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Occasional survey

Chronic renal insufficiency in children and adolescents: the 1996 annual report of NAPRTCS*

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Abstract. The 1996 annual report of the Chronic Renal Insufficiency Arm of the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) summarizes descriptive data and highlights important features on 1,725 patients from 130 centers. This database contains information on patients with an estimated glomerular filtration rate (GFR) $\leq$75 ml/min per 1.73 m^2 as calculated by the Schwartz formula, who were treated on or after 1 January 1994. Thus this report reflects 2 years of data entry. Analysis of the data revealed that nearly two-thirds of patients registered had a structural anomaly. On average, patients were 1.5 standard deviations below age- and sex-specific norms for height, and 0.6 standard deviations below weight norms. Mean serum creatinine for the entire group was 2.4 mg/dl and 68% of patients had a baseline GFR of at least 25 ml/min per 1.73 m^2. The mean hematocrit for all children at registration was 33.3$\pm$6.3%, and did not vary among age groups. Overall, 30.9% of patients had a hematocrit $<$30%. Only 12.8% of patients were receving Epoetin therapy. Although still in infancy, the Chronic Renal Insufficiency Arm of the NAPRTCS database in providing important insights into this disorder.

Key words: Chronic renal insufficiency – Creatinine – Epoetin – Growth hormone

Introduction

The North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) is an initiative which originated in 1987. At that time, information was voluntarily shared on pediatric renal transplant recipients from 87 centers in the United States and Canada [1]. The goal at origination was to collect data, describe standard clinical practices, and analyze outcomes for this population. The long-term objective was to identify factors which affect morbidity and mortality, and to ultimately improve the standard of care. As this effort evolved, the number of participating centers grew, and in 1992 the initiative was expanded to collect and evaluate data on pediatric dialysis patients [2]. A second expansion in 1994 added enrollment and data entry on pediatric patients with chronic renal insufficiency (CRI). This expansion of NAPRTCS provides a unique opportunity to closely study natural progression of pediatric patients with CRI. In addition, it will be possible to track patients' progression from renal insufficiency to renal replacement therapy with dialysis and transplantation, as the database matures. As of January 1996, the NAPRTCS database contained information on 6,892 children and adolescents receiving care at 130 centers in the United States, Canada, Mexico, and Costa Rica. The purpose of this report is to summarize descriptive data and highlight important features of the 1,725 patients enrolled in the CRI arm of this research effort.

Patients and methods

Patients are eligible for enrollment in the CRI arm of NAPRTCS if they are younger than 21 years at their first reported clinic visit and have an estimated glomerular filtration rate (GFR) $\leq$75 ml/min per 1.73 m^2 as calculated by the Schwartz formula [3, 4]. Data on diagnosis, selected laboratory values, concomitant medications, and medical events are collected and sent to the data coordinating center (DCC) of NAPRTCS at the time of patient registration and every 6 months thereafter. Collection of data on the CRI patients was begun in Septembe 1994. Data were reported retrospectively to include the first patient visit occurring on or after 1 January 1994. The information in this report includes all data received in the DCC through 16 January 1996. Enrollment data have been received on 1,725 patients with 6- and 12-month follow-up data on 1,008 and 508 patients, respectively. Standard descriptive statistical analyses were performed by the DCC.

*North American Pediatric Renal Transplant Cooperative Study (for participating NAPRTCS Centers, see end of article)

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Table 1. Primary renal disease by age

	<2 years		2–6 years		6–12 years		12–20 years	
	n	%	*n*	%	*n*	%	*n*	%
All patients	287	100	343	100	600	100	495	100
Primary diagnosis								
Obstructive uropathy	78	27.2	111	32.4	161	26.8	101	20.4
A/hypo/dys/plastic kidney	103	35.9	81	23.6	104	17.3	55	11.1
Reflux nephropathy	11	3.8	20	5.8	72	12.0	52	10.5
Other	34	11.8	33	9.6	71	11.8	62	12.5
FSGS	1	0.3	11	3.2	30	5.0	62	12.5
Polycystic kidney disease	11	3.8	26	7.6	26	4.3	10	2.0
Syndrome of agenesis	19	6.6	9	2.6	24	4.0	9	1.8
Cystinosis			6	1.7	18	3.0	2	0.4
Hemolytic uremic syndrome	4	1.4	12	3.5	13	2.2	10	2.0
Unknown	2	0.7	3	0.9	11	1.8	12	2.4
Medullary cystic disease					11	1.8	7	1.4
Systemic immunological disease					10	1.7	44	8.9
Pyelo/interstitial nephritis	1	0.3	3	0.9	10	1.7	14	2.8
Familial nephritis					9	1.5	14	2.8
Renal infarct	15	5.2	17	5.0	9	1.5	4	0.8
Chronic glomerulonephritis	1	0.3	2	0.6	6	1.0	9	1.8
MG type I			1	0.3	0.5	0.8	9	1.8
MG type II					4	0.7	4	0.8
Idiopathic crescentic GN			1	0.3	1	0.2	3	0.6
Wilms' tumor			3	0.9	1	0.2	2	0.4
Congenital nephrotic syndrome	6	2.1	3	0.9	1	0.2		
Oxalosis					1	0.2		
Sickle cell nephropathy					1	0.2	2	0.4
Membranous nephropathy			1	0.3	1	0.2	5	1.0
Drash syndrome	1	0.3						
Diabetic glomerulopathy							3	0.6

FSGS, Focal segmental glomerulosclerosis; MG, membranoproliferative glomerulonephritis; GN, glomerulonephritis

Results

Patient characteristics

Of the 1,725 patients entered in the CRI registry, 67% were male and 60% were white. At time of entry into the study, 35% of patients were between 6 and 12 years of age, 17% were less than 2 years of age, and only 3.5% were over 18 years. The most common primary diagnoses were obstructive uropathy (26%), renal aplasia, hypoplasia, dysplasia (20%), reflux nephropathy (9%), focal segmental glomerulosclerosis (6%), and polycystic kidney disease (4.2%). Nearly two-thirds of patients registered had a structural anomaly. Table 1 lists all diagnoses assigned to patients and shows primary diagnosis with a breakdown for different age groups. Table 2 shows primary renal diagnosis and percentage biopsy confirmation.

Data on baseline renal function at entry were collected on patients. When corrected for body surface area, the youngest patients (0–1 years) had the lowest mean GFR at 28.5 ml/min per 1.73 m^2, compared with a mean GFR in older patients (13–20 years) of 38.1 ml/min per 1.73 m^2. Overall, 68% of all patients had a baseline GFR of at least 25 ml/min per 1.73 m^2. Calculated GFR data by age are presented in Table 3. Follow-up data on renal function were available on 497 patients for a 1-year period. These follow-up data are presented in Table 4.

Information on selected medical events prior to study enrollment was collected. At the time of registration, 41% of all children had undergone urological surgery and 38% had had a urinary tract infection. Urological intervention was greatest (62%) in the 1,038 children with primary renal diseases associated with urological abnormalities, i.e., renal aplasia/dysplasia, obstructive uropathy, pyelonephritis or interstitial nephritis, and reflux nephropathy. Not unexpectedly, 91% of those with obstructive uropathy had required surgery. Fifty-four percent of children with urological abnormalities had had a urinary tract infection prior to enrollment and 41% were receiving prophylactic antibiotics. During the post-registration observation periods, urinary tract infections were reported in 12%, 11%, and 13.0% of children during consecutive 6-month intervals.

At the time of enrollment, 9% of children had a history of seizure and 4% were receiving anticonvulsant therapy (Table 5). A history of a seizure was most frequent (25.8%) in those with a GFR <10 ml/min per 1.73 m^2. Similarly, anticonvulsant treatment was utilized more frequently in those with the worst renal function. The frequency of seizure prior to enrollment did not vary by patient age. In each age group, those with the lowest GFR were more likely to have had a seizure. During each 6-month interval following registration, seizures occurred in 1.2%–2.4% of children.

Table 2. Primary renal diagnoses and percentage biopsy confirmation

	Total patients		Biopsy confirmation data[a]		
	n	%	*n*	No. with biopsy	Percent with biopsy
All patients	1,725	100.0	1,675	413	24.7
Primary diagnosis					
Obstructive uropathy	451	26.1	438	36	8.2
A/hypo/dys/plastic kidney	343	19.9	337	23	6.8
Other	200	11.6	192	49	25.5
Reflux nephropathy	155	9.0	148	13	8.8
FSGS	104	6.0	102	96	94.1
Polycystic kidney disease	73	4.2	72	21	29.2
Syndrome of agenesis	61	3.5	59	5	8.5
Systemic immunological disease	54	3.1	54	48	88.9
Renal infarct	45	2.6	43	2	4.7
Hemolytic uremic syndrome	39	2.3	38	9	23.7
Unknown	28	1.6	26	6	23.1
Pyelo/interstitial nephritis	28	1.6	26	13	50.0
Cystinosis	26	1.5	24	3	12.5
Familial nephritis	23	1.3	23	13	56.5
Chronic glomerulonephritis	18	1.0	18	14	77.8
Medullary cystic disease	18	1.0	17	9	52.9
MG type I	15	0.9	15	15	100.0
Congenital nephrotic syndrome	10	0.6	9	8	88.9
MG type II	8	0.5	8	8	100.0
Membranous nephropathy	7	0.4	7	7	100.0
Wilms' tumor	6	0.3	6	5	83.3
Idiopathic crescentic GN	5	0.3	5	4	80.0
Diabetic glomerulopathy	3	0.2	3	2	66.7
Sickle cell nephropathy	3	0.2	3	3	100.0
Drash syndrome	1	0.1	1	1	100.0
Oxalosis	1	0.1	1	0	0.0

[a] Biopsy confirmation data available on only 1,675 patients

Table 3. Baseline renal function, by age

			Age at entry (years)									
	All patients		0–1		2–5		6–12		13–17		>17–20	
Calculated GFR[a]	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Total	1,725	100.0	287	100.0	343	100.0	600	100.0	434	100.0	61	100.0
ALL												
<10	68	3.9	41	14.3	3	0.9	15	2.5	7	16	2	3.3
10–25	484	28.1	104	36.2	92	26.8	155	25.8	113	26.0	20	32.8
25–50	698	40.5	100	34.8	156	45.5	233	38.8	184	42.4	25	41.0
50–75	475	27.5	42	14.6	92	26.8	197	32.8	130	30.0	14	23.0

GFR, Glomerular filtration rate

[a] Schwartz calculated creatinine clearance (ml/min per 1.73 m^2)

Metabolic status

Information on laboratory values at the time of study enrollment revealed considerable variability. The mean values were all within the normal ranges including: serum calcium 9.5 ± 1.1 mg/dl (mean $\pm$ SEM), inorganic phosphorus 5.1 ± 1.2 mg/dl, alkaline phosphatase 265 ± 154 IU/ml, CO_2 22.4 ± 4.0 mEq/l, and albumin 4.0 ± 0.6 g/dl. However, there was some variation among different age groups, with the calcium ranging from 10.2 ± 0.1 mg/dl in those <2 years to 9.2 ± 0.1 mg/dl in those 13–20 years. Similarly the phosphorus varied from 5.7 ± 0.1 mg/dl in those <2 years, in whom a higher level is normal, to 4.8 ± 0.1 mg/dl in those 13–20 years. The CO_2 did not vary among age groups. Data were collected on parathyroid hormone (PTH) level based on the upper limit of the normal range for the assay utilized at the participating study center. Levels greater than twice the upper limit of normal were considered elevated. The PTH level was unknown in half the patients for whom a response was given on the enrollment form. Of those for whom the PTH was known (842/1,671), 65% had values less than twice the upper normal limit and 35% had levels more than twice the upper normal limit. The frequency of elevated PTH levels varied

Table 4. Schwartz calculated GFR (ml/min per 1.73 m^2)

	n	Baseline		6 Months		12 Months	
		Mean	SE	Mean	SE	Mean	SE
All patients	497	38.5	0.76	38.2	0.82	38.1	0.90
Age of entry (years)							
0–1	90	29.4	1.72	34.0	1.83	37.7	2.27
2–5	110	40.4	1.62	39.8	1.84	40.5	1.98
6–12	172	40.6	1.28	39.2	1.36	38.0	1.49
13–17	116	39.6	1.45	37.6	1.62	35.3	1.69
18–20	8	55.4	4.03	54.0	6.60	48.0	8.22

Table 5. Frequency of seizures[a] and treatment with anticonvulsant agents as baseline, differences by age and renal function

	Percentage of patients	
	History of seizure	Anticonvulsant treatment
Patient age		
<2 years	9.1%	4%
2–5 years	7.9%	2%
6–12 years	9.5%	4%
13–20 years	9.1%	5%
GFR[b]		
<10	25.8%	15%
10–25	8.3%	4%
25–50	7.6%	4%
50–75	9.5%	3%

[a] Patients with a history of seizure prior to study enrollment
[b] Calculated using Schwartz formula (ml/min per 1.73 m^2)

slightly with age as 28.6%, 26.7%, 35.8%, and 43.2% of those <2, 2–5, 6–12, and 13–20 years of age, respectively, had abnormal values. The frequency of PTH levels more than twice the upper normal limit (in those with known values) also varied with GFR (ml/min per 1.73 m^2). Elevated PTH levels were reported in 67.9% of those with GFR <10, 57.1% of those with GFR 10–25, 27.7% with GFR 25–50, and 9.1% of those with GFR 50–75 ml/min per 1.73 m^2.

In order to maintain metabolic balance, 45% of children were receiving oral vitamin D compounds, 40% calcium compounds, 1% aluminum hydroxide, and 41% alkali treatment at baseline. The use of these agents varied somewhat with patient age (Table 6). Calcitriol was used by 37% of children of all ages; however, it was used more frequently in older children. Other vitamin D compounds were used in 8% of children overall, with more frequent use in those <6 years. Alkali therapy was required more frequently in those <6 years (55%) than in those 6–12 years (41%) or 13–20 years (24%). Supplemental enteral nutrition was required by 11% of children overall; however, 26% of those <2 years and 22% of those 2–5 years required supplements. The use of enteral supplementation was most frequent in those with the worst renal function (GFR <10 ml/min per 1.73 m^2): 37% of those <2 years and 67% of those 2–5 years were receiving enteral supplements. Overall, parenteral nutrition was used infrequently (1%); however, it was utilized in 6% of patients with GFR <10 ml/min per 1.73 m^2.

The mean blood pressure at baseline varied among age groups (Table 7). The mean systolic blood pressure ($\pm$SD) varied from 102 ± 16 mmHg in those <2 years to 126 ± 16 mmHg in those 13–20 years. The mean diastolic blood pressure varied from 59 ± 13 mmHg in those <2 years to 76 ± 13 in those 13–20 years. The frequency of antihypertensive treatment also varied directly by age, with its use required in 12%, 26%, 24%, and 54% of those <2, 2–5, 6–12, and 13–20 years, respectively. Antihypertensive treatment was required more frequently in those with CRI as a result of polycystic kidney disease (83%) or glomerulonephritis (71%), than in those with structural renal disease (19%) (Table 8). There was not a significant difference in the use of antihypertensive medications by age group within diagnostic categories. In fact, a portion of the difference in use by age may be related to the primary disease.

Anemia

The mean hematocrit for all children at registration was $33.3\% \pm 6.3\%$ and did not vary among age groups. Overall,

Table 6. Concomitant drug therapy: percentage of patients in each age group treated at baseline

	<2 years	2–5 years	6–12 years	13–20 years
Supplemental enteral nutrition	26%	22%	7%	1%
Calcitriol	18%	36%	43%	41%
Other vitamin D compounds	12%	16%	6%	3%
Calcium carbonate	26%	35%	38%	33%
Calcium acetate	1%	1%	3%	7%
Other calcium supplements	3%	4%	4%	2%
Aluminum hydroxide	0%	1%	1%	0%
Alkali therapy	55%	56%	41%	24%

Table 7. Mean blood pressure and treatment at baseline

Patient age	Systolic blood pressure[a]	Diastolic blood pressure[b]	Antihypertensive treatment
<2 years	102±16	59±13	12%[b]
2–5 years	105±14	63±11	26%
6–12 years	113±16	68±13	34%
13–20 years	126±16	76±13	54%

[a] Mean ± SD
[b] Percentage of patients in each age group receiving antihypertensive treatment

Table 8. Differences in the use of antihypertensive medications by primary renal disease

Primary renal disease	No. of patients	Antihypertensive treatment (% patients)
All patients	1,719	34%
Structural renal diseases[a]	852	19%
Polycystic kidney disease	73	83%
Glomerulonephritis[b]	211	71%
Pyelonephritis/interstitial nephritis	183	40%
Renal infarct	44	23%
Hemolytic uremic syndrome	39	59%
Other	317	35%

[a] Includes renal dysplasia/aplasia/hypoplasia, obstructive uropathy, and syndrome of agenesis of abdominal musculature
[b] Includes FSGS, systemic immunological disease, chronic glomerulonephritis, membranoproliferative glomerulonephritis, membranous and idiopathic crescentic glomerulonephritis

Table 9. Frequency of anemia and treatments for anemia: differences by age and renal function

	Percentage of patients				
	Hematocrit			Treatments	
	≤30%	31%–32.9%	>33%	Oral iron	Epoetin
All patients	30.9%	13.0%	56.1%	26%	12.8%
Patient age					
<2 years	37.9%	13.0%	47.0%	18%	21.3%
2–5 years	24.3%	15.0%	60.3%	36%	12.6%
6–12 years	31.4%	15.4%	55.2%	43%	10.7%
13–20 years	30.7%	9.5%	59.8%	41%	10.7%
GFR[a]					
<10	62.9%	11.3%	25.8%	44%	44.1%
10–25	48.1%	16.8%	35.1%	44%	26.7%
25–50	25.7%	13.3%	61.0%	36%	8.2%
50–75	13.1%	8.1%	78.7%	8%	1.1%

[a] Calculated using Schwartz formula (ml/min per 1.73 m^2)

30.9% of patients had a hematocrit <30% (Table 9). An additional 13% had mild anemia with hematocrit values 31%–32.9%. The frequency of a baseline hematocrit <30% varied among age groups and was most common in those <2 years (37.9%). The frequency of anemia varied, not unexpectedly, with the GFR. Significant anemia (hematocrit <30%) was present in 62.9% of those with a calculated GFR <10 ml/min per 1.73 m^2 and 13.1% of those with a GFR 50–75 ml/min per 1.73 m^2. In order to treat the anemia, 26% of patients were receiving oral iron supplementation and 12.8% were receiving Epoetin treatment. The frequency of Epoetin treatment varied with renal function with 44.1% of those with GFR <10 ml/min per 1.73 m^2 receiving this treatment and only 1.1% of those with GFR 50–75 ml/min per 1.73 m^2. Erythrocyte transfusions had been required in 11% of patients prior to registration. Additional transfusions were given to 2.4% of the patients during the 6 months following registration. The overall frequency of Epoetin treatment was unchanged over the period of follow-up, with its use in 14.7%, 15.0%, and 15.0% of those with data available at 6, 12, and 18 months, respectively.

Growth

Data on height and weight at time of entry are available on 1,701 patients. No data are available on age at diagnosis of

Table 10. Height (SDS) during 1st year of chronic renal insufficiency follow-up in patients with baseline height <3rd percentile (SDS <–1.88)

		Baseline SDS	12-Month SDS	Delta SDS
rhGH Therapy[a]	(n = 15)	–3.00 ± 0.16	–2.56 ± 0.17	0.44 ± 0.13
Control[b]	(n = 133)	–3.08 ± 0.10	–2.84 ± 0.11	0.25 ± 0.08

rhGH, Recombinant human growth hormone
[a] Patients were receiving rhGH therapy at baseline, 6 months, and 12 months
[b] Patients were not receiving rhGH at baseline, 6 months, or 12 months

Table 11. Characteristics at baseline and 12 months in patients with baseline height <3rd percentile (SDS <–1.88)

	Baseline CRI visit				12 Month CRI visit			
	rhGH Therapy[a]		Control[b]		rhGH Therapy[a]		Control[b]	
	n	%	*n*	%	*n*	%	*n*	%
All patients	15	100.00	133	100.00	15	100.0	133	100.00
Age group (years)								
0–1	1	6.7	37	27.8	–	–	26	19.5
2–5	3	20.0	36	27.1	2	13.3	36	27.1
6–12	5	33.3	40	30.1	7	46.7	45	33.8
13–17	6	40.0	20	15.0	6	40.0	23	17.3
>17	–	–	–	–	–	–	3	2.3
Tanner stage								
I	13	86.7	106	75.7	11	73.3	103	77.4
II	1	6.7	9	6.8	1	6.7	7	5.3
III	1	6.7	7	5.3	1	6.7	9	6.8
IV	–	–	1	0.8	1	6.7	1	0.8
V	–	–	4	3.0	–	–	6	4.5
Missing	–	–	6	4.5	1	6.7	7	5.3

[a] Patients were receiving rhGH therapy at baseline, 6 months, and 12 months
[b] Patients were not receiving rhGH at baseline, 6 months, or 12 months

CRI or height and weight standard deviation scores (SDS) at time of diagnosis of CRI. On average, patients were 1.5 SD below age- and sex-specific norms for height, and 0.6 SD below weight norms. Standardized height deficits were greatest for younger patients, and nearly half of the patients less than 5 years of age at entry had a height below the 3rd percentile for age and sex (SDS ≤–1.88). Thirty-five percent of patients 6–12 years old, 26.7% of those 13–17 years old, and 18.6% of those 18–20 years old fell below the 3rd percentile for height. Female patients and those with worse renal function at baseline tended to have greater height deficits, although it is interesting to note that many children fell below the 3rd percentile for height (SDS ≤–1.88) despite a calculated GFR greater than 25 ml/min per 1.73 m^2. Although differences in the duration of CRI among patients with the same degree of renal impairment at entry may account for this finding, it should be noted that even among patients <1 year of age at entry, there is not a straightforward relationship between height SDS and GFR. Baseline characteristics, including Tanner stage, CO_2, and PTH values, were not different in the groups of patients whose height was above and below the 3rd percentile for age (SDS <–1.88).

Growth data were available on 497 patients at 1 year post entry. Only 15 of 133 (11%) patients whose height was <3rd percentile (SDS <–1.88) at entry, received recombinant growth hormone (rhGH) during the period of follow-up. The baseline and follow-up SDS scores for these patients are detailed in Table 10. Table 11 details the age and Tanner scores for patients with baseline height <3rd percentile (SDS <–1.88). These data reveal similar ranges of age and Tanner stage in patients who received rhGH compared with those who did not, and thus do not support the concept that the untreated patients were excluded because of advanced pubertal development.

Discussion

This report summarizes data on 1,725 children at 130 centers. This newest arm of the NAPRTCS database, the CRI arm, will ultimately provide important information concerning the course and natural progression of CRI in children. Although data collection in this arm was only initiated in 1994, sufficient information is already available to provide insights into the etiology of CRI in children, standard treatment of this disorder, and to define the anticipated consequences of CRI. Some of the analyses may be limited by selection of patients who are enrolled in the study. The data that a patient begins chronic dialysis treatment or receives a renal transplant can be clearly delineated. The selection of patients for enrollment in the CRI

arm of NAPRTCS may be influenced by referral patterns to pediatric nephrologists, the impact of the organization of clinical programs on identification of eligible patients, and the ease of recognition of children with estimated GFR <75 ml/min per 1.73 m^2. Selection of patients for enrollment will influence assessments of the frequency of treatment with nutritional supplementation, GH, and Epoetin. Patient characteristics are described at study enrollment, not at presentation to the participating centers. It is possible that this will change as the database matures. Interestingly, the distribution of diagnoses varies slightly from that of the transplantation arm of NAPRTCS, where obstructive uropathy was less frequent (16.5%) and focal glomerulosclerosis more frequent (11.6%) [5]. This may reflect patient selection practices or the use of a GFR <75 ml/min per 1.73 m^2 as an enrollment criteria, with 68% of patients having a GFR of at least 25 ml/min per 1.73 m^2.

Overall 41% of children had undergone urological surgery prior to enrollment. This fact stresses the importance of close working relationships between pediatric urologists and pediatric nephrologists in the care of children with CRI. Such relationships may aide in the early establishment of optimum metabolic control. Prior to enrollment, 9% of children had had a seizure. The etiology of the seizures in this CRI population is unclear, but warrants further evaluation. There is no information in the registry about the presence of hypertension, electrolyte disorders, or infectious processes at the time of the seizures. However, seizures prior to enrollment were more common in those with the lowest GFR, who would be more likely to have electrolyte abnormalities. Of interest, dialysis-associated seizures have been described in 7% of children and adolescents receiving dialysis [6]. The frequency of hemodialysis-associated seizures was greatest (29%) in those with a history of seizure prior to the initiation of dialysis. Antihypertensive medications were frequently required in children with CRI. Not unexpectedly the need for these medications was greatest in adolescents and in those with polycystic kidney disease or glomerulonephritis.

Anemia is a frequent consequence of renal failure due to both erythropoietin and iron deficiency. In previous assessment of anemia in children with CRI, there has been considerable interpatient variability; however, anemia has been noted in most children with a GFR $<20-35$ ml/min per 1.73 m^2 [7]. As reported in this registry, anemia (hematocrit $<33\%$) was present in 74% of those with a GFR <10 ml/min per 1.73 m^2, despite the use of Epoetin in 44% of these children. This may reflect recent initiation of the Epoetin treatment. Sixty-five percent of those with a GFR 10–25 ml/min per 1.73 m^2 were anemic. In fact only 61% of those with a GFR 25–50 ml/min per 1.73 m^2 had a hematocrit level $\geq 33\%$. A level of 33% was chosen to indicate anemia as that level is at least 2 SD below the mean for all children older than 6 months. A greater proportion of those less than 2 years of age had a hematocrit level $<30\%$. This may be in part due to the expected physiological nadir in hematocrit in those <6 months; however, fewer children in this age group were receiving iron supplementation (18%). It is likely that the frequency of treatment with iron and Epoetin will increase with ongoing treatment of CRI at the participating centers, although this trend has not yet been documented. Of interest, 75% of all children on dialysis are receiving iron supplementation and $>90\%$ are receiving Epoetin afte 12 months on dialysis [5].

The mean height SDS was –1.5 at study enrollment with a significant proportion of children having heights below the 3rd percentile. Preliminary growth data confirm the clinical suspicion that growth retardation is not solely based on level of renal dysfunction. Further study is warranted to elucidate other factors (i.e., age of onset of renal insufficiency, underlying renal diagnosis, etc.) that significantly impact growth in this patient population. Although published data suggest that children with pre-terminal renal failure may significantly benefit from treatment with rhGH [8–10], the current database reveals that only a small percentage of patients with a height <3rd percentile for age received rhGH. The presence of factors that may have influenced use of this medication (i.e., presence of other growth-limiting medication or condition, previous malignancy, severe bone disorder, anticipated transplant, family preference) are not readily available in the present database and deserves further study. Intervention during treatment for CRI is necessary as the height deficit is greater in children in the NAPRTCS registry at the time of transplantation (mean SDS –2.16) [5].

Although still in its infancy, the CRI arm of the NAPRTCS database is providing important insights into this disorder. Over the next decade, we can expect to increase our knowledge of CRI in pediatric patients, and add important information to the existing body of literature on this topic [11, 12].

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Participating NAPRTCS centers

Center	City/state	Principal investigator
Albert Einstein College of Medicine	Bronx, N.Y., USA	Ira Greifer
Alfred I. duPont Institute	Wilmington, Del., USA	Farahnak Assadi
All Children's Hospital-St Petersburg	St Petersburg, Fla., USA	Sharon Perlman
Arizona Children's Renal Center	Tucson, Ariz., USA	Amira Al-Uzri
Arkansas Children's Hospital	Little Rock, Ark., USA	Eileen Ellis
Arnold Palmer Hospital	Orlando, Fla., USA	Jorge Ramirez
BC Children's Hospital	Vancouver, Canada	David S. Lirenman
Babies Hospital	New York, USA	Martin A. Nash
Boston City Hospital	Boston, Mass., USA	Melanie Kim
Bowman Gray School of Medicine	Winston-Salem, N.C., USA	William B. Lorentz
Bridgeport Hospital	Bridgeport, Conn., USA	Thomas Kennedy
Cardinal Glennon Hospital	St Louis, Mo., USA	Ellen Wood
Carolina's Medical Center	Charlotte, N.C., USA	Roberta Gray
Cedars-Sinai Medical Center	Los Angeles, Calif., USA	Elaine Kamil
Children's and Infants Diagnostic Center	Margate, Fla., USA	Michael Freundlich
Children's Hospital Med Center-Cincinnati	Cincinnati, Ohio, USA	Paul T. McEnergy
Children's Hospital Medical Center-Akron	Akron, Ohio, USA	Ian Dresner
Children's Hospital National Medical Center	Washington, D.C., USA	Kanwal Kher
Children's Hospital and Med Center-Seattle	Seattle, Wash., USA	Sandra L. Watkins
Children's Hospital at Albany	Albany, N.Y., USA	Rod E. Urizar
Children's Hospital of Alabama	Birmingham, Ala., USA	Edward C. Kohaut
Children's Hospital of Michigan	Detroit, Mich., USA	Shermine Dabbagh
Children's Hospital of Oklahoma	Oklahoma City, Okla., USA	James Wenzl
Children's Hospital of Orange County	Orange, Calif., USA	Dorit Ben-Ezer
Children's Hospital of Philadelphia	Philadelphia, Pa., USA	Kathy Jabs
Children's Hospital of Pittsburgh	Pittsburgh, Pa., USA	Demetrius Ellis
Children's Hospital of Winnipeg	Winnipeg, Manitoba, Canada	Malcolm Ogborn
Children's Hospital of the King's Daught	Norfolk, Va., USA	Irene Restaino
Children's Hospital-Boston	Boston, Mass., USA	John Herrin
Children's Hospital-Columbus	Columbus, Ohio, USA	Mark I. Mentser
Children's Hospital-Denver	Denver Colo., USA	Gary M. Lum
Children's Hospital-Los Angeles	Los Angeles, Calif., USA	Carl M. Grushkin
Children's Hospital-New Orleans	New Orleans, La., USA	Matti Vehaskari
Children's Hospital-Oakland	Oakland, Calif., USA	Rose Ellen Morrel
Children's Kidney Center-Buffalo	Buffalo, N.Y., USA	Leonard Feld
Children's Memorial Hospital-Chicago	Chicago, Ill., USA	Richard A. Cohn
Children's Mercy Hospital-Kansas City	Kansas City, Mo., USA	Bradley A. Warady
Children's Renal Center-Galveston	Galveston, Tex., USA	Luther B. Travis
Christ Hospital	Parkridge, Ill., USA	Kenneth Miller
Cleveland Clinic Foundation	Cleveland, Ohio, USA	Ben H. Brouhard
Columbia Hospital at Medical City Dallas	Dallas, Tex., USA	Ronald Hogg
Columbia Presbyterian	Denver, Colo., USA	M. Katherine Fitting
Connecticut Children's Medical Center	Hartford, Conn., USA	Majid Rasoulpour
Cook Children's Medical Center	Ft Worth, Tex., USA	Watson C. Arnold
Department of Pediatrics/PSP	Lackland AFB, Tex., USA	Robert Haws
Duke University Medical Center	Durham, N.C., USA	John W. Foreman
East Carolina University	Greenville, N.C., USA	Lou Anne Baldree
East Tennessee State University	Johnson City, Tenn., USA	Ahmad Wattad
Egleston Children's Hospital at Emory University	Atlanta, Ga., USA	Barry L. Warshaw
Emanuel Children's Hospital	Portland, Ore., USA	Randy Jenkins

Participating NAPRTCS centers (continued)

Center	City/state	Principal investigator
Fairfax Hospital for Center	Annandale, Va., USA	Glenn Bock
Geisinger Medical Center	Danville, Pa., USA	Oscar R. Oberkircher
Hospital Infantil De Mexico	Mexico City, Mexico	Ricardo Munoz Arizpe
Hospital Nacional de Ninos	San Jose, Costa Rica	Gilbert Madriga Campos
Hospital St Justine	Montreal, Quebec, Canada	Marie-Jose Clermont
Hospital for Sick Children-Toronto	Toronto, Ontario, Canada	Diane Hebert
J.W. Riley Hospital for Children	Indianapolis, Ind., USA	Sharon Andreoli
Jefferson Medical College	Philadelphia, Pa., USA	Ruth Gottlieb
Johns Hopkins University	Baltimore, Md., USA	Barbara Fivush
LAC+USC Medical Center	Los Angeles, Calif., USA	Donna Elliott
Loma Linda University Medical Center	Loma Linda, Calif., USA	Shobha Sahney
Long Island College Hospital	Brooklyn, N.Y., USA	Matthew Kaplan
Loyola University Medical Center	Maywood, Ill., USA	Donald Moel
Lutheran General Children's Medical Center	Park Ridge, Ill., USA	Ronald Kallen
Maine Medical Center/Pediatric Associates	Portland, Me., USA	Matt Hand
Massachusetts General Hospital	Boston, Mass., USA	Julie Ingelfinger
Mayo Clinic	Rochester, Minn., USA	Dawn S. Milliner
Medical College Hospital at Toledo	Toledo, Ohio, USA	Martin DeBeukelaer
Medical College of Georgia	Augusta, Ga., USA	Coral D. Hanevold
Medical College of Virginia	Richmond, Va., USA	James C.M. Chan
Medical College of Wisconsin	Milwaukee, Wis., USA	Cynthia Pan
Medical University of South Carolina	Charleston, S.C., USA	John Orak
Michigan State University	East Lansing, Mich., USA	Donald Kaufman
Michigan State University-Kalamazoo	Kalamazoo, Mich., USA	Alfonso Torres
Milton S. Hershey Medical Center	Hershey, Pa., USA	Steven J. Wassner
Montreal Children's Hospital	Montreal Quebec, Canada	Lorraine Bell
Mount Sinai Medical Center	New York, USA	Kenneth V. Lieberman
New England Medical Center	Boston, Mass., USA	Michael Linshaw
New York Hospital	New York, USA	Valerie Johnson
New York Medical College	Hawthorne, N.Y., USA	Amir Tejani
North Shore University Hospital	Manhasset, N.Y., USA	Manju Chandra
Oregon Health Sciences University	Portland, Ore., USA	Marc B. Lande
Pediatric Consultants	Reno, Nev., USA	Michael Pokroy
Phoenix Children's Hospital	Phoenix, Ariz., USA	Mel Cohen
Rainbow Babies and Childrens Hospital	Cleveland, Ohio, USA	Ira D. Davis
Rhode Island Hospital	Providence, R.I. USA	Andrew S. Brem
Robert C. Byrd HSC-Charleston	Charleston, W.Va., USA	Myra L. Chiang
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Rush-Presbyterian-St. Luke's Medical Center	Chicago, Ill., USA	Bettina A. Ault
SUNY Health Science Center	Syracuse, N.Y., USA	Frank S. Szmalc
SUNY Health Science Center at Brooklyn	Brooklyn, N.Y., USA	Anup Singh
Schneider Children's Hospital	New Hyde Park, N.Y., USA	Bernard Gauthier
Scottish Rite Hospital	Dunwoody, Ga., USA	Julius Sherwinter
St. Christopher's Hospital for Children	Philadelphia, Pa., USA	H. Jorge Baluarte
St. Barnabas Medical Center	West Orange, N.J., USA	Isabel Roberti
St. Francis Renal Institute-Honolulu	Honolulu, Hawaii, USA	James E. Musgrave
St. Louis Children's Hospital	St Louis, Mo., USA	S. Paul Hmiel
Stanford University Medical Center	Palo Alto, Calif., USA	Susan Conley
State University of New York-Stony Brook	Stony Brook, N.Y., USA	Frederick J. Kaskel
Sunrise Medical Center	Las Vegas, Nev., USA	Ragini Fredrich
Texas Children's Hospital	Houston, Tex., USA	Eileen D. Brewer
Tulane Medical Center	New Orleans, La., USA	Frank G. Boineau
UC Davis Medical Center	Sacramento, Calif., USA	Sudesh Makker
UCI Medical Center	Orange, Calif., USA	Deepak Rajpoot
UCLA School of Medicine	Los Angeles, Calif., USA	Robert Ettenger
UCSF Children's Renal Center	San Francisco, Calif., USA	Donald E. Potter
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Univ of Tenn/Le Bonheur Children's Hospital	Memphis, Tenn., USA	Shane Roy III
University Hospital-London	London, Ontario, Canada	David J Hollomby
University of Alberta Hospital	Edmonton, Alberta, Canada	Frances E. Harley
University of California at San Diego	San Diego, Calif., USA	Stanley A. Mendoza
University of Florida	Gainesville, Fla., USA	Robert S. Fennell
University of Illinois	Chicago, Ill., USA	Eunice G. John
University of Iowa Hospitals	Iowa City, Iowa, USA	Craig Porter
University of Kentucky Medical Center	Lexington, Ky., USA	Elizabeth Jackson
University of Louisville School of Medicine	Louisville, Ky., USA	Harold Harrison
University of Maryland Hospital	Baltimore, Md., USA	Roberto Jodorkowsky

Participating NAPRTCS centers (continued)

Center	City/state	Principal investigator
University of Massachusetts Medical Center	Auburn, Mass. USA	William Primack
University of Miami/Children's Hospital Center	Miami, Fla., USA	Jose Strauss
University of Michigan	Ann Arbor, Mich., USA	Aileen Sedman
University of Minnesota Hospital	Minneapolis, Minn., USA	Thomas E. Nevins
University of Mississippi Medical Center	Jackson, Miss., USA	Radharkrishma Baliga
University of Missouri	Columbia, Mo., USA	Ted. D. Groshong
University of Nebraska Medical Center	Omaha, Neb., USA	Helen Lovell
University of Rochester	Rochester, N.Y., USA	Melissa Gregory
University of South Florida	Tampa, Fla., USA	Alfonso Campos
Tennessee Medical Center	Knoxville, Tenn., USA	Maricarmen Malagon
University of Texas HSC at Houston	Houston, Tex., USA	Ronald Portman
University of Texas HSC at San Antonio	San Antonio, Tex., USA	Ihsan Elshihabi
University of Texas Southwest Med Center	Dallas, Tex., USA	Steven R. Alexander
University of Utah	Salt Lake City, Utah, USA	Richard Siegler
University of Vermont	Burlington Vt., USA	Ann P. Guillot
University of Virginia	Charlottesville, Va., USA	Robert L. Chevalier
University of Wisconsin Hospital	Madison, Wis., USA	Aaron Friedman
Valley Children's Hospital	Fresno, Calif., USA	Jerome Murphy
Vanderbilt University Medical Center	Nashville, Tenn., USA	Stanley Lee
Westchester County Medical Center	Valhalla, N.Y., USA	Robert A. Weiss
Wyler Children's Hospital	Chicago, Ill., USA	Andrew Aronson
Yale University School of Medicine	New Haven, Conn., USA	Karen Gaudio

Literature abstract

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Are short normal children at a disadvantage? The Wessex growth study

A. Bruce Downie, Jean Mulligan, Robert J. Stratford, Peter R. Betts, and Linda D. Voss

Objective. To examine whether short stature through childhood represents a disadvantage at around 12 years.
Design. Longitudinal non-intervention study of the physical and psychological development of children recruited from the community in 1986 – 7 after entry into primary school at age 5 – 6 years; this is the second psychometric assessment made in 1994 – 5 after entry into secondary school at age 11 – 13 years.
Setting. Southampton and Winchester health districts.
Subjects. 106 short normal children (< 3rd centile for height when recruited) and 119 controls of average stature (10th – 90th centile).
Main outcome measures. Psychometric measures of cognitive development, self concept development, behaviour, and locus of control.
Results. The short children did not differ significantly from the control children on measures of self esteem (19.4 v 20.2), self perception (104.2 v 102.4), parents'' perception (46.9 v 47.0), or behaviour (6.8 v 5.3). The short children achieved significantly lower scores on measures of intelligence quotient (IQ) (102.6 v 108.6; $P < 0.005$), reading attainment (44.3 v 47.9; $P < 0.002$), and basic number skills (40.2 v 43.5; $P < 0.003$) and displayed less internalisation of control (16.6 v 14.3; $P < 0.001$) and less satisfaction with their height ($P < 0.0001$). More short than control children, however, came from working class homes ($P < 0.05$). Social class was a better predictor than height of all measures except that of body satisfaction. Attainment scores were predicted by class and IQ together rather than by height. Height accounted for some of the variance in IQ and locus of control scores.
Conclusions. These results provide only limited support for the hypothesis that short children are disadvantaged, at least up until 11 - 13 years old. Social class seems to have more influence than height on children's psychological development.