Chapter 18: Report of the Paediatric Renal Registry

Summary

The demographics of the paediatric ERF population have changed little from previous reports, though it is now clear that the population is continuing to grow rather than plateauing as was inferred in last year's report. The total number of patients in paediatric renal units in April 2004 was 836, with a male to female ratio of 1.56:1. There remains a high prevalence of ERF in the South Asian population with an even higher incidence, suggesting that the prevalence is likely to rise in years to come.

The aetiology of ERF in childhood varies with both gender and ethnicity. Overall, renal dysplasia is the most common cause followed closely by glomerular disease. Obstructive dysplasia is now the third most common cause. Obstructive uropathy and renal dysplasia are both significantly more common in males. Amongst the ethnic minority groups the distribution of diseases causing ERF is different with a high incidence of autosomal recessively inherited diseases. As a consequence, the gender distribution in the ethnic minority population is less weighted towards males.

There has been a fall of 1.3% over the past 12 months in the proportion of patients with a functioning allograft. Looking at the proportion of patients in individual renal units transplanted, there is a linear relationship between the proportion of transplants obtained from living donors and the proportion of prevalent patients with allografts, confirming the relative shortage of cadaveric organs. Both the proportion of and the absolute number of patients on haemodialysis has risen, though the majority are still treated with automated peritoneal dialysis. CAPD is only regularly employed by two renal units.

At presentation, 21.6% of patients have paediatric specific co-morbidities; the single most common problem being developmental delay which is present in 8.8%. Co-morbidity at presentation is significantly more common in those presenting under the age of 8 years and in those taken on for dialysis in paediatric units over the age of 16 years. Intellectual disability affects 17% of the paediatric ERF population on cross-sectional analysis with this disability being moderate or severe in 7%. Physical disability is the next most common problem with visual and auditory disability being relatively rare. Overall, the presence of disability does not appear to prevent patients receiving a transplant.

Almost 28% of patients who were on dialysis on 1st April 2004 had been on dialysis for two or more consecutive years, with 7% having been on dialysis for five or more years. Over one third of those who had been on dialysis for more than two years were from ethnic minority groups. The majority of patients on dialysis for prolonged periods were on haemodialysis.

With the large numbers of paediatric patients with obstructive uropathy as a cause of ERF, the outcome of transplantation into the abnormal bladder is important. On cross-sectional analysis the outcome of transplantation into the bladders of patients with obstructive uropathy is no different to that of patients with renal dysplasia as a cause of ERF. However, looking specifically at those with abnormal bladder function requiring intermittent catheterisation, bladder augmentation or a urinary diversion, the outcome is worse with a $10\,\mathrm{mls/min/1.73\,m^2}$ reduction in median GFR.

Introduction

Progress towards the development of a system of continual data acquisition for analysis is ongoing with regard to paediatric data for the Renal Registry. To date, information is only being transmitted to the Registry directly from a limited number of renal units. For this reason, the body of this report contains data from our annual data trawl as reported in previous years.

In this report, the demographics of ERF in childhood in the UK, are described together with a focus on co-morbidity and disability in the paediatric population. Also discussed are the demographics of patients on long-term dialysis and the outcomes of transplantation into abnormal bladders.
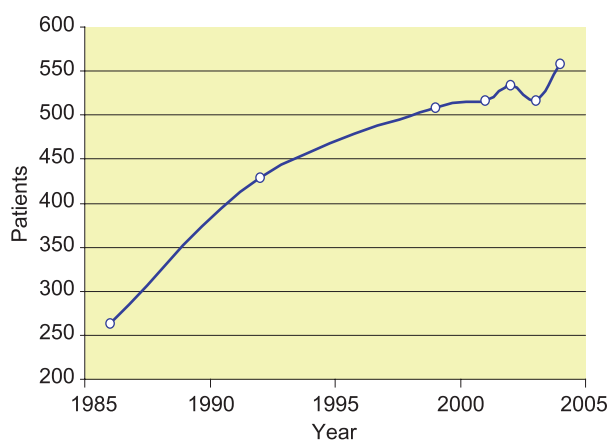
Paediatric ERF population

The paediatric arm of the Renal Registry currently contains data on 1,697 patients treated for ERF within paediatric units. Of these, 1,023 are male and 674 are female, giving an overall male to female ratio of 1.52 : 1. Of these, 138 patients are known to have died and many have been transferred to adult services. Some of those transferred will also have died at some point after transfer. The patients reported to the registry who appeared to remain under the care of paediatric units on 1st April 2004 numbered 836. Of these patients, there was no current data submission for 52. Thirty two of these 52 patients were over the age of 16 at the time and had probably been transferred to adult units. For the purpose of analysis, data available on the remaining 804 patients was used.

The figure of 804 current patients signifies a rise in the total number under active treatment in paediatric units, countering the small fall in prevalence in our report for 2003. Table 18.1 shows the total number of patients broken down according to gender and ethnicity, together with the numbers of these who were under 18 years of age in April 2004 and those who were under 15 years of age at this time. Figure 18.1 shows the growth in patient numbers for those under the age of 15 years

Figure 18.1: ERF patients below the age of 15 years, by year of data collection

and Table 18.2 shows the population changes for all age-groups. Although in our last report it was felt that growth in the population had reached a plateau, this appears not to be the case. Figure 18.2 shows the age distribution of the population compared with that in 2002 and 2003. It is clear from this that there is no specific trend in the ages of patients being treated.

The overall gender distribution also remains unchanged with a male to female ratio in the order of 1.5 : 1. The gender distribution across the paediatric age spectrum is shown in Figure 18.3 and Table 18.3. Male predominance is greatest in the early years of childhood but persists throughout the paediatric age range. This is secondary to specific diagnoses only seen in male patients which are discussed in the section on ERF diagnoses.

Returning to Table 18.1 and the ethnic distribution of the population, two things are

Table 18.1: Current prevalent patients by gender and ethnicity

	Patients	Male	Female	Ratio	Total %
Total	804	490	314	1.56 : 1	100.0
White	668	414	254	1.63 : 1	83.0
Asian	110	57	53	1.08 : 1	13.6
Black	15	10	5	2.00 : 1	1.8
Other	11	9	2	4.50 : 1	1.6
<18 years	781	476	305	1.56 : 1	97.1
<15 years	558	349	209	1.67 : 1	69.4

Table 18.2: ERF population by age and year of data collection

	Patient prevalent data						
Age (yrs)	1986	1992	1999	2001	2002	2003	2004
0–1.9		16	18	13	14	10	12
2–4.9		55	46	56	58	56	51
5–9.9		150	151	146	147	141	166
10–14.9		208	293	301	315	310	329
15–19.9			253	274	259	256	244
Total <15	263	429	508	516	534	517	558
Total <20			761	790	793	773	802
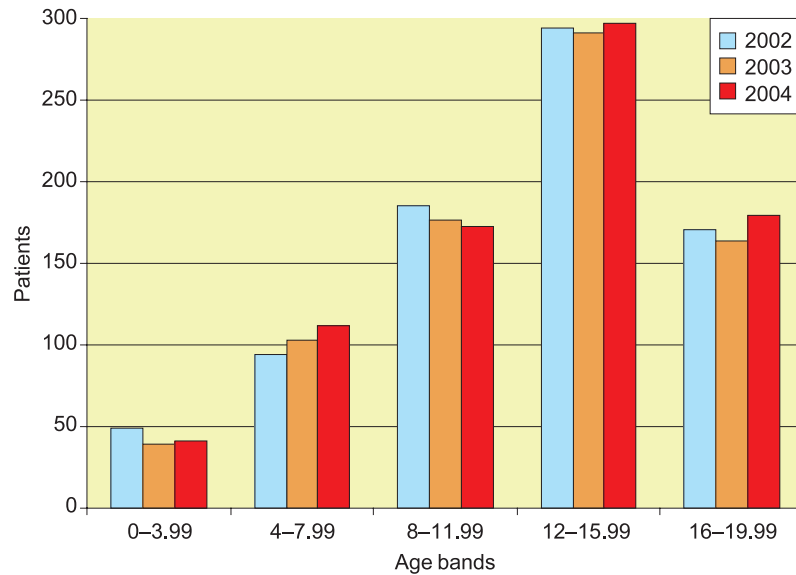
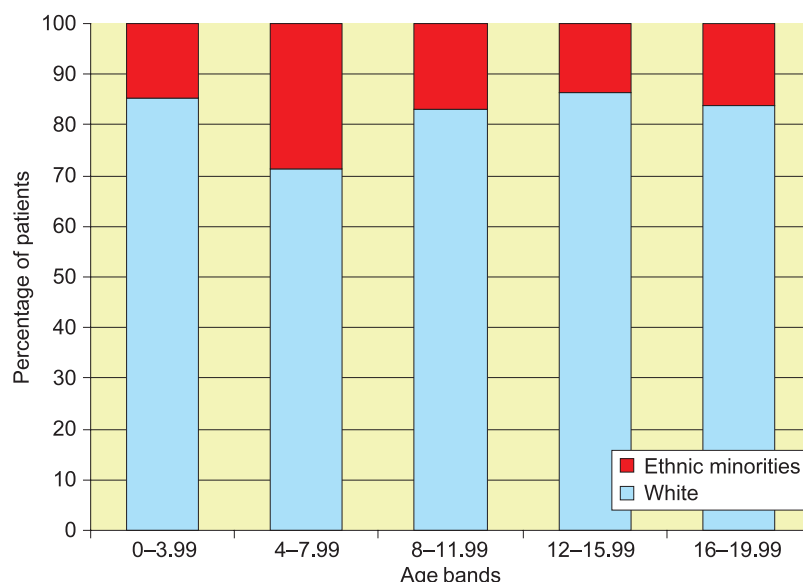**Figure 18.2: Prevalent paediatric ERF population 2002–2004 by age**
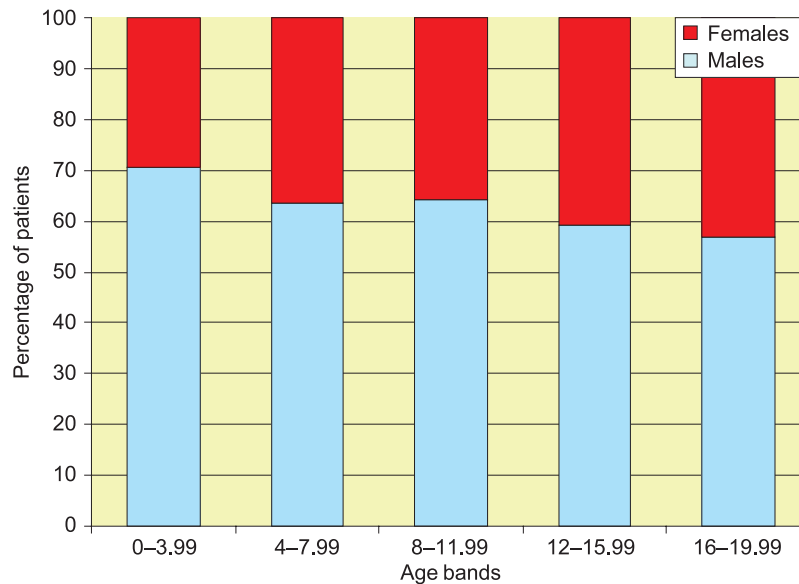
Figure 18.3: Gender distribution of the paediatric ERF population

clear. Firstly, as expected, the majority (83.0%) of the ERF population are White. However the observation that 17.0% come from ethnic minority groups, demonstrates that ethnic minorities are over-represented within the ERF population as these groups comprise just 7.9% of the total UK population. Within this, the greatest over-representation is from the South Asian community who form 13.6% of the paediatric ERF population, whilst just 4% of the general UK population is of South Asian origin. This is dealt with further in the section on prevalence. The other feature of note in Table 18.1 is that the male to female ratio is much lower in the South Asian population than in the White population. This difference is statistically significant ($p = 0.046$, Fisher's exact test). This relates to the different causes of ERF in the South Asian population and is dealt with further below.

Table 18.3: Age and gender distribution of the ERF population

Age (yrs)	Patients	Total %	Males	Females	Ratio
0–3.9	41	5.1	29	12	2.42 : 1
4–7.9	112	14.0	71	41	1.73 : 1
8–11.9	173	21.6	111	62	1.79 : 1
12–15.9	297	37.0	176	121	1.36 : 1
16–19.9	179	22.3	102	77	1.32 : 1
All <20	802	100.0	489	313	1.56 : 1

Figure 18.4: Ethnic distribution of the paediatric ERF population

**Table 18.4: Age and ethnic distribution of the ERF population**

Age (yrs)	Patients	White	South Asian	Black	Other
0–3.9	41	35	6	0	0
4–7.9	112	80	22	5	5
8–11.9	173	144	25	3	1
12–15.9	297	257	35	2	3
16–19.9	179	150	22	5	2
All <20	802	666	110	15	11

Table 18.4 shows a breakdown of the population according to ethnicity and age. This is shown graphically in Figure 18.4. There appears to be an excessive proportion of South Asian patients between the ages of 4 and 8 years. Grouping the populations into two groups of "White" and "ethnic minority" to allow meaningful analysis, the difference between the age distributions of the White and ethnic minority populations are statistically significant (Chi-square = 13.53, p = 0.009).

Whilst the UK has a large ethnic minority population, it is well recognised that this population is not evenly distributed across the UK. Indeed, 50% of the ethnic minority population reside in the Greater London area with significant pockets of ethnic minorities in other specific regions whilst some regions have very few citizens from ethnic minorities. Table 18.5 shows the distribution of the patients according to ethnicity within the 13 paediatric ERF units in the UK. The determinants of the number of patients being actively treated in each unit are both the size of the population covered and the proportion of this population that belongs to the ethnic minorities. Whilst 6 of the 13 renal units have very low proportions of patients from the ethnic minorities (under the 8% figure that constitutes the overall proportion of the ethnic minority citizens in the population), 4 units have an ethnic minority population over 20% (Figure 18.5). As discussed in previous reports, this will have implications for the provision of resources.

Table 18.5: Ethnicity distribution by unit

Centre	White	South Asian	Black	Other	Patients	% ethnic minority
Belfast	31	0	0	0	31	0.0
Birmingham	47	14	2	1	64	26.5
Bristol	50	2	0	0	52	3.8
Cardiff	29	1	0	0	30	3.3
Glasgow	54	3	0	0	57	5.2
GOSH	106	29	9	6	150	29.3
Guys	64	9	4	1	78	12.9
Leeds	48	15	0	0	63	23.8
Liverpool	34	1	0	0	35	2.9
Manchester	66	25	0	1	92	28.2
Newcastle	50	0	0	1	51	2.0
Nottingham	78	10	0	1	89	12.3
Southampton	11	1	0	0	12	8.3
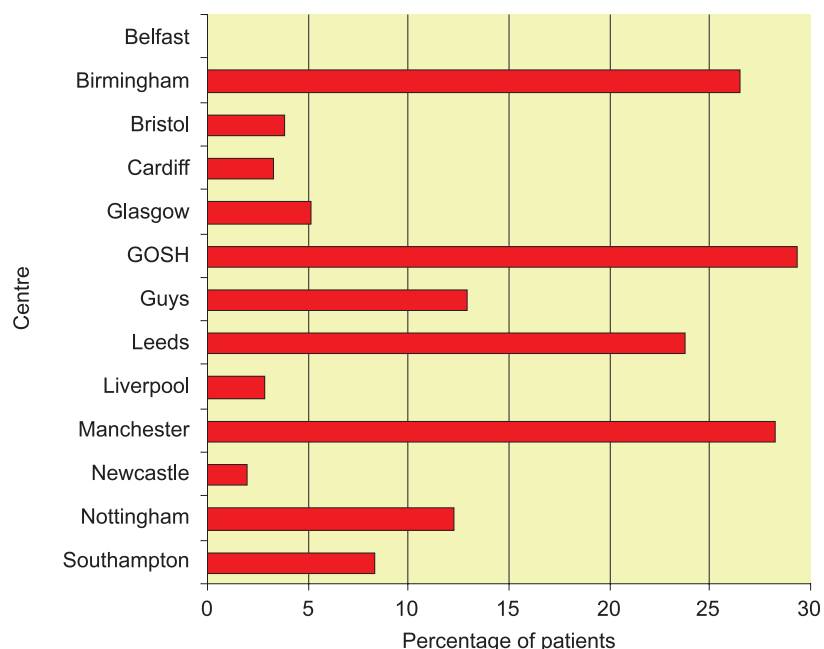
Figure 18.5: Percentage of each unit's patients from ethnic minority groups

Prevalence and take-on rate

Data on the UK population divided according to age and ethnic background was taken from the Office for National Statistics' Website (www.statistics.gov.uk). Data for this report is based upon population estimates for mid-2004 which themselves are based upon the United Kingdom Census of 2001. Table 18.6 shows the UK population in thousands according to age. For ethnicity, the statistics only allowed for the calculation of a total population under the age of 16 in each ethnic group. This is an important calculation as the proportion of children within ethnic minority families varies tremendously.
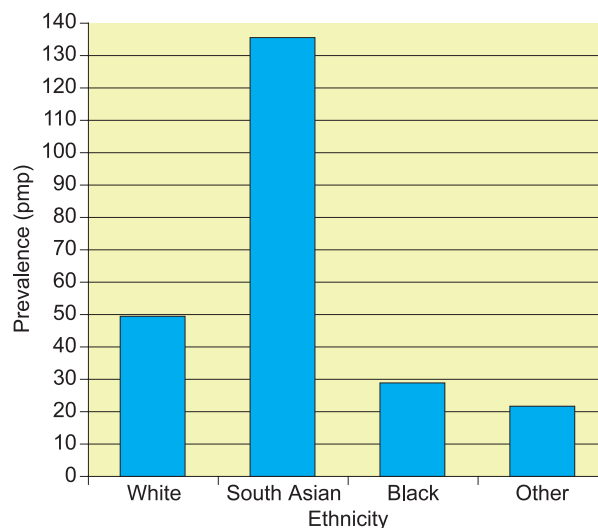
19% of the White population are under the age of 16, compared to 23% of the Indian population, 29% of the Black population and 38% of the Bangladeshi population. Failure to take account of the increased proportion of children in some of the ethnic minority populations can lead to an over-inflated prevalence and take-on rate.

Table 18.7 shows the prevalence of ERF according to age and gender. These figures are comparable to those in previous registry reports and to those published by the USRDS. The prevalence appears to drop over the age of 16 years but this is secondary to the transfer of

Table 18.6: Projected UK population in mid 2004 (thousands)

Age (yrs)	Total	Male	Female
0–3.9	2,708	1,387	1,321
4–7.9	2,829	1,449	1,380
8–11.9	2,967	1,521	1,446
12–15.9	3,142	1,613	1,529
16–19.9	3,142	1,617	1,524
<15	10,867	5,570	5,297
<18	13,222	6,780	6,442
<20	14,788	7,587	7,201
Total pop	59,835	29,271	30,564

Figure 18.6: Prevalence of ERF in children by ethnicity

patients to adult renal units. In reality, the prevalence of ERF continues to rise with age. This will be clarified once all renal units can submit data electronically to the UK Renal Registry, allowing for continuity of analysis between paediatric and adult centres. As prevalence data obtained by the paediatric Registry is currently unreliable above the age of 16 years, only patients below this age were included for the calculation of prevalence by ethnicity. Figure 18.6 shows the prevalence of ERF in children according to ethnicity. These figures are calculated taking account of the increased proportion of children comprising the ethnic minority population as detailed above. Whilst the prevalence of ERF in the White population is similar to that reported from other developed nations, the prevalence in those from the South Asian community is almost three times as high. This difference in prevalence between the two communities is highly significant (Chi-square = 82.52, p < 0.0001). The reason for this seems to reside in the different patterns of renal pathology seen in this population as discussed below. The prevalence of ERF in the Black population appears to be lower than might be

expected. Again, this is likely to be related to the patterns of disease seen in this population. The prevalence of ERF in the Black population is much higher than that reported from Nigeria (although reporting systems there are poor) but lower than that reported in the US. The difference in prevalence between the Black and the White population fails to meet statistical significance (Chi-square = 2.477, p = 0.1155).

To reduce the year to year variability seen when the number of new patients are relatively small, the acceptance rate has been calculated using an average of the patients accepted onto the ERF programme over the 5 years up to 1st April 2004. Table 18.8 shows the patients accepted onto the paediatric ERF programme over the past 5 years. This incidence data is shown graphically according to ethnicity rather than age in Figure 18.7. The picture for take-on rate shows an identical pattern to that for prevalence. The take-on rate for South Asians

Table 18.7: Prevalence of ERF per million childhood population

Age (yrs)	All patients		Males		Females	
	Patients	Prevalence	Patients	Prevalence	Patients	Prevalence
0–3.9	41	15.1	29	20.9	12	9.1
4–7.9	112	39.6	71	49.0	41	29.7
8–11.9	173	58.3	111	73.0	62	42.9
12–15.9	297	94.5	176	109.1	121	79.2
16–19.9	179	57.0	102	63.1	77	50.5
<15	558	51.4	349	62.7	209	39.5

Table 18.8: Take on rate for patients with ERF per million childhood population

	All patients		Males		Females	
Age (yrs)	Patients	Take on rate	Patients	Take on rate	Patients	Take on rate
0–3.9	23	8	14	10	9	7
4–7.9	16	5	9	6	7	5
8–11.9	26	9	14	9	12	9
12–15.9	37	12	19	12	18	12
<15	93	9	51	9	42	8
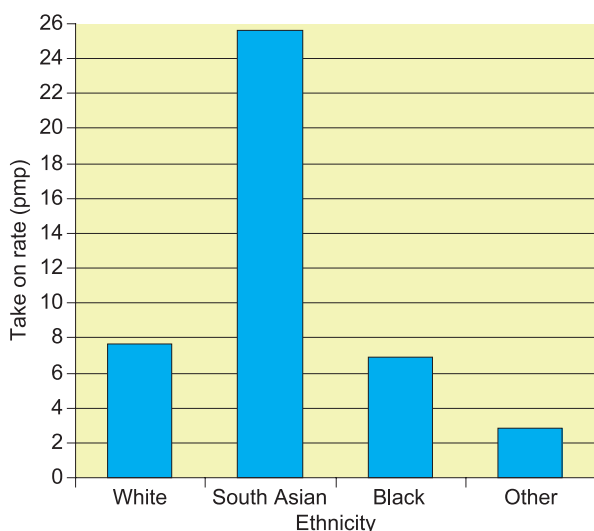
Figure 18.7: Take on rate for children starting RRT by ethnicity

is 3.35 times that of the White population. Currently the prevalence of ERF in the South Asian population is 2.75 times that of the White population. This would suggest that the proportion of South Asians on the paediatric ERF programme is likely to continue rising.

Causes of ERF in Children

The return rate for ERF diagnosis was higher than for any other data item with 96.3% of current patients having an ERF diagnosis allocated. To give a true picture of the distribution of diagnoses, all patients presenting after 1st April 1996 (when data collection began) were analysed even if they had been transferred or died. Using the current population for this analysis gives a false picture as those with specific diseases associated with early onset ERF in childhood are over-represented because of their lengthy stay in paediatric care, whilst those with later onset ERF are under-represented because they are transferred after just a brief period of paediatric care.

Primary ERF diagnoses were available for 845 patients presenting after 1st April 1996. These diagnoses have been grouped into 12 broad categories. Table 18.9 shows the distribution of patients between these categories. When analysed this way renal dysplasias remain the most common group of disorders causing ERF in childhood, closely followed by glomerular

Table 18.9: ERF diagnostic grouping for 845 patients presenting after 1st April 1996

Diagnostic group	Patients	Males	Females	Ratio
Dysplasia	198	124	74	1.68 : 1
Glomerulopathy	195	88	107	0.82 : 1
Obstructive uropathy	131	116	15	7.73 : 1
Reflux nephropathy	67	32	35	0.91 : 1
Tubulo-interstitial diseases	63	34	29	1.17 : 1
Congenital nephrotic syndrome	45	18	27	0.67 : 1
Metabolic diseases	41	23	18	1.28 : 1
Reno-vascular problems	31	16	15	1.06 : 1
Polycystic kidney disease	24	8	16	0.50 : 1
CRF of uncertain aetiology	23	11	12	0.92 : 1
CRF from drug nephrotoxicity	17	12	5	2.40 : 1
Malignancy & associated disease	10	5	5	1.00 : 1

diseases. Obstructive uropathy is the third most common group. For those groups of disorders comprising more than one diagnosis, a further breakdown of cause is given in Tables 18.10–18.19.

Within the renal dysplasia group, the most common diagnosis is renal dysplasia itself. Of these 164 patients with renal dysplasia, 40 (24.4%) had an associated syndromic diagnosis, chromosomal anomaly or other congenital anomalies. Ten of this subgroup had associated developmental delay at presentation whilst just 7 of the remaining 124 patients with renal dysplasia as a cause of ERF had developmental delay. This significant increase in developmental delay at presentation ($p = 0.0014$, Fisher's exact test) in children with other congenital problems

Table 18.10: Diagnoses for patients with renal dysplasia

Diagnoses in renal dysplasia group	Patients	Males	Females	Ratio
Renal dysplasia	164	102	62	1.65 : 1
Multicystic dysplastic kidneys	11	5	6	0.83 : 1
Prune belly syndrome	8	8	0	
Renal hypoplasia	7	3	4	0.75 : 1
Branchio-oto-renal syndrome	3	3	0	
Lawrence Moon Bardet Biedl syndrome	3	1	2	0.50 : 1
Megacystis megaureter	2	2	0	

Table 18.11: Diagnoses for patients with glomerulopathy

Diagnoses in glomerulopathy group	Patients	Males	Females	Ratio
Primary focal segmental glomerulosclerosis	83	40	43	0.93 : 1
Diarrhoea positive HUS	17	8	9	0.89 : 1
Henoch Schoenlein nephritis	13	4	9	0.44 : 1
Diarrhoea negative HUS	11	3	8	0.38 : 1
GN (unspecified)	10	6	4	1.50 : 1
Alport's syndrome	9	8	1	8.00 : 1
IgA nephropathy	9	5	4	1.25 : 1
Mesangio-capillary GN type 1	9	4	5	0.80 : 1
Crescentic GN	8	4	4	1.00 : 1
Proliferative GN	6	2	4	0.50 : 1
Systemic lupus erythematosis	6	1	5	0.20 : 1
Anti GBM disease	3	0	3	
Mesangio-capillary GN type 2	3	0	3	
Microscopic polyarteritis nodosa	3	1	2	0.50 : 1
Wegner's granulomatosis	3	2	1	2.00 : 1
Macroscopic polyarteritis nodosa	1	0	1	
Vasculitis (unspecified)	1	0	1	

Table 18.12: Diagnoses for patients with obstructive uropathy

Diagnoses in Obstructive uropathy group	Patients	Males	Females	Ratio
Posterior urethral valves	98	98	0	
Neuropathic bladder	13	3	10	0.30 : 1
Bladder outlet obstruction*	11	9	2	4.50 : 1
Congenital obstructive uropathy**	7	4	3	1.25 : 1
Acquired obstructive uropathy	2	2	0	

*Excluding posterior urethral valves.
**Excluding bladder outlet obstruction.

Table 18.13: Diagnoses for patients with tubulo-interstitial disease

Diagnoses	Patients	Males	Females	Ratio
Nephronophthisis	51	26	25	1.04 : 1
Primary interstitial nephritis	7	5	2	2.50 : 1
Bartter's syndrome	2	1	1	1.00 : 1
Nephrocalcinosis	1	0	1	
Renal tubular acidosis	1	1	0	
Tubular disorders (other)	1	1	0	

Table 18.14: Diagnoses for patients with congenital nephrotic syndrome

Diagnoses	Patients	Males	Females	Ratio
CNS unspecified	20	5	15	0.33 : 1
Finnish type	17	8	9	0.89 : 1
Diffuse mesangial sclerosis	5	4	1	4.00 : 1
Focal segmental glomerulosclerosis	3	1	2	0.50 : 1

Table 18.15: Diagnoses for patients with metabolic diseases

Diagnoses	Patients	Males	Females	Ratio
Cystinosis	34	19	15	1.27 : 1
Primary hyperoxaluria type 1	3	2	1	2.00 : 1
Mitochondrial cytopathy	3	1	2	0.50 : 1
Metabolic disease (other)	1	1	0	

Table 18.16: Diagnoses for patients with reno-vascular disease

Diagnoses	Patients	Males	Females	Ratio
Cortical necrosis	20	9	11	0.82 : 1
Renal vein thrombosis	7	5	2	2.50 : 1
Renal artery stenosis	2	1	1	1.00 : 1
Renal trauma	2	1	1	1.00 : 1

Table 18.17: Diagnoses for patients with polycystic kidney disease

Diagnoses	Patients	Males	Females	Ratio
Recessive PKD	18	5	13	0.38 : 1
PKD (other)	4	2	2	1.00 : 1
Dominant PKD	1	1	0	
Tuberous sclerosis with PKD	1	0	1	

Table 18.18: Diagnoses for patients with CRF from drug nephrotoxicity

CRF from drug nephrotoxicity	Patients	Males	Females	Ratio
Calcineurin inhibitor nephrotoxicity	13	10	3	3.30 : 1
Cytotoxic drug nephrotoxicity	4	2	2	1.00 : 1

Table 18.19: Diagnoses for patients with malignant disease

Diagnoses	Patients	Males	Females	Ratio
Wilms' tumour	7	3	4	0.75 : 1
Wilms' nephropathy	3	2	1	2.00 : 1

is not surprising but has not previously been quantified. Even excluding diagnoses such as prune belly syndrome, where the patients are by definition male, renal dysplasia is a more common cause of renal failure in males than females (Table 18.10). This is not offset by the slightly increased frequency of reflux nephropathy as a cause of ERF in females (Table 18.9) and contributes significantly to the overall preponderance of males with ERF.

Within the group of patients with glomerular disease as a cause of ERF, it can be seen from Table 18.11 that primary focal segmental glomerulosclerosis is the single most common disorder accounting for 43% of all cases. Diarrhoea associated haemolytic uraemic syndrome and Henoch Schoenlein nephritis are the next two most common problems and together these three disorders, which are rare causes of ERF in adults, account for 58% of paediatric patients with ERF from glomerulopathy.

Within the group of patients with obstructive uropathy as a cause of ERF, the vast majority (74.8%) have posterior urethral valves. This by definition is limited to males and is the other major contributor to the preponderance of males in the paediatric ERF population. Within the small group with ERF secondary to a neuropathic bladder, females significantly outnumber males.

For those patients with tubulo-interstitial disease, nephronophthisis was the predominant diagnosis accounting for 80.9% of cases. Twenty seven percent of these (14 of 51) were in-patients who also had a syndromic diagnosis, chromosomal abnormality or congenital abnormality recognised at presentation. Six of this group had developmental delay evident at presentation, 3 of these were in the group who had a syndromic diagnosis.

For those with congenital nephrotic syndrome, 44% are in the ''unspecified group'', the majority of these will be presumed to have Finnish type disease. In many centres, after a typical presentation with congenital nephrotic syndrome, obtaining a firm histological diagnosis is not felt to be a procedure where the benefits outweigh the risks or influence management.

Cystinosis is the main cause of ERF in those with metabolic disease whilst cortical necrosis predominates in those with ERF from reno-vascular problems. Recessive polycystic kidney disease, not surprisingly, accounts for 75% of those with polycystic disease leading to ERF. What is surprising in this group is the preponderance of females in a disease with autosomal recessive inheritance.

Renal failure from drug nephrotoxicity is presented as a separate group for the first time. Although it only accounts for 1.5% of patients it is an important group as the numbers appear to be increasing and, theoretically, it is a preventable cause of renal failure. Whilst historically this group comprised patients who had renal failure secondary to the toxicity of cytotoxic drugs used to treat malignancy, now the majority of patients have renal failure secondary to calcineurin inhibitor toxicity. Of these 13 patients, 4 were documented to have a liver allograft, four a heart allograft and one heart and lungs grafted.

Wilms' tumour is the only malignancy causing ERF in this paediatric group. Some children with the WT1 mutation are documented to be in established renal failure from the associated nephropathy without ever developing a tumour. In some instances this will be because elective bilateral native nephrectomy has been undertaken after making a diagnosis to prevent the progression to malignancy.

ERF aetiology and ethnicity

The pattern of disease causing ERF in children varies between ethnic groups and this accounts for much of the difference noted above in the incidence and prevalence of ERF in the different ethnic groups. Table 18.20 shows the diagnostic groups detailed above but broken down according to ethnicity rather than gender. Dysplasia, glomerulopathy and obstructive uropathy predominate in the White population, these 3 groups accounting for 64.1% of patients. In South Asian patients there is a more even spread across the groups with only 48.4% of patients having dysplasia, glomerulopathy or obstructive uropathy. In the Black population glomerulopathy alone accounts for 64.7% of patients, with dysplasia being relatively rare and no cases of obstructive uropathy

Table 18.20: Ethnic distribution of ERF diagnostic groups

Diagnostic group	White	South Asian	Black	Other
Dysplasia	176	19	3	0
Glomerulopathy	155	25	11	4
Obstructive uropathy	112	17	0	2
Reflux nephropathy	58	6	1	2
Tubulo-interstitial diseases	46	15	0	2
Congenital nephrotic syndrome	29	16	0	0
Metabolic diseases	29	12	0	0
Reno-vascular problems	29	2	0	0
Polycystic kidney disease	17	5	1	1
CRF of uncertain aetiology	16	6	1	0
CRF from drug nephrotoxicity	15	2	0	0
Malignant disease	9	1	0	0

Table 18.21: Ethnic distribution of ERF combined diagnostic groups

Combined diagnostic groups	White	South Asian	Black	Other
Group 1	346	42	4	4
Group 2	155	25	11	4
Group 3	121	48	1	3
Group 4	69	11	1	0

Group 1 = Dysplasia + Obstructive + Reflux
Group 2 = Glomerulopathy
Group 3 = Tubulo-interstitial disease + Metabolic disease + PKD + CNS
Group 4 = Reno-vascular disease + Malignant disease + Drug nephrotoxicity + CRF of uncertain aetiology

being included in this cohort. This different pattern of disease in the Black population is the likely cause of the low incidence and prevalence in this group.

To allow meaningful statistical analysis of the pattern of disease, these have been further grouped into four categories. The first of these contains patients who have structural problems and includes patients from the dysplasia, obstructive uropathy and reflux nephropathy groups. The second is just for patients with glomerulopathy. The third contains the patients with mostly inherited diseases – tubulo-interstitial disease, metabolic disease, congenital nephrotic syndrome and polycystic disease. The fourth group contains the other remaining patients. The results of this regrouping are shown in Table 18.21. Whilst 50% of White patients belong to group 1, the largest single group in the South Asian population is group 3. This comprises 38% of the patients and demonstrates the importance of inherited disease in the aetiology of renal failure in this population. The difference in the distribution of disease groups between the White and South Asian populations is significant (Chi square = 23.78, p < 0.0001). This difference remains significant when the White population is compared to the total ethnic minority population (Figure 18.8).
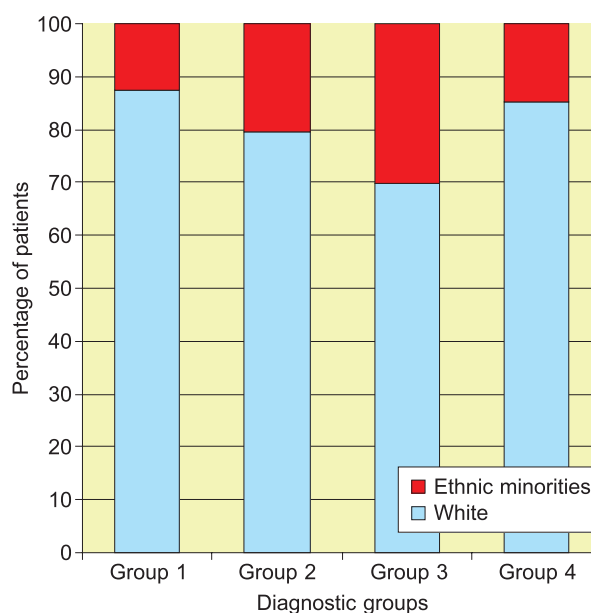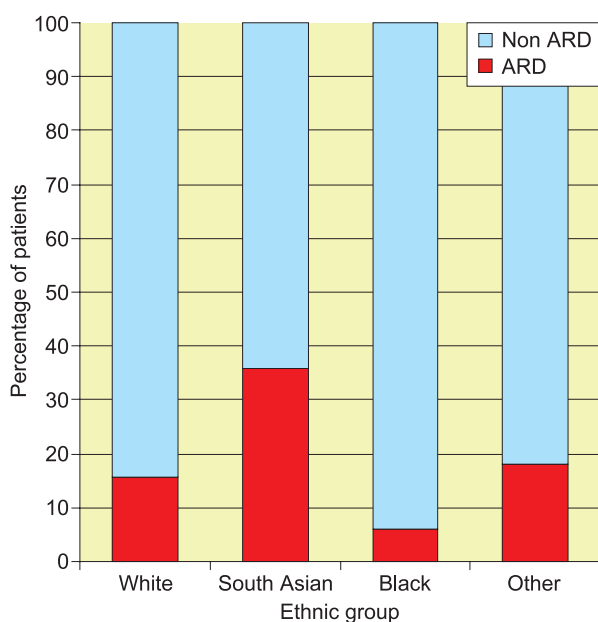

Figure 18.8: Ethnic distribution of the grouped ERF diagnoses

Table 18.22: Ethnic distribution disease by inheritance

Disease inheritance	White	South Asian	Black	Other
Autosomal recessive	108	45	1	2
Autosomal dominant	5	0	0	0
Sex linked	6	2	1	0
Mitochondrial disease	3	0	0	0
Not directly inherited	569	79	15	9

To confirm that these findings are due to inherited diseases, compounded in the South Asian community by a high frequency of consanguineous marriage, these data have been analysed according to the known usual inheritance of each pathology. This is shown in Table 18.22.

Almost 80% of patients have diseases leading to renal failure which are not directly inherited. Of the rest, 90% are diseases which are inherited in an autosomal recessive manner. The higher proportion of patients with autosomal recessive disease in the South Asian population compared with the White population is very significant (p < 0.0001, Fisher's exact test, Figure 18.9). This suggests that consanguinity and consequent autosomal recessive disease is a large factor in the high incidence and prevalence of ERF in the South Asian community. Reducing the frequency of autosomal recessive disease in the South Asian community to that of the White population would lead to a 26%

reduction in incidence and prevalence. Such a reduction would make the incidence of ERF in the South Asian community 18.9 per million population. Thus, although significantly reduced, the incidence would still be 2.48 times that of the White population (compared with a current incidence ratio of 3.35). Clearly, there are other factors that also contribute to the high incidence of ERF in children in the South Asian population.

Current treatment of paediatric ERF patients

Details of treatment modality on 1st April 2004 were available for 786 of the 804 patients (97.5%). The distribution of treatments is shown in Figure 18.10. A total of 195 patients were on dialysis whilst 591 (75.2%) had a functioning allograft. Of those with a functioning graft, 151 (25.5%) had grafts from living donors (LD) whilst the majority (74.5%) had cadaveric (CAD) grafts. Peritoneal dialysis was the preferred mode of dialysis management with 58% of dialysis patients being treated this way. Of these 111 patients, 99 were on automated

Figure 18.9: Autosomal recessive disease (ARD) as a cause of ERF by ethnicity
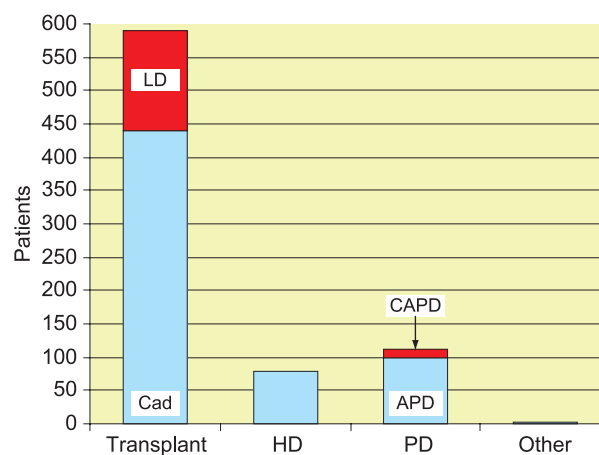
Figure 18.10: Distribution of patients by modality on 1st April 2004
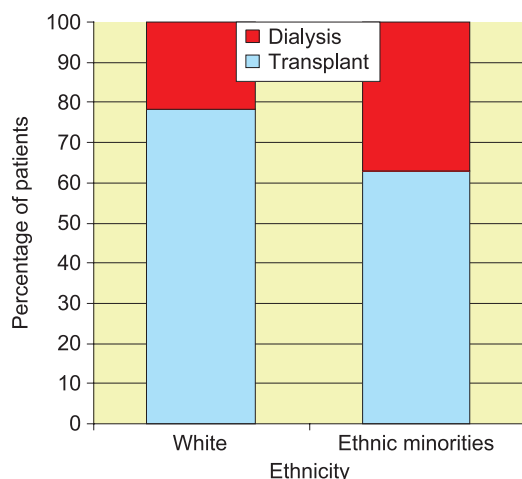
Figure 18.11: Distribution of dialysis and transplant patients by ethnicity
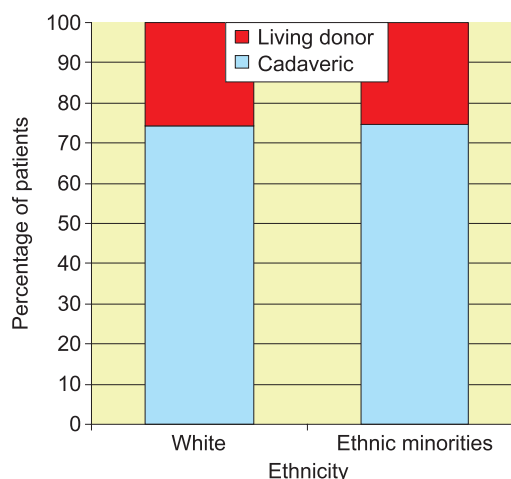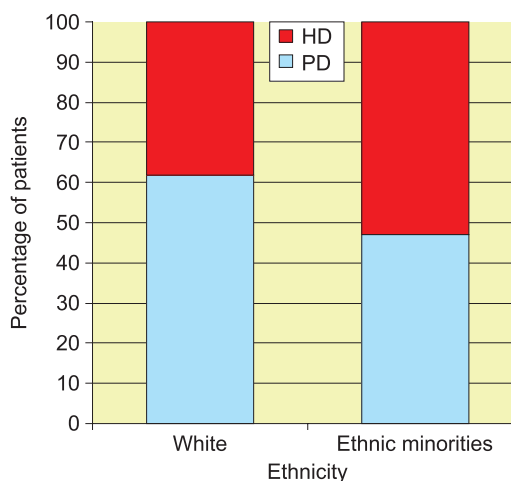

Figure 18.12: Distribution of transplant patients by ethnicity

Figure 18.13: Distribution of dialysis patients by ethnicity

peritoneal dialysis whilst just 12 were on CAPD. Two patients were not receiving any active treatment at the time. In one patient active management had been ceased whilst in the other the patient was between dialysis modalities and was surviving on residual renal function.

As in previous years, a significantly greater proportion of the White population had a functioning allograft compared with the ethnic minority groups (p = 0.0003, Fisher's exact test, Figure 18.11). For those who did have a functioning allograft, there was no difference in the proportion that had a graft from a living donor rather than a cadaveric graft between the ethnic minority groups and the White population (Figure 18.12.) Thus, despite the difficulty in getting cadaveric grafts for ethnic minority patients, there has been no move towards the more aggressive promotion of living donor transplantation. This explains the excessive proportion of ethnic minority patients being treated with dialysis (Table 18.23).

For those patients on dialysis, almost two thirds of the White population were being treated with peritoneal dialysis whilst over 50% of the ethnic minority population were on haemodialysis (Figure 18.13). Whilst in previous years the difference between dialysis modality in the White and ethnic minority populations was statistically significant, this year it was not (p = 0.0925, Fisher's exact test). The reason for this is shown in Figure 18.14, which compares the dialysis population for 2003 and 2004.

Table 18.23: Modality on 1st April 2004 by ethnicity

Modality	White	South Asian	Black	Other
Transplant (All)	508	68	8	7
Transplant (Cadaveric)	378	53	5	4
Transplant (Living donor)	130	15	3	3
Haemodialysis	54	21	3	2
Peritoneal dialysis	88	18	3	2
Other	2	0	0	0
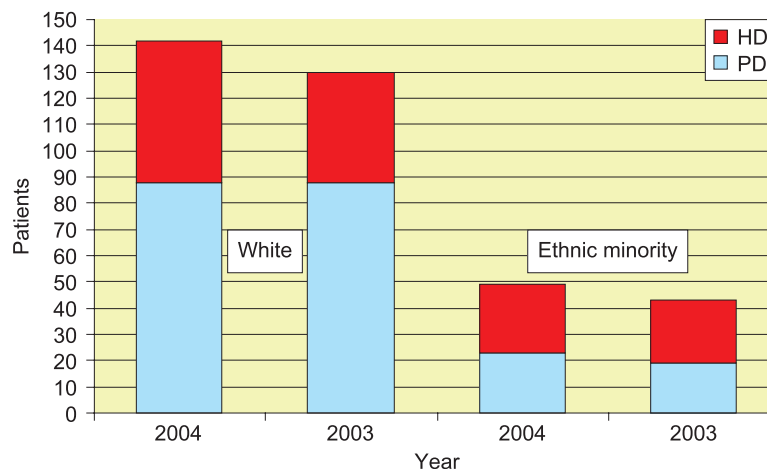
Figure 18.14: Change in the numbers of dialysis patients between 2004 and 2003 by ethnicity

Whilst for the ethnic minority groups there has been an equal increase in both the haemodialysis and peritoneal dialysis population, in White patients the number of peritoneal dialysis patients has been static whilst the haemodialysis population has grown. This change is related to the management of long-term dialysis patients and those returning to dialysis after allograft failure as peritoneal dialysis remains the primary initial treatment modality in this population.

Differences exist between renal units in the proportion of patients transplanted and, for those remaining on dialysis, the proportions using each dialysis modality available. Table 18.24 shows a breakdown of the number of patients with a functioning allograft or on

dialysis according to treatment centre. The proportion of patients with a functioning allograft varies widely from 49–91%. In part, this difference will undoubtedly relate to the ethnic distribution of the population covered by the treatment centre. Another factor is the individual centre's approach to living donation. Table 18.25 shows the proportion of engrafted patients in each treatment centre who have living donor allografts. Again, there is a wide variation from 3% to almost 86%. Currently, 10 of the 13 regional paediatric nephrology units within the UK are performing transplantation. By allocating all patients to their transplanting centre, it is possible to compare the proportion of transplanted patients with living donor allografts to the overall proportion
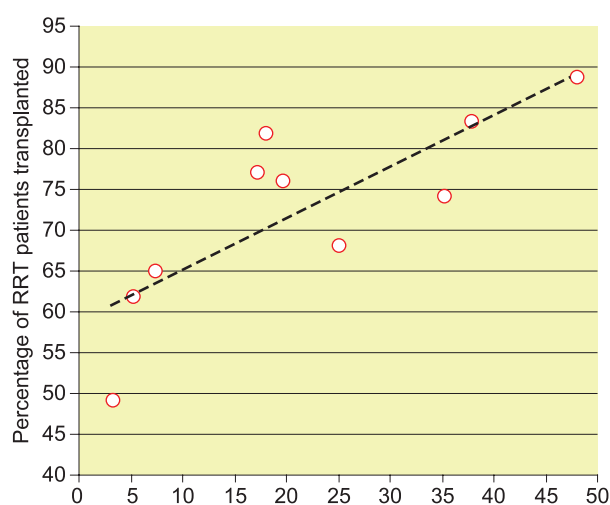
Table 18.24: Proportion of patients transplanted by centre

Renal unit	Patients			
	Transplant	Dialysis	Total	% grafted
Belfast	19	12	31	61.9
Birmingham	31	32	63	49.2
Bristol	41	12	53	77.4
Cardiff	23	7	30	76.7
Glasgow	45	9	54	83.3
GOSH	116	31	147	78.9
Guys	72	5	77	93.5
Leeds	41	22	63	65.1
Liverpool	22	7	29	75.8
Manchester	70	22	92	76.1
Newcastle	32	15	47	68.1
Nottingham	72	16	88	81.8
Southampton	7	5	12	58.3
Total	**591**	**195**	**786**	**75.2**

Table 18.25: Living donor vs cadaveric allografts by centre

Renal unit	Patients with allografts			
	Living donor	Cadaveric	Total	% living donor
Belfast	1	18	19	5.3
Birmingham	1	30	31	3.2
Bristol	9	32	41	22.0
Cardiff	2	21	23	8.7
Glasgow	17	28	45	37.8
GOSH	41	75	116	35.3
Guys	32	40	72	44.4
Leeds	3	38	41	7.3
Liverpool	4	18	22	18.1
Manchester	14	56	70	20.0
Newcastle	8	24	32	25.0
Nottingham	13	59	72	18.1
Southampton	6	1	7	85.7
Total	**151**	**440**	**591**	**25.5**

of transplanted patients. These data are shown in Figure 18.15. There is a clear correlation between the proportion with living donor allografts and the overall proportion engrafted ($p = 0.0053$). These differences between renal units may relate to both the populations served and also the approach to living donation taken. These data emphasise the shortage of deceased donor grafts; if there were an unlimited supply of grafts, the transplantation rates between centres would not vary in this way. More research in this area is required to see if an alteration in approach could improve the living donor transplant rates in some centres.

With regard to dialysis modality, there is wide variation between renal units in the proportion of patients receiving peritoneal rather than haemodialysis. Interpretation of these snapshot data, however, is difficult as the numbers are small and the situation is very fluid with patients moving from one modality to another. One thing that does stand out is the popularity of APD with CAPD only being a regular treatment option in one renal unit (Table 18.26).

Table 18.26: Dialysis modality by centre

Renal unit	Patients with allografts			
	CAPD	APD	HD	% PD
Belfast	0	6	6	50.0
Birmingham	0	20	12	62.5
Bristol	0	8	4	66.7
Cardiff	0	2	5	28.5
Glasgow	0	4	5	44.4
GOSH	1	22	8	74.2
Guys	0	2	3	40.0
Leeds	0	14	4	77.7
Liverpool	0	6	1	85.7
Manchester	8	5	9	59.1
Newcastle	0	5	10	33.3
Nottingham	0	6	10	37.5
Southampton	2	0	3	40.0
Total	**11**	**100**	**80**	**58.1**

Figure 18.15: Percentage of grafted patients with living donor graft by centre

Co-morbidity in paediatric ERF patients

In addition to the well recognised co-morbid conditions that influence outcome in both adults and children with ERF, there are a number of problems that are specific to those commencing ERF as children, though with successful management of ERF, these will also have an impact upon management in adult units in time. The paediatric registry documents the presence or absence of a number of specific co-morbid features at presentation with ERF. These include cerebral palsy, developmental delay, chromosomal anomalies, non-renal tract congenital abnormalities, syndromal diagnoses, neural tube defects and congenital heart disease. Figure 18.16 shows the incidence of these problems amongst 868 patients presenting with ERF between the 1st April 1996 and 1st April 2004. Overall, 21.7% of patients had one or more of these co-morbid problems at presentation. The most common of these is developmental delay affecting 8.9% of patients. This figure will actually be an under-estimate of the true incidence of developmental delay as, in those patients presenting at birth or within infancy, developmental delay may not be apparent at the time of presentation.

Table 18.27 shows the numbers of patients with and without these co-morbid problems at the time of presentation with ERF, broken down according to age at presentation. It is

Table 18.27: Presentation co-morbidity by age at ERF start

| Age band	Normal	Co-morbidity	Total	% with co-morbidity
0–3.9	129	52	181	28.7
4–7.9	88	31	119	29.4
8–11.9	166	35	201	17.4
12–15.9	245	54	299	18.1
16–19.9	52	16	68	23.5

clear that these co-morbidities are more common in the younger age-groups. Comparing patients starting ERF management below the age of 8 years with those starting between 8 and 16 years of age, there is a significant difference in the incidence of co-morbidity ($p = 0.0013$, Fisher's exact test). Over the age of 16 years there seems to again be a high incidence of patients with co-morbidity starting ERF treatment. This is likely to be because patients with these co-morbidities will be kept on and treated in paediatric units initially whilst patients without co-morbidity in this age-group will often start ERF treatment in an adult unit.

Co-morbidity is not associated with ethnic origin. Of 706 White patients in this cohort, 156 had co-morbidities at presentation, whilst 32 of 159 patients from ethnic minorities were affected by these. There was, however, an association between co-morbidity at presentation and gender with females being more frequently
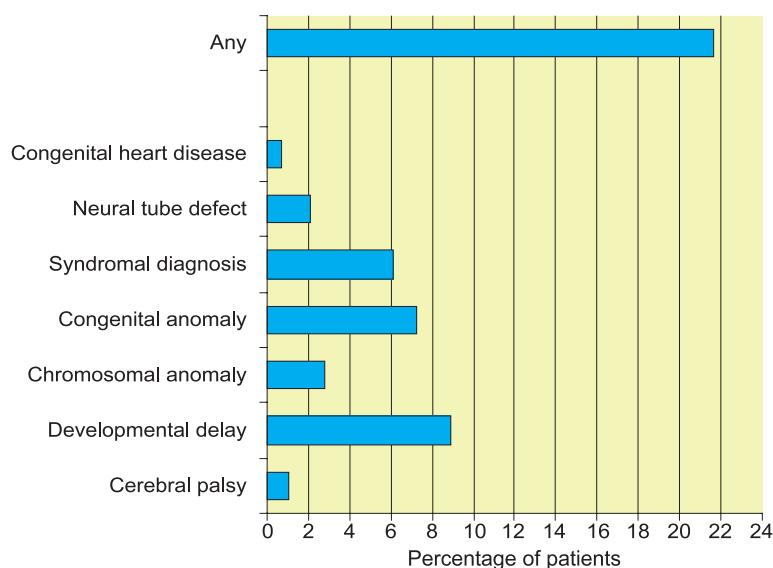
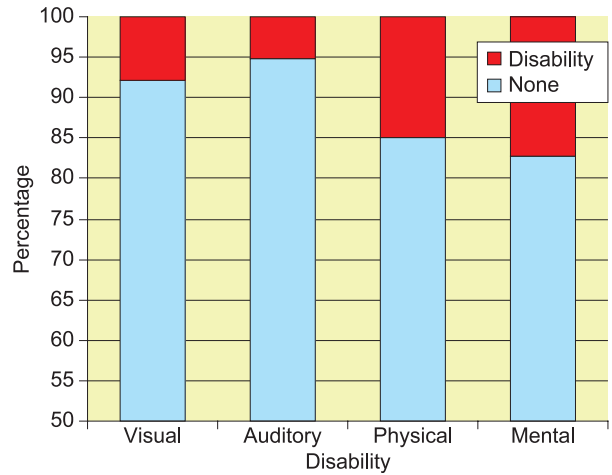**Figure 18.16: Percentage of patients with co-morbidity noted at presentation**
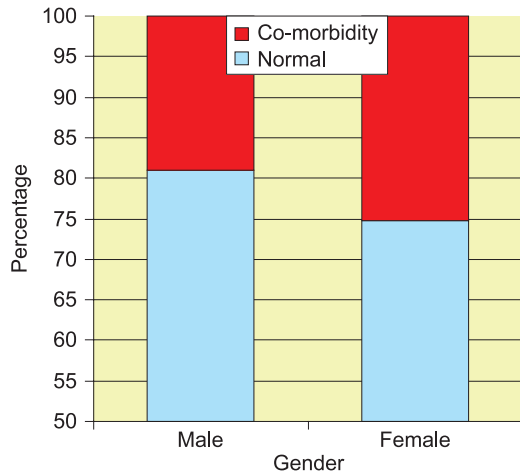
Figure 18.17: Presentation co-morbidity by gender

Figure 18.18: Prevalence of disability in the ERF population

affected than males (p = 0.0301, Fisher's exact test, Figure 18.17). This seems to be related to the aetiology of renal failure with the large number of young boys with either posterior urethral valves or renal dysplasia as a cause of ERF reducing the proportion of patients with other pathologies associated with co-morbid problems.

The collection of data about ongoing and new co-morbidity is difficult when dealing with a cohort of children with widely ranging problems and backgrounds. To allow comparisons to be made, the annual data collection tool includes four broad questions about the presence or absence of disability in four areas. These are visual disability, auditory disability, physical disability and mental disability. Each of these disabilities is graded as "none", "mild", "moderate" or "severe". Current status records were available for 748 patients in 2004. Of these, the fields detailing disabilities were completed for 723 patients (96.7%). Table 18.28 shows the results of the analysis of these records. Mental disability was the most common problem with 17.2% of patients having some degree of disability in this area

and 7.3% having moderate or severe disability. The proportions of patients showing any disability in these areas or just moderate or severe disability in these areas are shown graphically in Figures 18.18 and 18.19. There was no significant difference in the prevalence of moderate or severe physical or mental disability between the genders nor was there any association between these disabilities and ethnicity. The disappearance of the association between female gender and mental impairment on current analysis when compared with presentation is secondary to the appreciation of disability in those boys presenting with ERF in infancy. Whether these patients have acquired disability as a complication of ERF management or were destined to have these disabilities anyway is impossible to determine from the available information.

Table 18.28: Levels of disability in the current ERF population

Disability	None	Mild	Moderate	Severe
Visual	666	41	10	6
Auditory	685	15	12	11
Physical	615	66	33	9
Mental	599	71	42	11
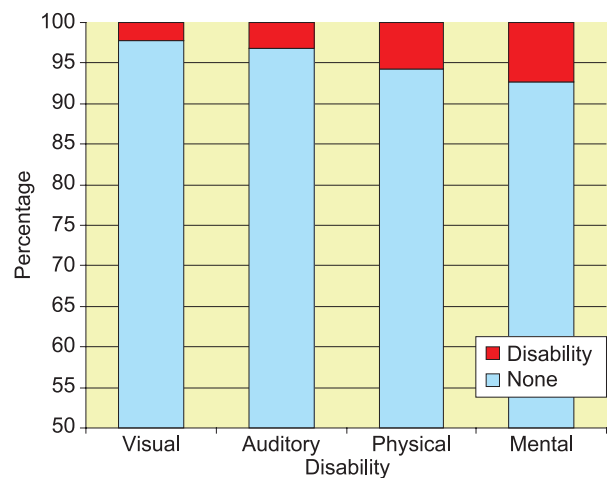
Figure 18.19: Prevalence of significant disability in the ERF population
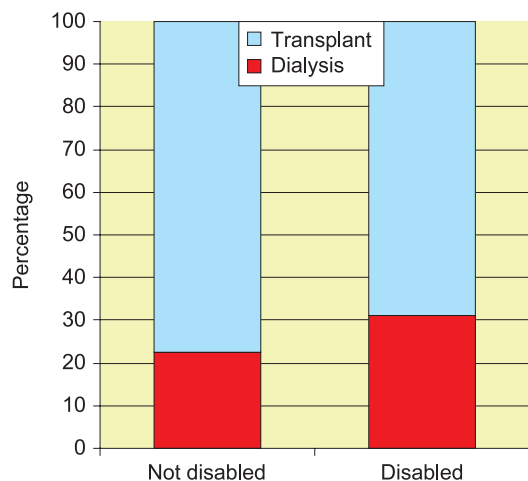
Figure 18.20: Treatment modality in those with moderate or severe mental and/or physical disability compared with patients with no disability

There are undoubtedly some patients in whom their degree of disability and the nature of this disability influences ERF management. Looking at the population as a whole, however, this was not the case. Figure 18.20 shows those patients with moderate or severe mental or physical disability compared to those with no disability. Although the proportion of patients on dialysis, rather than having a functioning allograft, is greater in the group of patients with disabilities, this did not reach statistical significance (p = 0.1087, Fishers exact test).

Patients on long-term dialysis

The overall mortality rate for children on renal replacement therapy is 25–30 times higher than expected for age[1,2,3]. Cardiovascular events cause up to 50% of these deaths[1,2,3].

Overall, children on dialysis have a 4-fold risk of death compared to children with a functioning renal transplant. There was no difference in mortality between children receiving a pre-emptive transplant and those who had received up to 24 months of dialysis pre-transplant[1]. However, those who have "relatively long-term dialysis", defined as having more days of RRT on dialysis than with a functioning transplant, have a mortality hazard ratio of 7.2 compared to children receiving RRT as a functioning transplant but not dialysis[2]. Those children with relatively long-term haemodialysis have a higher mortality rate than those on relatively long-term peritoneal

Table 18.29: Duration of continuous dialysis treatment for current patients

Dialysis duration (yrs)	Patients	Previous allograft	No previous allograft
<1	65	8	57
1–1.9	54	7	47
2–2.9	25	4	21
3–3.9	18	2	16
4–4.9	8	2	6
⩾5	13	1	12

dialysis. This may reflect the more complex medical problems or longer total duration of dialysis of children who need to be on haemodialysis, as most paediatric units favour peritoneal dialysis as the initial mode of dialysis where possible. Prolonged peritoneal dialysis was associated with a significant increase in aortic valve calcification when compared to haemodialysis[4].

Apart from the increased mortality risk, cumulative dialysis duration of more than 4 years was associated with a 3.4-fold increased risk of the full-scale IQ being ⩾1 SD below the mean[5].

Of the 191 patients being treated with dialysis in paediatric units on the 1st April 2004, a previous treatment history was available for 183 (95.8%). One hundred and eleven of these patients had been on dialysis for less than two years whilst 80 had been on dialysis for over two years. Table 18.29 shows the duration of continuous dialysis therapy for this cohort. Although in clinical practice, prolonged dialysis used to be associated with the wait for a second allograft in sensitised patients, only 9 of the patients who had been on dialysis for over two years had previously had a transplant. Thirteen patients, 7% of the dialysis population, had been on dialysis for 5 or more years. As would be expected from the information given in the current treatment section, there was an excess of ethnic minority patients on dialysis for a prolonged period. Of 51 patients who had been on dialysis continually for 2 or more years and had not previously received an allograft, 19 (37.2%) were from ethnic minority groups.

For those patients being treated with long-term dialysis, there were more on haemodialysis

than peritoneal dialysis. Thirty of the 64 patients on continuous dialysis for 2 or more years were on peritoneal dialysis whilst 34 were on haemodialysis. In part, this will be related to ethnicity as we know haemodialysis is used more in patients from ethnic minority groups who form over a third of this cohort. However, in many cases this will be secondary to loss of peritoneal access or peritoneal function. Twelve of the patients in this cohort had switched from peritoneal dialysis to haemodialysis whilst just one patient moved from haemodialysis to peritoneal dialysis. Clearly this is a concern, both with regard to long-term co-morbidity and also with regard to the potential for ongoing dialysis. The majority of paediatric haemodialysis patients are dialysed through central venous catheters rather than arterio-venous fistulae. If patients are losing peritoneal function and then get central venous occlusion secondary to dialysis catheters, the potential for dialysis in these patients when they reach adulthood is greatly reduced.

Figure 18.21 shows the age distribution of the 64 patients who have been on dialysis continuously for two or more years. It is not surprising that there are fewer patients in the 0–3.9 year age-group considering that many of these patients would not have been in ERF for over two years. What is surprising is the dip in numbers in the 8–11.9 year age-group. There

is no clear reason for this and only future analyses will reveal whether this is a persistent trend.

Transplantation and the abnormal bladder

Obstructive uropathy from posterior urethral valves is one of the more common causes of chronic kidney disease in children. In one long-term series, 6% died from chronic renal failure, 16% developed ERF and 6% had ongoing chronic renal failure (creatinine greater than $150 \, \mu mol/l$)[6]. Children with posterior urethral valves and other children with primary neuropathic bladder or secondary nephropathy from bladder outlet obstruction are at risk of urinary infections and incontinence as a result of their abnormal bladders and upper urinary tracts. Of particular concern is the persistence of bladder dysfunction in the form of detrusor hyper-reflexia or poor bladder compliance with small capacity, that may result in a high pressure bladder, or detrusor failure with a hypotonic bladder where the bladder fails to empty resulting in recurrent infections. Modern management for these children now includes bladder augmentation cystoplasty to create a low pressure, high capacity bladder and clean intermittent catheterisation to achieve bladder emptying.
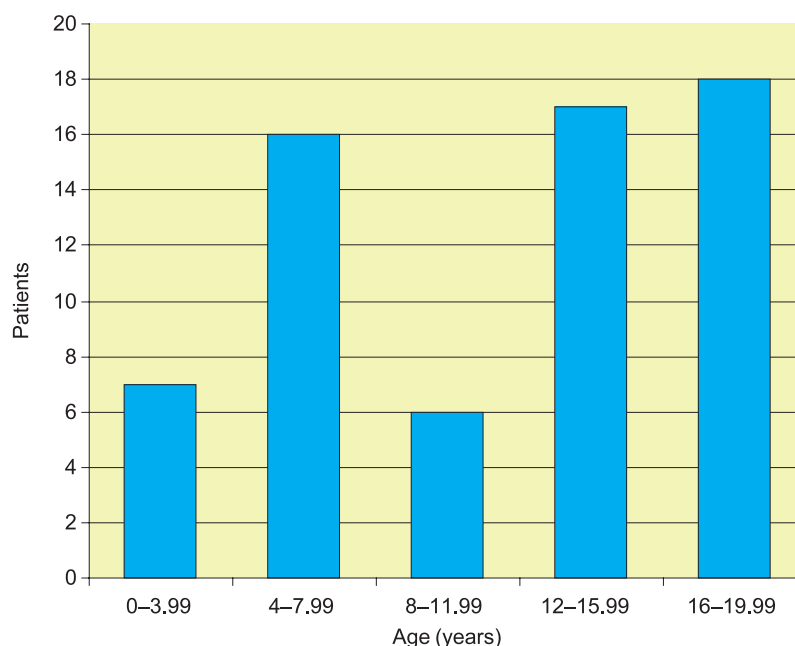

Figure 18.21: Patients on dialysis for two or more years, by current age

There is some debate as to the outcome of renal transplantation in these children. In the early days of transplantation, patients with "bad bladders" were considered unsuitable for transplantation. Historically, it has been asserted that children with posterior urethral valves have a worse outcome following renal transplantation[7,8]. More recently, however, a number of authors have reported good outcomes both for transplantation into abnormal bladders including those with augmented bladders and urinary diversions; graft and patient survival being in the range of 70–80% and 85–100% at 5 years respectively[9].

Theoretically, the paediatric Registry ought to be an ideal source of data for the comparison of outcomes of transplantation into normal and abnormal bladders. Unfortunately this becomes difficult once one takes into account that data collection is only annual, complications such as urinary sepsis are often not recorded and at present the lack of continuous data tracking patients through both their childhood and adult careers. In addition, to assess outcome solely related to bladder function, one needs to take account of other factors that lead to allograft dysfunction and loss such as matching, rejection, immunosuppression, non-urinary tract infection and recurrent renal disease. In an attempt to overcome these analytical difficulties we have compared two cohorts of current patients. In the April 2004 review of paediatric patients there were 109 patients with a functioning allograft whose original cause of renal failure was bladder related obstructive uropathy. As expected posterior urethral valves was the cause in 92 of these patients with 8 patients having a neuropathic bladder and 9 patients having obstructive uropathy from bladder outlet obstruction that was not posterior urethral valves. The second cohort consisted of 146 patients for whom the primary cause of renal failure was renal dysplasia and who were documented to have a functionally normal bladder. Using this cohort for comparison removed the potential confounding factors of recurrent disease and systemic disease and previous immunosuppression. Also, the observed male to female ratio in paediatric patients with ERF from renal dysplasia went some way to counter the gender differences between the groups, where, by definition, the vast majority of those with obstructive uropathy would be male.
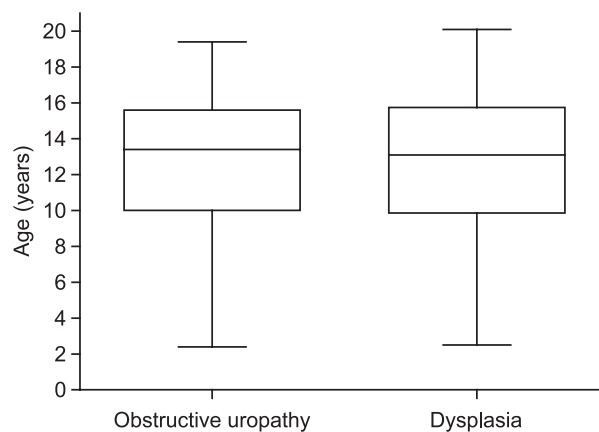
Figure 18.22: Age distribution of patients with obstructive uropathy compared to those with renal dysplasia

As predicted by selection, all those in the renal dysplasia cohort had normal bladder function and passed urine normally. There was no reliable record of how many of these patients suffered from urinary tract infections or had native or transplant vesico-ureteric reflux. For the cohort with renal failure from obstructive uropathy, 67 were thought to have normal bladder function or at least a "safe" bladder requiring no intervention. Sixteen patients were on clean intermittent catheterisation alone, 10 patients had a bladder augmentation and were on clean intermittent catheterisation, 5 patients had an ileal loop urinary diversion and in 11 patients the nature of the bladder and mode of drainage was not clearly defined.

There was no difference in the age distribution of the two cohorts (Figure 18.22). As expected, there was a preponderance of males in the obstructive uropathy group with 102 of the 109 patients in this group being male compared to 100 of 146 patients in the dysplasia group ($p < 0.0001$, Fisher's exact test). Similarly, there was no difference between the two groups with regard to the age of the allograft (Figure 18.23).
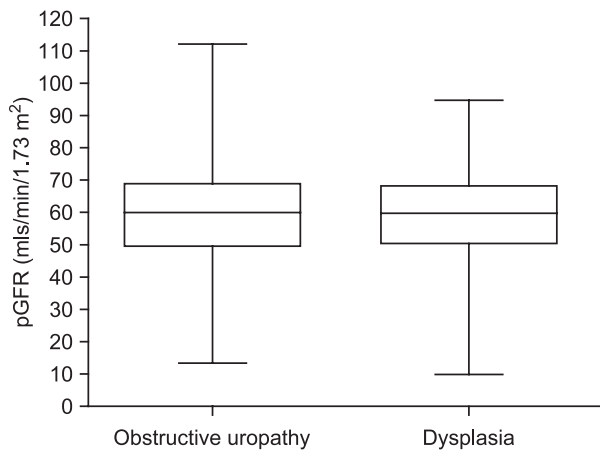
To assess renal function in these groups, predicted GFR from the patient height and serum creatinine using a single constant of 40 was used:

$$\text{ie pGFR} = \frac{40 \times \text{Height}}{\text{plasma creatinine}}$$

The results of this analysis are shown in Figure 18.24. There was no significant difference
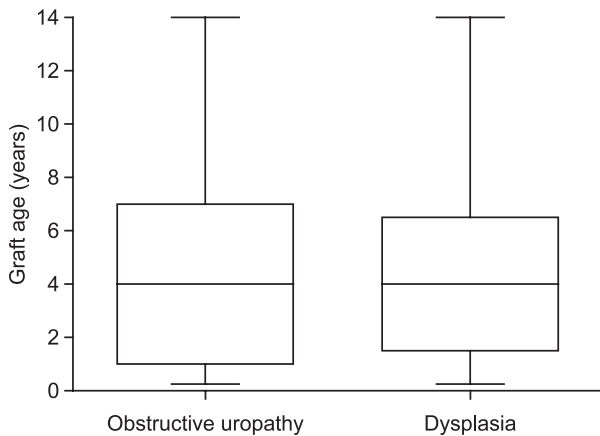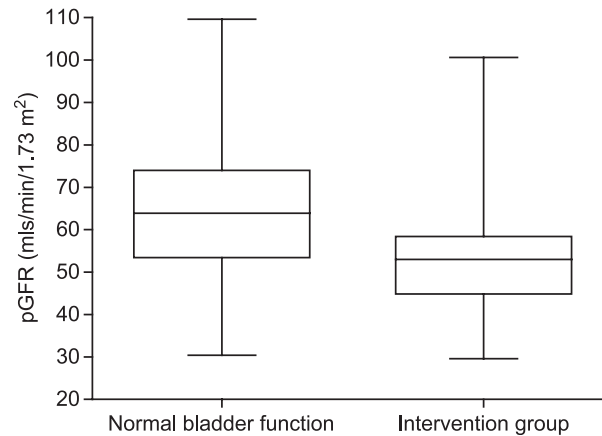
Figure 18.23: Graft age distribution of patients with obstructive uropathy compared to those with renal dysplasia

Figure 18.25: Predicted GFR in transplanted patients with obstructive uropathy according to bladder type

Figure 18.24: Predicted GFR in transplanted patients with obstructive uropathy compared to those with renal dysplasia

between the distribution of predicted GFR between the two groups.

The failure to show any difference in function between the two groups could be because of successful interventive management in those with obstructive uropathy but it could also be secondary to the presence of a majority of patients in the obstructive uropathy group who were deemed to have normal bladder function. To assess the impact of having both obstructive uropathy as a cause of renal failure and subsequent bladder dysfunction, the predicted GFR of those patients requiring clean intermittent catheterisation, bladder augmentation or urinary diversion (intervention group) were compared with patients who had obstructive uropathy as a cause of renal failure but in

whom bladder function was normal (normal bladder function group). The patients were matched for both chronological and graft age. The results of this analysis are shown in Figure 18.25. Although the range of GFR's between the two groups remains similar, the distributions are different, with the median GFR in the patients with abnormal bladder function ($53.0\,\mathrm{mls/min/1.73\,m^2}$) being significantly lower than that of those with normal bladder function ($63.9\,\mathrm{mls/min/1.73\,m^2}$) (p = 0.0048 Wilcoxon signed rank test).

These data confirm that bladder function is an important determinant of graft function and hence graft longevity. More longitudinal studies are required to determine which aspects of bladder dysfunction and intervention are related to poor outcome.

Conclusions

Demography

- The demographics of the paediatric ERF population are unchanged.

- The growth of the paediatric ERF population has not plateaued but continues to increase.

- There remains a high incidence and prevalence of ERF in South Asian children.

- This is in part accounted for by an increased incidence of genetic diseases in this group.

- These patients are more likely to be on haemodialysis and less likely to have a functioning allograft than White patients.

- A greater proportion of the paediatric population are on dialysis than in previous years.

- There is a linear relationship between the proportion of living related transplants being performed and the proportion of the population who are transplanted – confirming the shortage of cadaveric allografts.

Co-morbidity

- 21.6% of children have one or more paediatric specific co-morbidity at presentation with ERF.

- The most common of these is developmental delay affecting 8.7%.

- Co-morbidity is significantly more common in those presenting below the age of 8 years and in those commencing dialysis in paediatric units over the age of 16 years.

- On cross-sectional analysis, intellectual disability affects 17% of the paediatric ERF population with 7% having moderate or severe impairment.

- Overall, the presence of disability does not seem to influence patient management (with regard to progression to transplantation).

Patients on prolonged dialysis

- 27.9% of paediatric dialysis patients have been on dialysis for 2 or more consecutive years.

- 7% have had 5 or more consecutive years of dialysis.

- 37.2% of those patients on dialysis for two or more consecutive years are from ethnic minority groups.

- Haemodialysis is the most common modality of treatment in this population.

Transplantation into the abnormal bladder

- Overall, allograft function is no different between patients who have had obstructive uropathy as a cause of renal failure compared to those who had renal dysplasia.

- Compared to those with a functionally normal bladder, allograft function is significantly worse in those who have a significant functional bladder abnormality requiring intermittent catheterisation, bladder augmentation or urinary diversion.

Acknowledgements

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