Neuropsychological profile of children with kidney transplants

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Abstract

Background. Varying results on the cognitive outcome of children who have undergone kidney transplantation (KTx) have raised concern for specific neurocognitive difficulties.

Methods. Fifty children with KTx were assessed at a mean age of 11.1 (SD 3.2; range 6.3–16.4), on average 6.9 (SD 3.6; range 1.0–14.1) years post-operatively. A standardized test of intelligence [Wechsler Intelligence Scale for Children (WISC-III)] and neuropsychological tests from NEPSY-II were administered. The neuropsychological profile of KTx children was compared to that of a control group matched for gender, age and maternal education.

Results. The KTx children had a lower intelligence quotient (83.9) than the test norms (100.0, P < 0.001). On neuropsychological assessment, the KTx group scored generally lower than the control group did (P < 0.001). The difference was evident in both the verbal and visuospatial domains, on a sub-test of complex auditory attention, verbal working memory and facial affect recognition. When children with neurological co-morbidity were excluded, the remaining group still scored lower than the controls did on Comprehension of Instructions (P = 0.06), Design Copying (P = 0.007) and Affect Recognition (P = 0.018). A better cognitive outcome was mainly associated with the absence of neurological co-morbidity, younger age, shorter disease duration and sustained kidney function. Children with congenital nephrosis had a similar outcome to those with other diagnoses.

Conclusions. KTx children exhibit a pattern of effects in their cognitive outcome in which both the visuospatial and language domains are affected, but visual memory and simple auditory attention remain intact. Patients without neurological co-morbidity exhibit impairment in receptive language, visuospatial functions and in recognizing emotional states.

Keywords: cognitive outcome; congenital nephrosis of the Finnish type; neurodevelopment; neuropsychological test; pediatric kidney transplantation

Introduction

Studies on cognitive outcome after kidney transplantation (KTx) have reported intelligence in the low average to average range in school-age children [1–5]. The majority of patients have attended school and followed the normal curriculum [4–6]. Despite these encouraging reports, concern for specific neurocognitive difficulties lingers.

More detailed studies on neurocognitive development remain few. Falger et al. [1] found impairment in performance intelligence and motor performance among KTx children, even in the absence of neurological co-morbidity. Qvist et al. [5] found performance within the normal range in attention and executive functions, language, visuospatial processing, and memory and learning. These reports compared the performance of KTx children to normative data from test norms. Two studies have used a matched control group. Fennel et al. (1984) found greater improvement in performance intelligence and math in the KTx group than in the control group in assessments undertaken before the initiation of dialysis and 1-month post-KTx; the KTx children now reached the level of the control group. In verbal intelligence, however, both groups had very similar scores at each assessment. Additionally, no differences were found between groups at 1-year post-KTx on measures of intelligence, achievement, problem solving, verbal memory or attention. However, the groups were matched for intelligence, which explains their similar cognitive level [2]. In a more recent study, Brouhard et al. [6] found KTx children to perform significantly poorer on measures of non-verbal intelligence and achievement (spelling, reading and arithmetic) than do their siblings.

The present study aimed to evaluate comprehensively the cognitive level and neuropsychological profile of KTx children. To obtain knowledge about neurocognitive functioning in relation to age expectations, KTx children were compared to a matched control group.

Materials and methods

Children included in the study had undergone kidney or kidney–liver transplantation at least 1 year prior to assessment, attended medical
follow-up at the Helsinki University Central Hospital (HUCH), were be-
tween 6.0 and 16.5 years of age (born between November 1991 and
September 2003) and had Finnish or Swedish as their first language. Of
a total of 62 patients, 2 had died post-Tx and one patient had an acute
clinical condition which precluded testing. One patient whose first lan-
guage was neither Finnish nor Swedish and another child with severe
tetraplegia and cerebral palsy were excluded. One child was unable to
complete the assessments due to psychological distress. Of the remaining
56 patients, 6 declined to participate in the study. Of the six patients who
decided to participate, one had cerebral palsy, sensorineural hearing loss
and attended a special school. One patient was born prematurely, had
suffered from asphyxia and experienced seizures and posterior reversible
leukoencephalopathy syndrome. The four remaining patients had a normal
neurological outcome.
A total of 50 children (22 girls and 28 boys) who had undergone
transplantation between February 1993 and January 2008 participated in
the study. Two patients had received haemodialysis after a failure of
peritoneal dialysis and two received haemodialysis only. The rest had
received peritoneal dialysis. As many as 39 (78%) were deceased donor
organ recipients. Five patients had undergone a combined liver–kidney
Tx; four had a re-Tx. In two cases, the first transplant was a kidney, and
the re-transplant was a combined liver–kidney. As background character-
istics, variables came from the latter Tx. The immunosuppressive med-
cication cyclosporine A was used in 24 patients and tacrolimus in 26, both
in combination with methylprednisolone. In addition, most patients used
either azathioprine (n = 32) or mycophenolate mofetil (n = 17). Ten
patients had received growth hormone treatment. For clinical data, see
Table 1.
The control group was formed from the Finnish NEPSY-II standard-
ization sample in which 923 children aged 3–15 years were assessed
individually [7]. Data were collected during the years 2007–2008. The
control group underwent no Wechsler Intelligence Scale for Children
(WISC-III) evaluation. For each child with KTx, one child of the same
gender, approximate age and maternal educational level (four levels) was
randomly chosen. All children in the control group attended school with a
normal curriculum, and none had any neurological diagnosis.

Table 1. Clinical data for 50 patients with kidney transplants

<table>
<thead>
<tr>
<th>Measures</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>n (%)</td>
</tr>
<tr>
<td>CNF with mutations in the nephrin gene (NPHSI)</td>
<td>22 (44)</td>
</tr>
<tr>
<td>Autosomal recessive polycystic kidney disease</td>
<td>5 (10)</td>
</tr>
<tr>
<td>Renal dysplasia</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Urethral valve</td>
<td>4 (8)</td>
</tr>
<tr>
<td>Renal insufficiency of unknown aetiology</td>
<td>3 (6)</td>
</tr>
<tr>
<td>Hypoxalalia</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (20)</td>
</tr>
<tr>
<td>Pre-transplantation data</td>
<td>Mean (SD) Range</td>
</tr>
<tr>
<td>Age at inclusion on the waiting list, years</td>
<td>2.9 (3.4) 0.4 to 13.0</td>
</tr>
<tr>
<td>Time on dialysis, years</td>
<td>1.4 (1.2) 0.01 to 5.8</td>
</tr>
<tr>
<td>Waiting time for KTx, days</td>
<td>290.5 (269.4) 17.0 to 1067.0</td>
</tr>
<tr>
<td>Transplantation data</td>
<td>Mean (SD) Range</td>
</tr>
<tr>
<td>Age at first KTx, years</td>
<td>3.7 (3.5) 0.67 to 13.4</td>
</tr>
<tr>
<td>Intensive care unit stay after KTx, days</td>
<td>2.3 (0.8) 1.0 to 5.0</td>
</tr>
<tr>
<td>Hospital stay after KTx, days</td>
<td>30.9 (11.9) 18.0 to 64.0</td>
</tr>
<tr>
<td>Height at KTx, z-scores</td>
<td>–1.6 (1.6) –9.0 to 0.7</td>
</tr>
<tr>
<td>Weight for height index at KTx, %</td>
<td>7.4 (17.5) –20.0 to 83.0</td>
</tr>
<tr>
<td>Data at time of evaluation</td>
<td>Mean (SD) Range</td>
</tr>
<tr>
<td>Age, years</td>
<td>11.1 (3.2) 6.3 to 16.4</td>
</tr>
<tr>
<td>Follow-up time since KTx, years</td>
<td>6.9 (3.6) 1.0 to 14.1</td>
</tr>
<tr>
<td>Height, in z-scores</td>
<td>–1.3 (1.1) –4.2 to 1.3</td>
</tr>
<tr>
<td>Weight for height index, %</td>
<td>11.9 (28.7) –11.0 to 152.0</td>
</tr>
<tr>
<td>GFR, mL/min/1.73 m²</td>
<td>47.5 (14.8) 14.0 to 88.0</td>
</tr>
<tr>
<td>Serum creatinine, μmol/L</td>
<td>98.7 (62.3) 38.0 to 452.0</td>
</tr>
</tbody>
</table>

Procedure
The ethics review board at HUCH approved the study. Written consent
came from one caregiver of each child. The children were recruited for the
study during their annual re-evaluation visit to HUCH or an appointment
was made by telephone to assess the child at the hospital closest to home.
The first author and two trained psychology students performed the assess-
ments between May 2007 and September 2009. At the time of assessment,
all patients were medically stable but had a weakened kidney function;
19% had values near normal [glomerular filtration rate (GFR) > 60 mL/
min/1.73 m²] and 81% below normal (GFR < 60 mL/min/1.73 m²).

纠纷
The short form of the Finnish version of the WISC-III [8] served as an
evaluation of cognitive capacity (the WISC-IV was not available in Fin-
ish). Three scales were compiled: the estimated Verbal Intelligence Quo-
tient (VIQ; sub-tests Information, Similarities and Comprehension), the
Performance Intelligence Quotient (PIQ; sub-tests Picture Completion,
Picture Arrangement and Block Design) and the Full-Scale Intelligence
Quotient (FSIQ). One patient exceeded the age criteria and did not take the
WISC-III.

The NEPSY-II [7, 9] comprises 29 sub-tests from six domains of
development. According to the test manual, the selection of sub-tests is
according to the child’s age and clinical needs. Ten sub-tests were adminis-
tered: the Auditory Attention and Response Set (Attention and
Executive Functions domain), Speeded Naming and Comprehension of
Instructions (Language domain), Visuomotor Precision (Sensorimotor
domain), Memory for Designs, Memory for Faces, Word List Interfer-
ence (Memory and Learning domain), Design Copying and Geometric
Puzzles (Visuospatial Processing domain) and Affect Recognition
(Social Perception domain). These sub-tests provided a comprehensive
profile across all domains. One patient did not wish to take part in the
NEPSY-II assessment.

Parents also completed a form on demographic, educational and social
variables. Information on medical variables and rehabilitation services
came from medical records. Kidney function was evaluated as serum

c\text{observed height }/C0\text{mean height for age}/SD.

c\text{ratio of weight (kg) for height (cm) to the mean weight for height ratio in the normal population.}

Normal values > 90 mL/min/1.73 m², near normal > 60 mL/min/1.73 m².

Normal values for children aged 6–12 years 10–76 μmol/L, girls aged 13–16 years 15–90 μmol/L and boys aged 13–16 years 20–95 μmol/L.
neurological co-morbidity versus control group) [11]. Missing observations

variance with the group as the independent variable and the sub-test scores as

profile analysis was carried out using repeated measures analysis of var-

t-test. For the NEPSY-II, a

corrected standard scores. The WISC-III scores were compared to the
test norms with the Student’s one-sample corrected using the Bonferroni correction. Medical/background variables

significance were two tailed (P < 0.05). Partial eta squared (ηp²) served as an indicator of effect size.

Results

Background characteristics

Patient and control groups did not differ with respect to
gender (28 boys and 21 girls), age [KTx 11.2 (SD 3.2) versus control group 11.0 (SD 3.0) years, P = 0.829] or
maternal education (33 comprehensive school or secondary level, 16 lower or higher tertiary level).

Of the 50 patients, 33 (66%) were considered to have a normal neurological outcome and 17 patients (34%) had neurological co-morbidity or severe risk factors post-KTx (Table 2). Thirty-four patients (68%) attended age-appropriate classes according to the normal curriculum.

Ten patients (20%) attended full-time special education and seven (14%) attended part-time special education (three in mathematics, three in mathematics and a foreign language and one not specified). Of these patients, three (6%) also had a postponed school start and three (6%) had repeated a school grade.

Global intelligence

KTx children obtained significantly lower intelligence scores compared to the test norms and performed in the low average range (FSIQ = 2 SD < 70). All of the patients with low FSIQs were able to speak, lived with their families and attended school (full-time or part-time special education). All but one were ambulatory. In 17 patients (35%), PIQ was significantly lower than VIQ (15–55 score difference), whereas 6 patients (12%) had a significantly lower VIQ than PIQ (15–40 score difference).

Patients with neurological co-morbidity or risk factors had significantly lower scores than did children without major neurological co-morbidity, particularly that affecting

neurocognition (P = 0.005). Design Copying (P = 0.007) and Affect Recognition (P = 0.018) sub-tests.

Congenital nephrosis of the Finnish type

For a comparison of background characteristics between children with CNF and other diagnoses, see Table 4. Of the non-CNFX children, 86% had a congenital disease.

Table 2. Description of children with neurological co-morbidity or severe post-transplantation risk factors

Co-morbidity/risk factor

n

Neurological co-morbidity

Mental retardation

Cerebral palsy due to asphyxia

Right-sided weakness, which later resolves

Alcohol exposure in utero

Birth at very low gestational age (VLGA) <32 weeks

with low birth weight (<2500 g) and hearing impairment

G-protein signalling disorder with damage to several organs

Townes-Brocks syndrome with increased intracranial pressure requiring a shunt and hearing impairment

Unspecified syndrome involving dysmorphic features

Severe visual impairment

Post-transplantation risk factors

Septis and hypertensive crises with pulmonary oedema

Absence seizures, probably due to high levels of ammonia

Herpes infection, hyponatremia and a single seizure

F

A single lone seizure was not considered a neurological sequela (n = 3).

normal (FSIQ – 2 SD < 70). All of the patients with low FSIQs were able to speak, lived with their families and attended school (full-time or part-time special education). All but one were ambulatory. In 17 patients (35%), PIQ was significantly lower than VIQ (15–55 score difference), whereas 6 patients (12%) had a significantly lower VIQ than PIQ (15–40 score difference).

Patients with neurological co-morbidity or risk factors had significantly lower scores than did children without major neurological co-morbidity, particularly that affecting PIQ (independent samples t-test: VIQ P = 0.015, PIQ P = 0.003 and FSIQ P = 0.005).

Neurocognitive test profile

The significant between-subject effect of group, F(1, 92) = 22.2, P < 0.001, ηp² = 0.195, indicated that KTx children scored generally lower than did the control group. The interaction of test and group was significant, F(Greenhouse-Geisser corrected df = 8.3, 765.6.) = 2.3, P = 0.016, ηp² = 0.025, indicating that the KTx and control groups did not have parallel test profiles in the NEPSY-II. For univariate analyses of the individual sub-test scores, see Figure 1.

When patients with neurological co-morbidity were excluded from the analyses, the significant between-subject effect of group, F(1, 77) = 8.8, P = 0.004, ηp² = 0.102, indicated that KTx children without neurological co-morbidity continued to score generally lower than did the control group. On the sub-test level, significant differences were found in the Comprehension of Instructions (P = 0.006), Design Copying (P = 0.007) and Affect Recognition (P = 0.018) sub-tests.

Congenital nephrosis of the Finnish type

For a comparison of background characteristics between children with CNF and other diagnoses, see Table 4. Of the non-CNFX children, 86% had a congenital disease.
Risk factors

In a bivariate correlation, VIQ, PIQ, FSIQ and those NEPSY-II sub-tests that showed a significant decrease in KTx recipients were chosen as outcome measures (Table 5). The following background variables strongly intercorrelated ($r_s$): the duration of kidney disease correlates 0.967 ($P < 0.001$) with age at KTx and 0.448 ($P = 0.001$) with follow-up time. Likewise, age at KTx and follow-up time correlated $−0.485$ ($P < 0.001$).

Discussion

We found a generalized effect on cognitive development in children with kidney failure and consequent KTx.
However, visual memory and simple auditory attention remained intact. Patients without neurological co-morbidity or risk factors had intelligence in the normal range and an age-appropriate outcome in auditory attention, visual and verbal memory, verbal fluency, visuomotor precision and non-motor visual processing. Specific difficulties were seen in receptive language, visuospatial functions and affect recognition. A better outcome was mainly associated with the absence of neurological co-morbidity, shorter disease duration, younger age and a better long-term kidney function.

Global intelligence

The global intelligence score (FSIQ 84) reported in our study is poorer than that reported in other studies (87–103) [1–5]. To obtain a complete picture of the population, how-study is poorer than that reported in other studies (87–103). The global intelligence score (FSIQ 84) reported in our study population has an FSIQ of 89, which is still notably lower than that reported by Falger et al. (median FSIQ 97).

Neuropsychological test profile

A pattern of effects on neurocognitive development was observed in the NEPSY-II. Compared to the matched controls, difficulties emerged in both the verbal and visuospatial domains, on a sub-test of complex auditory attention, verbal working memory and the recognition of emotional states. Visual memory and simple auditory attention remained intact. Previous studies have reported problems within non-verbal reasoning, measured as a significantly lower PIQ compared to VIQ [1]. In addition, studies have reported significantly lower psychomotor development compared to mental development in 44% of pre- and 36% of post-KTx infants [14]. An early study from 1984 reported the greatest pre- to post-KTx improvement in non-verbal problem solving [2]. In our study, 35% had significantly lower PIQ compared to VIQ, yet the difference was mainly observed in the group with neurological co-morbidity and non-CNF children. However, not all studies have confirmed more difficulties in PIQ compared to VIQ [2, 5]. In CNF, in particular, Qvist et al. [5] reported equal VIQ and PIQ in a group of patients transplanted before the age of five. Our results indicate that CNF patients have shorter illness duration and early KTx, which may alleviate visuospatial impairment in particular.

Patients without neurological co-morbidity had age-appropriate outcomes in auditory attention, visual and verbal memory, visuomotor precision, verbal fluency and non-motor visual processing. Specific difficulties arose in

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**Table 4. Comparison of 28 patients with CNF and 22 patients with other diagnoses**

<table>
<thead>
<tr>
<th>Data</th>
<th>CNF*</th>
<th>Other*</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gestational age, weeks 35.5 (2.3)</td>
<td>37.4 (2.3)</td>
<td>0.026</td>
<td></td>
</tr>
<tr>
<td>Height, cm 47.2 (3.0)</td>
<td>49.1 (2.2)</td>
<td>0.023</td>
<td></td>
</tr>
<tr>
<td>Birth weight, kg 2.5 (0.4)</td>
<td>3.3 (0.6)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Pre-transplantation data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration pre-KTx, years 1.9 (0.9)</td>
<td>4.3 (3.3)</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Time on dialysis, years* 1.5 (1.1)</td>
<td>1.3 (1.2)</td>
<td>0.670</td>
<td></td>
</tr>
<tr>
<td>Waiting time for KTx, days* 386 (315)</td>
<td>223 (213)</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Transplantation data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at first KTx, years 1.9 (0.9)</td>
<td>5.2 (4.1)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Weight for height index at KTx, %* 0.57 (8.5)</td>
<td>12.5 (20.7)</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>Data at time of evaluation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years 11.0 (3.4)</td>
<td>11.3 (3.1)</td>
<td>0.742</td>
<td></td>
</tr>
<tr>
<td>Follow-up time since KTx, years 8.2 (3.4)</td>
<td>5.8 (3.5)</td>
<td>0.016</td>
<td></td>
</tr>
<tr>
<td>Weight for height index, %* 0.55 (9.0)</td>
<td>20.8 (35.3)</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>Neurological co-morbidity* 7 (25%)</td>
<td>10 (45%)</td>
<td>0.773</td>
<td></td>
</tr>
</tbody>
</table>

*Data presented as mean (standard deviation).
*Total time on peritoneal or haemodialysis. For patients with re-transplants, time on dialysis and waiting time for KTx includes both first and second Tx.
*% = ratio of weight (kg) for height (cm) to the mean weight for height ratio in the normal population.
*Data presented as n (%). P-value is derived from a chi-square comparison.
Table 5. Correlations between cognitive outcome and selected background characteristics for 50 patients with kidney transplants

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>VQ</th>
<th>PIQ</th>
<th>FSIQ</th>
<th>Neurological co-morbidity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at follow-up</td>
<td>-0.365*</td>
<td>-0.331*</td>
<td>-0.351*</td>
<td></td>
</tr>
<tr>
<td>Age at KTx</td>
<td>-0.328*</td>
<td>-0.206*</td>
<td>-0.251*</td>
<td></td>
</tr>
<tr>
<td>Follow-up time</td>
<td>-0.312*</td>
<td>-0.312*</td>
<td>-0.312*</td>
<td></td>
</tr>
<tr>
<td>GFRb</td>
<td>-0.390**</td>
<td>-0.200</td>
<td>-0.337*</td>
<td></td>
</tr>
<tr>
<td>S-creatinineb</td>
<td>-0.326**</td>
<td>-0.200</td>
<td>-0.337*</td>
<td></td>
</tr>
<tr>
<td>aData expressed as Pearson's correlation coefficient. **P &lt; 0.01, *P &lt; 0.05, †P &lt; 0.10. bA higher GFR and lower serum creatinine indicate more efficient kidney function. The measures were obtained at the time of follow-up.</td>
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</tr>
</tbody>
</table>

Cognitive outcome and pediatric kidney transplantation

Concern has grown for an adverse neurodevelopmental outcome in children transplanted for CNF [5, 21]. These patients are severely ill from birth with a lower gestational age and birth weight [22, 23] and they are transplanted significantly earlier than are children with other diagnoses.
However, their cognitive outcome is surprisingly good; they score higher on all measures than do children with other diagnoses. Interestingly, this difference approached significance in the visuospatial domain. We found no other study reporting the cognitive outcome of CNF children alone. Qvist et al. [5] reported a high percentage of neurological sequelae on MRI among the first CNF patients who received a KTx. In our study, children with CNF did not have more neurological sequelae than did non-CNF children.

Risk factors

In our study, deteriorating kidney function was associated with poorer verbal ability, verbal working memory and complex auditory attention. Deterioration of memory functions with increasing blood urea nitrogen levels or decreasing creatinine clearance has been reported [13]. Among children with chronic kidney disease without KTx, GFR was a significant predictor of intellectual and academic outcomes [24]. In some studies, kidney function among KTx recipients failed to correlate with cognitive data [1, 14]. Our patients had a poorer GFR than did patients in several previous studies [4]. However, we used measured GFR (EDTA), which yields stricter values than does estimated GFR (e.g. calculated with the Schwartz formula [25]). In addition, kidney function tends to deteriorate over time [26–28]. Although other studies have assessed patients 1–6 years post-KTx [1, 5], our patients were assessed on average 7 years post-KTx.

Older age at KTx and at follow-up seem to associate negatively with cognitive outcome. Children with KTx later in life experience a longer disease duration, thus placing them at risk for more neurodevelopmental deficits. However, the strongest association occurred between neurological co-morbidity and poorer outcome observed on all sub-tests of the NEPSY-II. Early studies on paediatric KTx associated poorer cognitive outcome with early onset of kidney disease [2, 3] and longer disease duration pre-KTx [2]. In more recent studies, however, cognitive impairment has been associated with neurological co-morbidity [1], hypertensive crises and seizures during dialysis [5] and lower socio-economic status [1]. Today, early KTx may alleviate the effects of early onset of kidney disease, yet longer disease duration prior to KTx remains a risk factor for cognitive impairment. Since more demanding patients are accepted for KTx, an increase in neurological co-morbidity may result.

Limitations

The large intra-group age ranges in our study weaken these results. Additionally, we included all patients in the study, even patients with re-Tx and combined liver–kidney Tx. However, we used a comprehensive series of standardized neuropsychological tests designed for a wide age range. All children could be assessed using the same measures, yielding results generalizable across ages. Moreover, we included a healthy control group.

We report more developmental delay and neurological co-morbidity compared to age expectations and to other cohorts of KTx children. However, most of our patients had a congenital disease and received a KTx at a young age. Despite the difficulties of caring for these youngest and smallest patients, their long-term outcomes are quite reassuring. Early KTx with shorter disease duration alleviates later cognitive outcome, while neurological co-morbidity strongly associated with neurocognitive impairment. Poor kidney function at follow-up associated with poorer verbal skills, verbal working memory and complex auditory attention. There seems to be a tendency to under-recognize mental retardation and the need for special education in this patient population. We emphasize the importance of neuropsychological evaluation so that educational needs can be addressed. Children with neurological co-morbidity or longer disease duration are at risk for more general cognitive impairment, yet patients with normal intelligence may also have minor specific neurocognitive deficits and should be evaluated. With correct interventions the children’s learning can be optimized, thereby improving their future schooling and job opportunities and quality of life.

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Conflict of interest statement. None declared.

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