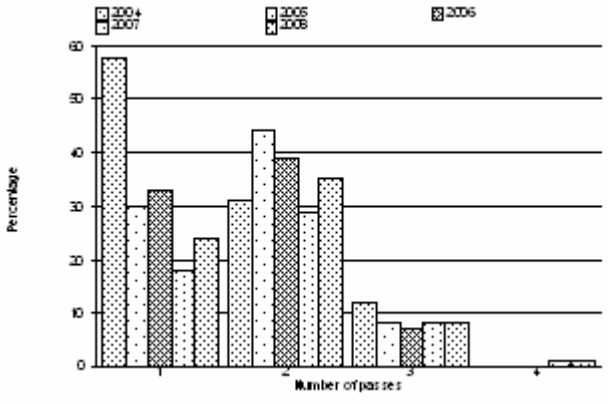


Figure 5.5.2: Number of passes, 2004-2008



5.5.2: Number of passes

The average number of passes for renal allograft biopsy remained unchanged over the last 5 years where majority had one or two passes only. In 2008, the average number of passes made during allograft biopsy was 1.78 (after censoring incomplete data) with only 1 allograft biopsy required more than 3 passes (Table & Figure 5.4.2).

Table 5.5.2: Number of passes, 2004-2008

Number of passes	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
1	30	58	21	30	39	33	22	18	30	24	142	29
2	16	31	31	44	46	39	36	29	43	35	172	35
3	6	12	6	8	8	7	10	8	10	8	40	8
4	0	0	0	0	0	0	1	1	1	1	2	0
Missing*	0	0	13	18	25	21	55	44	39	32	132	27
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

* No data information on number of passes

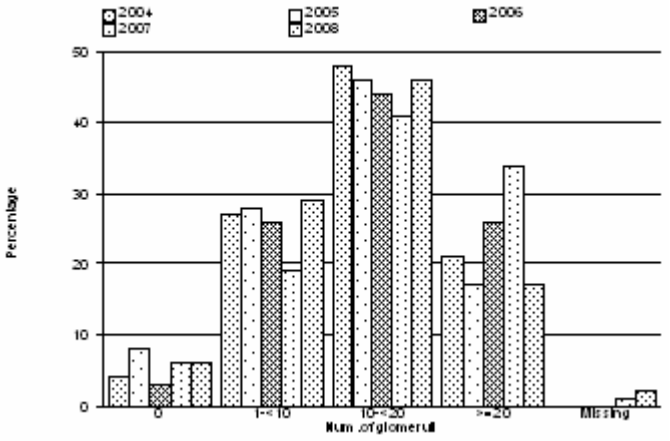
5.5.3: Number of glomeruli obtained on biopsy

With an average of 1.76 passes made during allograft biopsy, 69% of the renal allograft biopsies performed over the last 5 years yield at least 10 glomeruli (Table & Figure 5.4.3). Renal allograft biopsies that did not yield any glomerulus were uncommon and accounted for only 5%. This pattern remained unchanged over the last 5 years

Table 5.5.3: Number of glomeruli obtained on biopsy, 2004-2008.

Number of glomeruli obtained	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
0	2	4	6	8	4	3	7	6	7	6	26	5
1-9	14	27	20	28	31	26	23	19	36	29	124	25
10-19	25	48	33	46	52	44	51	41	57	46	218	45
>20	11	21	12	17	31	26	42	34	21	17	117	24
Missing/Unknown*	0	0	0	0	0	0	1	1	2	2	3	1
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

Figure 5.5.3: Number of glomeruli obtained on biopsy, 2004-2008



5.5.4: Type of complications

Over the last 5 years, complications from renal allograft biopsy were uncommon. In 2008 (after censoring missing data), 97% of all biopsies do not have any complications while a major complication was only reported in 1 allograft biopsy (Table 5.5.4).

Table 5.5.4: Type of complications, 2004-2008

Type of complications	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
No complication	49	94	53	75	95	81	68	55	88	72	353	72
Mild complication[a]	1	2	1	1	1	1	3	2	2	2	8	2
Severe complication[b]	0	0	1	1	0	0	1	1	1	1	3	1
Missing / Unknown[c]	2	4	16	23	22	19	52	42	32	26	124	25
Total	**52**	**100**	**71**	**100**	**118**	**100**	**124**	**100**	**123**	**100**	**488**	**100**

[a] Mild complication is defined as presence of gross hematuria, perirenal collection, hematoma, or AVM that do not require intervention

[b] Severe complication is defined as presence of hypotension or complications requiring intervention.

[c] No data information for complications

5.6: Histological diagnosis

Acute rejection has remained the most common histological diagnosis (Table 5.6) and in 2008 accounted for 49% of all allograft biopsies. The number of allograft biopsies with histological diagnosis of acute rejection has increased over the last 5 years with a corresponding decrease in the number of allograft biopsies with the histological diagnosis of calcineurin inhibitor toxicity and chronic allograft nephropathy (Figure 5.6). This may be a result of the changing pattern in the calcineurin inhibitors usage among nephrologists in recent years.

Furthermore, the numbers of allograft biopsies with histological diagnosis of acute rejection continue to increase despite a decreased in the number of allograft biopsies performed for acute graft dysfunction (37% in 2008), suggesting that in recent years, acute rejection in renal allograft may not present with the classical acute rise in serum creatinine and may instead manifest as chronic graft dysfunction.

Chronic allograft nephropathy, calcineurin inhibitor toxicity and acute tubular necrosis remained the next three commonest histological diagnosis and in 2008 accounted for 46% of all allograft biopsies.

Table 5.6: Histological diagnosis, 2004-2008

Histological diagnosis	2004		2005		2006		2007		2008		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Acute rejection	24	34	25	32	55	33	57	43	52	49	213	38
Borderline rejection	3	4	9	12	5	3	3	2	1	1	21	4
Calcineurin inhibitor toxicity	14	20	21	27	29	17	18	13	16	15	98	18
Chronic allograft nephropathy	10	14	11	14	39	23	26	19	16	15	102	18
Acute tubular necrosis	14	20	8	10	21	13	20	15	17	16	80	14
PTLD**	1	1	0	0	6	4	1	1	0	0	8	1
De novo	0	0	0	0	0	0	0	0	0	0	0	0
Recurrent GN	4	6	2	3	5	3	1	1	3	3	15	3
Diabetic nephropathy	0	0	0	0	5	3	1	1	0	0	6	1
Others	1	1	2	3	2	1	7	5	2	2	14	3
Total	**71**	**100**	**78**	**100**	**167**	**100**	**134**	**100**	**107**	**100**	**557**	**100**

* Patients may have more than 1 diagnosis classification
**Post Transplant Lymphoproliferative disease

Figure 5.6: Histological diagnosis, 2004-2008